

zenes of 1,2,4 orientation appeared as an unresolved peak; the retention time was identical with that of **10**, **11**, or **12**; the infrared spectrum of eluted material was very complex, and the nmr spectrum closely resembled that of an authentic mixture of **10**, **11**, and **12**; on the basis of the nmr spectrum, this is taken to be a mixture of these three isomers. The combined yield of **10**, **11**, and **12** was 7%. 1-Bromo-3-chloro-5-iodobenzene (**7**) appeared in 18% yield; identification was by the match of infrared and nmr spectra with those of an authentic sample, by melting point and mixture melting point with authentic **7**, and by retention time analysis. A mixture of substances diagnosed as bromochloriodobenzenes of 1,2,4 orientation appeared in 23% yield; the retention time was that of **6**, **13**, or 1-iodo-3-bromo-4-chlorobenzene, a mixture of which was inseparable on the column employed; the infrared and nmr spectra of an eluted sample were complex, and the nmr spectrum showed absorptions characteristic of **6** and **13** as well as further absorptions which, however, could not be attributed to 1-iodo-3-bromo-4-chlorobenzene; this mixture is believed to comprise unreacted **6**, product **13**, and at least one further bromochloriodobenzene of 1,2,4 orientation. Following a trace of an unidentified product, a trace of 1-chloro-3,5-diiodobenzene (**9**) appeared; identification was by retention time and the near-match of the infrared spectrum of an eluted sample with that of authentic **9**. The last clearly defined fraction, which appeared in trace amounts,

was a mixture of 1-chloro-2,4-diiodobenzene (**14**) and 1-chloro-3,4-diiodobenzene (**15**); identification was by retention time and by the fact that infrared and nmr spectra matched almost perfectly those of an authentic mixture of **14** and **15**.

Reactions of 1-Iodo-2,4,6-tribromobenzene (16). From 10-min exposure of **16** (0.005 mol) to potassium anilide (0.01 mol) in 500 ml of ammonia, a mixture of products was obtained. By glpc analysis on an SE-30 column, product fractions were eluted in the order in which they are now discussed. The first four products were 1,3,5-tribromobenzene (**2**), in 44% yield, 1,2,4-tribromobenzene (**1**) (10%), 1-iodo-3,5-dibromobenzene (**4**) (1.6%), and 1-iodo-2,4-dibromobenzene (**3**) (4%), all identified by retention time and by the match of infrared spectra of eluted samples with those of the authentic compounds. The next fraction (7% yield) was subjected to further glpc on an SE-30/Bentone 34 column which effected partial resolution into two subfractions; the infrared spectra of the eluted subfractions indicated them to be composed, respectively, of 1,2,3,5-tetrabromobenzene (**17**) contaminated with 1,2,4,5-tetrabromobenzene (**18**), and of **18** contaminated with **17**. After an unidentified fraction in trace amount, unreacted **16** (12%) appeared; identification was by its infrared spectrum.

Further details concerning glpc materials and procedures, the analysis of various reaction mixtures, and the identification of specific products are given in the Dissertation of C. E. M.^{1a}

Experiments Which Illuminate the Mechanism of Base-Catalyzed Isomerization and Disproportionation of Trihalobenzenes¹

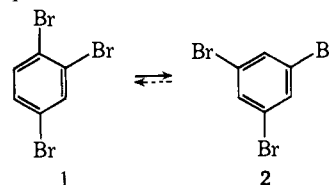
J. F. Bunnett* and Gianfranco Scorrano²

Contribution from the University of California,
Santa Cruz, California 95060. Received February 12, 1970

Abstract: On treatment with potassium anilide in 50% ammonia–50% diethyl ether at reflux (–29°), 1,2,4-tribromobenzene (**1**) isomerizes to its 1,3,5 isomer (**2**) and disproportionates to di- and tetrabromobenzenes. Potassium *tert*-butoxide (*tert*-BuOK) in DMF or HMPA at room temperature is also an effective catalyst. The fact that 1-chloro-2-fluoro-4-iodobenzene (**7**) and 1-chloro-2-fluoro-5-iodobenzene (**8**) do not interconvert on treatment with potassium anilide is evidence against a conceivable mechanism of 1,2 shift of iodine in an *o*-iodoaryl anion. Although isomerization of **1** is incomplete because **1** and **2** are nearly equal in free energy, **2** does not isomerize on treatment with potassium anilide in ammonia or with *tert*-BuOK in DMF. However, **2** does isomerize with cocatalysis by 1,2,3,5-tetrabromobenzene (**12**); this clarifies the reaction mechanism, which is now indicated to be the “seven-halogen” positive halogen transfer mechanism of Scheme II. In accord with the clarified mechanism, **7** and **8** do interconvert when 1-iodo-2,4,6-trichlorobenzene is supplied as cocatalyst. In HMPA, *tert*-BuOK brings about isomerization of **2** without requirement for cocatalysis, and equilibration between 1,2,4- and 1,3,5-triiodobenzene is easily effected, starting from either isomer; this exceptional reactivity is attributed to the high free energy of *tert*-BuO[–] in HMPA.

The isomerization of 1,2,4-tribromobenzene (**1**) to its 1,3,5 isomer (**2**) is catalyzed by NaNH₂³ or KNH₂ in ammonia, but much more effectively by potassium anilide.^{4,5} Some disproportionation to di- and tetrabromobenzenes also occurs. The action of potassium anilide in ammonia on 1-iodo-2,4-dibromobenzene or 1-iodo-2-bromo-4-chlorobenzene brings about redistribution of halogens between rings as well as isomerization.^{4,5} On the basis of these and other

observations, a mechanism involving series of positive halogen transfers from aryl halides to aryl anions has been proposed.^{4,5}



Closely related is the scrambling of the iodine atoms of 1,2,4-triiodobenzene which occurs on treatment with potassium anilide in ammonia, more rapidly than isomerization to 1,3,5-triiodobenzene.⁶ This also has been interpreted in terms of the positive halogen transfer mechanism.⁶

(1) Supported in part by grants from the National Science Foundation and by the Petroleum Research Fund administered by the American Chemical Society.

(2) Grateful recipient of a NATO Fellowship awarded by the Consiglio Nazionale delle Ricerche d'Italia, 1967–1968.

(3) J. H. Wotiz and F. Haba, *J. Org. Chem.*, **24**, 595 (1959).

(4) C. E. Moyer, Jr., and J. F. Bunnett, *J. Amer. Chem. Soc.*, **85**, 1891 (1963).

(5) (a) J. F. Bunnett and C. E. Moyer, Jr., *ibid.*, **93**, 1183 (1971);

(b) C. E. Moyer, Jr., Dissertation, Brown University, Providence, R. I., 1964.

(6) J. F. Bunnett and D. J. McLennan, *J. Amer. Chem. Soc.*, **90**, 2190 (1968).

Table I. Reactions of 1,2,4-Tribromobenzene (1) in Various Base-Solvent Systems

| Run no. | Solvent | Base | [1], <i>M</i> | [Base], <i>M</i> | [C ₆ H ₅ - NH ₂], <i>M</i> | Reaction time, min | Reaction products ^a | | | | |
|---------|---|-----------------------------------|------------------|---------------------|---|-----------------------|--------------------------------|-------------------|--|--|------------------------|
| | | | | | | | 2, % | 1, % | C ₆ H ₄ Br ₂ , % | C ₆ H ₂ Br ₄ , % | Br ⁻ , % |
| 1 | 50% NH ₃ - 50% ether ^b | KNH ₂ | 0.02 | 0.01 | | 120 | 22 | 55 | <i>c</i> | <i>c</i> | 15 |
| 2 | | KNH ₂ ^d | 0.02 | 0.01 | | 15 + 60 ^d | 3 | 80 | <i>c</i> | <i>c</i> | 20 ^d |
| 3 | | C ₆ H ₅ NHK | 0.02 | 0.01 | 0.01 | 30 | 27 | 62 | <i>c</i> | <i>c</i> | 4 |
| 4 | | | 0.02 | 0.01 | 0.01 | 120 | 52 | 36 | <i>c</i> | <i>c</i> | 11 |
| 5 | | | 0.02 | 0.01 | 0.01 | 480 | 48 | 33 | <i>c</i> | <i>c</i> | 13 |
| 6 | | | 0.02 | 0.10 | 0.10 | 120 | 19 | 36 | 5.7 ^e | Trace | 34 |
| 7 | DMF ^f | <i>tert</i> -BuOK | 0.08 | 0.064 | | 0.45 | 50.6 ^g | 49.4 ^g | <i>c</i> | <i>c</i> | <i>c</i> |
| 8 | | | 0.08 | 0.16 | | 1.08 | 50.9 ^g | 49.1 ^g | <i>c</i> | <i>c</i> | <i>c</i> |
| 9 | | | 0.14 | 0.22 | | 1,020 | 26.5 | 26.1 | <i>c</i> | <i>c</i> | <i>c</i> |
| 10 | | | 0.08 | 0.13 | | 5,400 | 36.3 | 38.4 | 6.9 | 4.5 | 20 |
| 11 | HMPA ^f | <i>tert</i> -BuOK | 0.71 | 0.13 | | 2.0 | 40.0 | 39.2 | 3.1 ^h | 1.2 ⁱ | 23 |
| 12 | | | 0.07 | 0.14 | | 79 | 27.3 | 27.2 | 4.7 ^j | 1.5 ⁱ | 38 |
| | | | | | | 2.67 | 30.7 | 45.5 | 8.7 | 3.3 | 9 |
| | | | | | | 1,500 | 22.4 | 39.7 | 7.2 | 2.8 | 12 |
| | | | | | | 1.08 | 18.9 | 34.6 | 14.1 ^k | 6.1 ⁱ | 23 |

^a Yields reckoned on basis of 1 introduced. ^b Reactions in 50% NH₃-50% diethyl ether were run at reflux (-29°). ^c Not determined. ^d CH₃I (0.01 *M*) added after 15 min; 100% iodide ion but no toluene derivatives were formed. ^e 5.2% para and 0.5% meta isomer. ^f Room temperature. ^g Percentages listed are of recovered neutral fraction. ^h 2.8% para and 0.3% meta isomer. ⁱ Glpc suggested ca. 75% 1,2,4,5 and 25% 1,2,3,5 isomer. ^j 4.1% para and 0.6% meta isomer. ^k 11.4% para and 2.7% meta isomer.

Although work heretofore has served to describe and to define many important features of these unusual reactions, it has left several questions unanswered. We now report a number of investigations, all related to the same theme but rather independent of each other, which collectively lead to a much better understanding of the scope and mechanism of these reactions.

Each section of this paper concerns one investigation and discussion follows presentation of results in each section, in order that the facts and principles that emerge from one investigation may be cited as appropriate in subsequent sections. Finally, there is a short unifying discussion.

I. The Efficacy of Various Base-Solvent Systems

We find that the isomerization of 1 can be carried out satisfactorily with potassium anilide base in 50% ammonia-50% diethyl ether solution, or with potassium *tert*-butoxide (*tert*-BuOK) base in dimethylformamide (DMF) or hexamethylphosphoramide (HMPA) solution. Representative experiments are summarized in Table I.

The ammonia-ether medium has advantages over neat ammonia in that some halogenated benzenes which have limited solubility in liquid ammonia are quite soluble in ammonia-ether. The first experiment in Table I indicates that a significant amount of isomerization can be brought about through the action of KNH₂ in ammonia-ether. Runs 3, 4, and 5 of Table I suggest that more isomerization occurs in 120 min than in 30 min, but that extending the reaction period to 480 min has no further beneficial effect.

In one potassium anilide catalyzed run (run 6), the di- and tetrabromobenzenes were carefully determined. Dibromobenzenes were formed in total yield of 5.7%, but tetrabromobenzenes only in trace amounts. Disproportionation of a tribromobenzene should form di- and tetrabromobenzenes in equivalent amounts; apparently subsequent reactions consume the tetrabromobenzenes much faster than the dibromobenzenes. Among the dibromobenzenes, the para isomer is pre-

dominant, being formed in ten times the yield of the meta, while no ortho isomer was detected.

In most experiments with potassium anilide base, an equimolar amount of free aniline was also present. In one experiment (not listed), aniline (0.19 *M*) was present in great excess over the base (0.01 *M*); of the tribromobenzenes isolated after 177 min, only 7% was the 1,3,5 isomer. The decelerating effect of excess aniline has been studied in greater detail by Bunnett and Feit.⁷

Dry, alcohol-free *tert*-BuOK in DMF or HMPA is very effective as an isomerization reagent.⁸ Within 1 min at room temperature, the extent of isomerization is as great as at much longer reaction times (*cf.* runs 7-10 and 11-12). However, excess *tert*-butyl alcohol (*tert*-BuOH) strongly retards the reaction. With 0.25 *M tert*-BuOH in DMF solution, 0.01 *M tert*-BuOK brought about only 2.2% isomerization in 22 hr, and 0.04 *M tert*-BuOK in DMF containing 9% of *tert*-BuOH by volume had produced no detectable isomerization after 43 hr.

In these systems, disproportionation to di- and tetrabromobenzenes is more pronounced than in potassium anilide catalyzed reactions (*cf.* runs 10 and 12). Again, about ten times as much *p*- as *m*-dibromobenzene is formed. Of the tetrabromobenzenes, the 1,2,4,5 isomer is formed in greater amount than the 1,2,3,5 isomer, and there is no evidence for the 1,2,3,4 isomer.

The speed and convenience of isomerizations catalyzed by *tert*-BuOK in DMF or HMPA make this the reagent of choice for effecting base-catalyzed isomerization of trihalobenzenes.

The facility of these reactions in DMF and HMPA might suggest the use of *tert*-BuOK in other dipolar

(7) J. F. Bunnett and I. N. Feit, *J. Amer. Chem. Soc.*, **93**, 1201 (1971).

(8) Indications of very slow isomerization-disproportionation of the present type obtained by Dr. Rae R. Victor, in her study of the action of *tert*-BuOK on oligohalobenzenes in 50% DMF-50% *tert*-BuOH and 50% HMPA-50% *tert*-BuOH,⁹ suggested the experiments with *tert*-BuOK in neat DMF or HMPA now described.

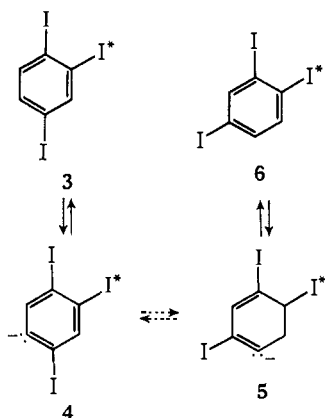
(9) J. F. Bunnett and R. R. Victor, *J. Amer. Chem. Soc.*, **90**, 810 (1968); R. R. Victor, Dissertation, Brown University, Providence, R. I., 1968.

aprotic solvents, such as dimethyl sulfoxide or *N,N*-dimethylacetamide. We advise against such attempts; *tert*-BuOK in such solvents is likely to cause dehalogenation to occur.⁹

II. The Possibility of a 1,2-Shift Mechanism

Disproportionation reactions, as of a tribromobenzene to di- and tetrabromobenzenes or of 1-iodo-2,4-dibromobenzene to **1**, are clearly intermolecular in character. It has been hypothesized that isomerizations^{4,5} and isotope scrambling reactions⁶ which occur under similar conditions are also intermolecular; the mechanisms proposed involve transfer of halogen atoms back and forth between aromatic rings. However, the fact that disproportionations are intermolecular does not rigorously exclude the possibility that isomerizations might be intramolecular.⁶ Reactions of quite different mechanism might just happen to occur under similar conditions.

Consider, for example, the reaction of 2-radiolabeled 1,2,4-triiodobenzene (**3**) with potassium anilide in ammonia, which effects a statistical redistribution of the radiolabel among the 1, 2, and 4 positions.⁶ Con-

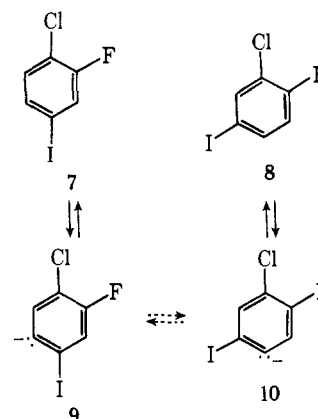


ceivably, transformation of **3** into its 1-labeled radioisomer **6** might occur by acid-base reaction to form 5-anion, **4**, then 1,2 shift of the 4-iodine of **4** to the erstwhile carbanionic center so as to form **5**, and finally protonation of **5** to form **6**. Obviously, further transformations of similar character could convert **6** into the 4-labeled radioisomer of **3**.

Although we know of no precedent for 1,2 shift of a halogen atom to a carbanionic site, such a shift does not seem improbable from *a priori* considerations. A three-membered ring intermediate making use of *d* orbitals of iodine or bromine is even conceivable. Moreover, 1,2-halogen migration accompanying a sigmatropic rearrangement has recently been described.¹⁰

As a test of the 1,2-shift possibility, we investigated the action of potassium anilide in ammonia or in ether-ammonia solution on 1-chloro-2-fluoro-4-iodobenzene (**7**) and on 1-chloro-2-fluoro-5-iodobenzene (**8**). If isomerization *via* 1,2 shift in *o*-iodophenyl anions were possible, **7** and **8** ought to interconvert *via* anions **9** and **10** under the conditions which brought about scrambling of the radiolabel of **3**. However, interconversion of **7** and **8** would not be expected according to the positive halogen transfer mechanism because chlorine (and presumably also fluorine) is not mobile

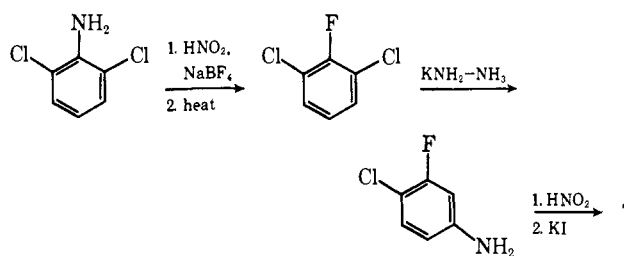
(10) C. W. Bird, *Chem. Commun.*, 1486 (1969).



with potassium anilide in ammonia and iodine in **7** or **8** is not ortho to another halogen and therefore should not be susceptible to being captured by an attacking aryl anion.⁵

In synthesis of **7**, a cine substitution was employed to advantage, as shown in Scheme I. 3-Fluoro-4-

Scheme I



chloroaniline was obtained in 66% yield by reaction of 1-fluoro-2,6-dichlorobenzene with KNH₂ in ammonia, doubtless *via* an aryne intermediate. Synthesis of **8** was straightforward.

The infrared and proton magnetic resonance spectra of isomer **7** were found to differ characteristically from those of isomer **8**.

Isomers **7** and **8** were separately exposed to potassium anilide in ammonia (under the conditions which effected scrambling of the radiolabel of **3**) or in ammonia-ether. In each case, reaction to form a considerable amount of iodide ion occurred but from 30 to 75% of unreacted chlorofluoroiodobenzene was recovered. The recovered C₆H₃ClFI had identically the same infrared and pmr spectra as the **7** or **8** introduced into the reaction. There was no evidence in either type of spectrum for isomerization to the other isomer. These experiments are summarized in Table II.

The failure of **7** and **8** to interconvert on treatment with potassium anilide constitutes strong evidence against the 1,2-shift mechanism.¹¹

III. Equilibration of 1,3,5- with 1,2,4-Tribromobenzene

In all of Moyer's experiments on the isomerization of **1** to **2** and in all the experiments of Table I, some

(11) It might be contended that, because **9** and **10** are not the thermodynamically favored aryl anions related to **7** and **8**, isomerization *via* 1,2 shift had no chance to occur. No doubt the hydrogens in **7** and **8** which are flanked by two halogens are the most acidic, but the complete exchange of all hydrogens of perdeuterated **1** on reaction with C₆H₅NHK in ammonia⁶ gives assurance that all possible aryl anions from 1,2,4-trihalobenzenes are generated under the conditions employed. Also, experiments concerning **7** or **8** and a good positive iodine donor, described below, affirm that **9** and **10** are generated under basic conditions.

Table II. Reactions of Chlorofluoroiodobenzenes with Potassium Anilide

| Run no. | C ₆ H ₃ ClFI substrate | Solvent | | [C ₆ H ₃ ClFI], M | [C ₆ H ₃ NHK], M | [C ₆ H ₃ NH ₂], M | Reaction time, min | C ₆ H ₃ ClFI recovered, % | I ⁻ formed, ^a % |
|---------|--|---------------------|----------|---|--|---|--------------------|---|---------------------------------------|
| | | NH ₃ , % | Ether, % | | | | | | |
| 13 | 7 ^b | 91 | 9 | 0.018 | 0.018 | 0.018 | 480 | 31 | 53 |
| 14 | 8 ^b | 91 | 9 | 0.018 | 0.018 | 0.018 | 480 | 30 | 53 |
| 15 | 7 | 50 | 50 | 0.020 | 0.010 | 0.010 | 120 | 47 | 29 |
| 16 | 8 | 50 | 50 | 0.020 | 0.010 | 0.010 | 120 | 54 | 30 |

^a Also, 3–6% of fluoride ion (by titration with lanthanum nitrate, using an F⁻-selective electrode) was formed in each experiment. ^b Data reported are averages from agreeing duplicate runs.

unrearranged **1** was always found in the product mixture at the end of reaction.⁵ No matter what the base or conditions or how long the reaction time, isomerization was never complete. This could easily be attributed to the attainment of a state of equilibrium, if it were not for the fact that **2** failed to revert to **1** to any detectable extent on treatment with potassium anilide in ammonia.

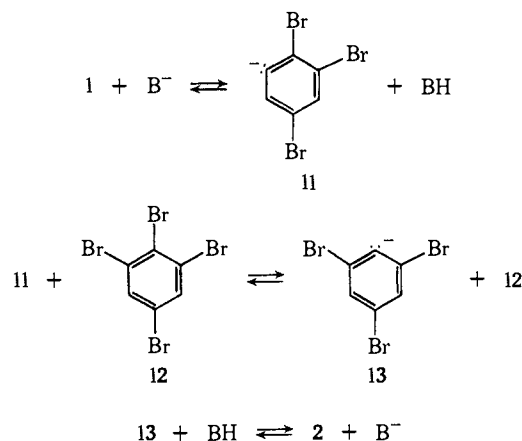
It was shown in the present work that **2** likewise fails to revert to **1** on treatment with potassium anilide in ammonia-ether or with *tert*-BuOK in DMF. Actually, the positive halogen transfer mechanism in its "six-halogen" version^{5a} would predict that **2** should not revert to **1** unless some **1** were supplied as a "primer." This is obvious from application of the principle of microscopic reversibility to Scheme V of Bunnett and Moyer.^{5a} Accordingly we exposed **2**, intentionally contaminated with 5% **1**, to potassium anilide in ammonia-ether, but found no evidence of transformation of **2** to **1**; the ratio of **2** to **1** in the product mixture was no greater than in the reactants (Table III, run 19). Substantially the same observation was made when a mixture of 95% **2** and 5% **1** was exposed to *tert*-BuOK in DMF (run 23).

It was then found that reversion of **2** to **1** occurs readily if a small amount of 1,2,3,5-tetrabromobenzene (**12**) is supplied as a cocatalyst. This cocatalytic effect was observed both with potassium anilide in ammonia-ether (Table III, runs 21 and 22) and with *tert*-BuOK in DMF (run 24). In both systems, the ultimate product ratio, of **2** to **1**, was virtually the same as in isomerizations which proceeded from **1**. With *tert*-BuOK in DMF, 1,2,3-tribromobenzene also was an effective cocatalyst for reversion of **2** to **1** (run 25). Bunnett and Feit⁷ have shown 1,2,4,5-tetrabromobenzene also to be a good cocatalyst.

The fact that **12** is an effective cocatalyst for reversion of **2** to **1**, whereas **1** is not, shows that the six-halogen version of the positive halogen transfer mechanism^{4,5} is inadequate. A fully acceptable mechanism for reversion of **2** to **1** must provide an essential role for the cocatalyst. This requirement is met by the seven-halogen version of the positive halogen transfer mechanism,^{5a} which is sketched in Scheme II.

As in the six-halogen version, the characteristic feature of this mechanism is positive halogen transfer from an aryl halide to an aryl anion. As sketched, it specifies tetrabromobenzene **12** as the functioning positive halogen donor in the key step, the second step in Scheme II. It should be noted that **12** is both consumed and formed in that step. In the forward direction as written, **11** takes positive bromine from the **2** position of **12**, and in so doing **11** is converted into **12**. In the reverse direction, **13** captures bromine

Scheme II



from the (equivalent) 1 or 3 position of **12**, forming **11** and regenerating **12**. This key step has a degree of symmetry. The first and third steps of Scheme II are straightforward acid-base reactions.

Rigorously, our experiments do not demonstrate that **12** itself is the functioning cocatalyst in the key step. It could be that some other species, some species that can be formed from **12** under the reaction conditions but not from **2**, plays the vital role. However, the simplicity and symmetry of Scheme II recommend it over others that might be conceived.

The efficacy of 1,2,3-tribromobenzene as a cocatalyst for reversion of **2** to **1** (Table III, run 25) may well be due to **12** formed through base-catalyzed reaction of **2** with its 1,2,3 isomer. 1,2,3-Tribromobenzene is well constituted to donate its 2-bromine to an aryl anion, inasmuch as the by-product 2,6-dibromophenyl anion would have two halogens ortho to its anionic center.^{5a}

If **12** is the functioning cocatalyst for reversion of **2** to **1**, the principle of microscopic reversibility requires that it must play the same role (but in the opposite direction) in isomerization of **1** to **2**. How can it be, then, that **1** isomerizes merely on treatment with base, without requirement for addition of **12** or other cocatalyst? One remote possibility that came to mind was that all the samples of **1** which had been used by Wotiz and Huba,³ by Bunnett and Moyer,⁵ and in our own earlier experiments were contaminated with traces of **12** or other cocatalyst. Accordingly we ultra-purified a good sample of **1**, by zone melting and glpc, so as to reduce its impurities content to less than 0.1%, as judged by glpc. However, reaction of the ultrapure **1** with *tert*-BuOK in DMF for 73 sec afforded 42% **2** as well as 2.3% di- and 0.6% tetrabromobenzenes. It was no less reactive than ordinary samples of **1**.

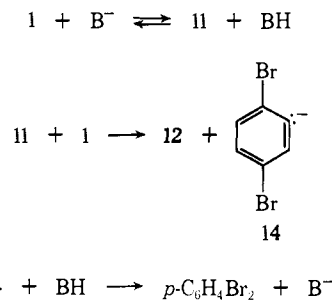
Table III. Behavior of 1,3,5-Tribromobenzene (2) on Treatment with Potassium Anilide in Ammonia-Ether or with *tert*-BuOK in DMF

| Run no. | Solvent | Base | [Base], M | [2], M | [C ₆ H ₅ NH ₂], M | Added substance, M | [Added substance], M | Reaction time, min | Recovered 2, % | 1, % | Reaction products ^a | | |
|---------|----------------------------|-----------------------------------|-----------|--------|---|--------------------|----------------------|--------------------|-------------------|-------------------|--------------------------------|---|---|
| | | | | | | | | | | | 2:1 | C ₆ H ₄ Br ₂ , % | C ₆ H ₃ Br ₃ , % |
| 17 | 50% NH ₃ -ether | C ₆ H ₅ NHK | 0.01 | 0.02 | 0.01 | | | 480 | 89 | Nil | Nil | Nil | 5 |
| 18 | DMF | <i>tert</i> -BuOK ^b | 0.22 | 0.14 | | | | 76 | 96 | Nil | Nil | Nil | 1 |
| 19 | 50% NH ₃ -ether | C ₆ H ₅ NHK | 0.01 | 0.02 | 0.01 | 1 | 0.001 | 120 | 73.2 | 3.5 | 21 | c | c |
| 20 | | | 0.01 | 0.01 | 0.01 | 1 | 0.01 | 30 | 39.6 | 35.8 | 1.1 | c | 4 |
| 21 | | | 0.01 | 0.02 | 0.01 | 12 | 0.0006 | 147 | 73.2 | 23.3 | 3.1 | 1.3 ^d | 12 |
| 22 | | | 0.01 | 0.02 | 0.01 | 12 | 0.0015 | 300 | 46.4 | 26.8 | 1.7 | 1.3 ^e | 29 |
| 23 | DMF | <i>tert</i> -BuOK | 0.22 | 0.27 | | 1 | 0.014 | 0.97 | 95.3 ^f | 4.7 ^f | 20 | c | c |
| | | | | | | | | 29 | 95.4 ^f | 4.6 ^f | 20 | c | c |
| | | | | | | | | 15,600 | 88.9 ^f | 11.1 ^f | 8.0 | c | c |
| 24 | | | 0.16 | 0.10 | | 12 | 0.0034 | 1.67 | 38.4 | 37.1 | 1.03 | g | c |
| 25 | | | 0.20 | 0.09 | | h | 0.0019 | 0.83 | 41.2 | 38.5 | 1.07 | 2.0 | 0.6 |

^a Unless otherwise stated, yields are based on total aryl bromides introduced. ^b *tert*-BuOK was prepared by evaporation to dryness under vacuum of a solution of *tert*-BuOK in *tert*-BuOH. ^c Not determined. ^d 1.0% para and 0.3% meta isomer. ^e 1.1% para and 0.2% meta isomer. ^f Percentages are of C₆H₃Br₃ products. ^g Present but not determined. ^h 1,2,3-C₆H₃Br₃.

The formation of tetrabromobenzenes in this experiment, as in other isomerizations of **1** (Table I and ref 5), is the reason that **1** can isomerize without addition of external cocatalyst. It forms its own cocatalyst by base-catalyzed disproportionation to di- and tetrabromobenzenes. The mechanism of Scheme III is postulated for the disproportionation.

Scheme III



The first and third steps of this mechanism are straightforward proton transfers. The second step involves a positive halogen transfer of the same type as in Scheme II. Indeed, the first two steps of Scheme III are identical with the first two steps of the six-halogen version of the positive halogen transfer mechanism for isomerization of **1** to **2**, as presented in Scheme V of Bunnett and Moyer.^{5a} As a mechanism for isomerization the six-halogen version requires that anion **14** seize a positive bromine from **12**, so as to form **1** and **13**, faster than it takes a proton from the medium, whereas the seven-halogen version requires no such uncomfortable assumption. On the other hand, the very likelihood that **14** would capture a proton rather than a positive bromine reinforces its suitability as a mechanism for disproportionation.

As set forth in Table I, disproportionation of **1** forms not only **12** and *p*-dibromobenzene, but also 1,2,4,5-tetrabromobenzene and small amounts of *m*-dibromobenzene. These results imply that disproportionation may involve not only attack of anion **11** on the 2-bromine of **1**, as shown in Scheme III, but also attack of 2,4,5-tribromophenyl anion on that bromine, and of either anion on the 1-bromine of **1**.

Tables I and III show the yield of dibromobenzenes to be always higher than that of tetrabromobenzenes, even when **12** is furnished as cocatalyst. Inasmuch as disproportionation of **1** or **2** should form di- and tetrabromobenzenes in equal proportions, this implies that the tetrabromobenzenes are preferentially destroyed in further reactions, probably in reactions which form arynes with liberation of bromide ion.

Inasmuch as **1** can, with catalysis by base, disproportionate to form **12** which is a cocatalyst for equilibration of **1** and **2**, one may ask why **1** did not itself show activity as a cocatalyst in runs 19 and 23 of Table III. The problem is probably a kinetic one. According to the mechanism of Scheme III, disproportionation of **1** should be second order in **1**, and therefore very slow when the concentration of **1** is low. It may be noted (Table III, run 23) that **1** apparently had some activity as a cocatalyst when the reaction time was exceptionally long.

The fact that **2** will not isomerize unless **12** or other cocatalyst is supplied constitutes compelling evidence against the 1,2-shift mechanism. If isomerization of **1**

to **2** had occurred *via* 1,2 shift, converting anion **11** directly into anion **13**, reversion of **13** to **11** and therefore of **2** to **1** should have occurred under the same conditions, so as to establish equilibrium starting from either **1** or **2** without need for cocatalysis.

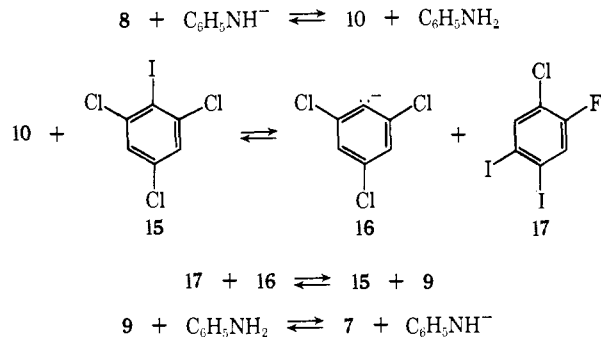
IV. Isomerization of 1-Chloro-2-fluoro-5-iodobenzene (**8**) with Cocatalysis

Although **8** does not isomerize on treatment with potassium anilide in ammonia or ammonia-ether, it seemed likely that it should isomerize if a suitable positive iodine donor cocatalyst were provided. The cocatalyst chosen was 1-iodo-2,4,6-trichlorobenzene (**15**) which is a good positive iodine donor because its iodine is flanked by two ortho chlorines.^{5a}

Reaction of equimolar amounts of **8**, **15**, potassium anilide, and aniline in 91% ammonia-9% ether afforded a mixture of isomerization product **7** (12.4%), unisomerized **8** (14.3%), 1,3,5-trichlorobenzene (46%), and four different chlorofluorodiodobenzenes (totaling 10.8%). Thus isomerization of **8** to **7** does occur under the influence of potassium anilide when a suitable cocatalyst is supplied.

This isomerization finds interpretation in a seven-halogen adaptation of the positive halogen transfer mechanism, as sketched in Scheme IV. The main

Scheme IV



features of Scheme IV are of a character adequately discussed above. Proton capture by **16** to form 1,3,5-trichlorobenzene is clearly a prominent further step. To the extent that it occurs, **17** and other chlorofluorodiodobenzenes (formed analogously) should accumulate in the system. The fact that the total yield of $\text{C}_6\text{H}_2\text{ClFI}_2$ isomers was less than of **16** at the end of the experiment indicates that they were consumed preferentially in further reactions, probably with liberation of iodide ion and formation of halogenated aromatic amines.

V. Reactions with *tert*-BuOK in Hexamethylphosphoramide (HMPA)

It is reported in Table I that isomerization of **1** to **2** occurs readily in this system. Experiments on the reversion of **2** to **1** are summarized in Table IV.

In HMPA, reversion of **2** to **1** occurs *without any need for a cocatalyst!* Within 1 min, a ratio of **2**:**1** is established which is substantially the same as from reactions starting from **1** (*cf.* Table I). Substantial amounts of disproportionation to di- and tetrabromobenzenes occur, and the ratio of *m*- to *p*-dibromobenzene increases with time, toward the thermodynamic ratio.

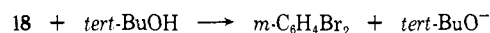
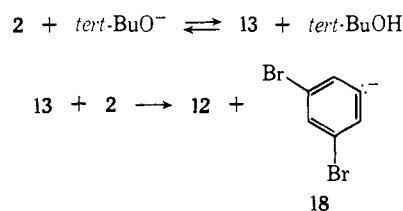
Table IV. Isomerization-Disproportionation of 1,3,5-Tribromobenzene Effected by *tert*-BuOK in HMPA^a

| Product | Product composition, ^b %, at reaction time | | |
|---|---|-----------------------|----------|
| | 1.0 min | 14.5 min | 1020 min |
| Recovered 2 | 28.0 | 26.4 | 20.8 |
| 1 | 49.1 | 45.1 | 38.3 |
| <i>p</i> -C ₆ H ₄ Br ₂ | 12.7 | 12.7 | 18.3 |
| <i>m</i> -C ₆ H ₄ Br ₂ | 3.0 | 8.0 | 12.4 |
| C ₆ H ₂ Br ₄ | 7.1 | 4.9 | 5.2 |
| Br ⁻ | 16 | 66 | 83 |
| 2 : 1 | 0.57 | Product ratio 0.58 | 0.54 |

^a Initial concentrations: **2**, 0.07 M; *tert*-BuOK, 0.13 M. ^b Percentages of di-, tri-, and tetrabromobenzenes determined are reported.

Isomerization of **2** without need for addition of a good positive bromine donor as cocatalyst implies that an aryl anion without halogen ortho to its anionic center plays a significant role as an intermediate. One can visualize disproportionation of **2** to form **12** and *m*-dibromobenzene, as sketched in Scheme V, and that

Scheme V



the **12** then cocatalyzes isomerization as in Scheme II.^{12a} By the rules which seem to be obeyed in ammonia, ammonia-ether, and DMF media, a species such as **18** should not have been energetically accessible.

The exceedingly high chemical potential of strongly basic anions in HMPA^{12b} is probably responsible for the occurrence of reactions in this medium which do not occur in the other media investigated. For example, the activity coefficient of chloride ion is estimated to be more than two orders of magnitude greater in HMPA than in DMF.^{12b} Reactions in HMPA start at such a high free-energy level that high-energy intermediates and transition states become attainable. In the present case, the equilibrium in the first step of Scheme V probably provides a high enough concentration of **13** to enable the second step, which otherwise would be very slow, to occur at an appreciable rate.¹³

VI. Tribromobenzene Isomer Proportions at Equilibrium

It is now clear that equilibration of **1** and **2** occurs under catalysis by base, in some cases with requirement

(12) (a) Carbanion-alkali metal cation salts are fully dissociated into free ions in HMPA: M. Szwarc, *Accounts Chem. Res.*, **2**, 87 (1969); (b) R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, **90**, 5049 (1968).

(13) The exceptionally high activity coefficient of bromide ion in HMPA^{12b} is also a factor to be considered; the transition state for expulsion of Br⁻ from *o*-bromoaryl anions to form arynes probably involves a large degree of C-Br bond scission¹⁴ and therefore also has a high activity coefficient; consequently bromide ion expulsion should be much retarded, thereby allowing higher concentrations of *o*-bromoaryl anions to be maintained.

(14) J. A. Zoltewicz and J. F. Bunnett, *J. Amer. Chem. Soc.*, **87**, 2640 (1965).

Table V. Isomerization-Disproportionation of Triiodobenzenes

| Solvent | C ₆ H ₃ I ₃ orientation | [C ₆ H ₃ I ₃], M | [<i>tert</i> -BuOK], M | Reaction time, min | Product yields | | Aryl iodides composition | | | | |
|---------|--|---|----------------------------|--------------------|------------------------------------|-----------------|--|--|--|--|---|
| | | | | | I ⁻ , ^a % | Aryl iodides, % | <i>p</i> -C ₆ H ₄ I ₂ , % | <i>m</i> -C ₆ H ₄ I ₂ , % | 1,2,4-C ₆ H ₃ I ₃ , % | 1,3,5-C ₆ H ₃ I ₃ , % | C ₆ H ₂ I ₄ , ^b % |
| DMF | 1,2,4 | 0.07 | 0.13 | 0.88 | 57 | 58 | 9.1 | 1.0 | 53.4 | 34.7 | 1.8 |
| | 1,3,5 | 0.08 | 0.13 | 1.33 | 45 | 72 | 5.0 | 3.2 | 34.0 | 57.1 | 0.7 |
| HMPA | 1,2,4 | 0.07 | 0.05 | 1.08 | 28 | 80 | 12.3 | 2.4 | 43.3 | 42.0 | |
| | 1,3,5 | 0.07 | 0.05 | 1.32 | 30 | 77 | 11.1 | 3.9 | 40.8 | 39.6 | 4.8 |

^a Iodide yield based on one I⁻ per C₆H₃I₃ introduced. ^b The C₆H₂I₄ isomers were isolated by glpc and recognized by their mass spectra: *m/e* 582, 455, 328, 201, and 74.

of addition of a cocatalyst such as **12**. In general, our experiments were not conducted in such a way as to affirm that equilibrium had actually been attained. In some it clearly was not. Nevertheless, there is a fair degree of consistency among several experiments, enough to suggest if not to establish the ratio of **2** to **1** at equilibrium.

In 50% ammonia-50% ether medium, the **2**:**1** ratio was not greater than 1.5 starting from **1**, or less than 1.7 starting from **2** (with cocatalysis by **12**). This implies an equilibrium ratio of about 1.6, at -29°. In DMF, the **2**:**1** ratio at equilibrium is indicated to be about 1.04, at *ca.* 25°. In HMPA, most experiments gave a ratio of about 0.55. In all three systems the ratio appears to be close to unity but somewhat dependent on the solvent and (in part) temperature.

The equilibrium isomer proportions among the dibromobenzenes, as determined in acid-catalyzed isomerization experiments, are about 6% ortho, 60% meta, and 34% para.¹⁵ The predominance of the meta over the ortho isomer is noteworthy; it is attributed to steric and dipole-dipole repulsions in the ortho isomer. Taking note that the three bromines in **2** are all meta related whereas those in **1** are (pair by pair) ortho, meta, and para related, and that the meta isomer prevails over both the ortho and the para in the dibromobenzene equilibrium, one might be surprised to find **1** and **2** to be almost equally favored in the triiodobenzene equilibrium.

This seeming paradox is, however, resolved by consideration of the symmetry numbers (σ)¹⁶ of **1** and **2** which are, respectively, 1 and 6. There is a symmetry contribution to the entropy of a species of magnitude $-R \ln \sigma$; in the present case, this has no effect on the entropy of **1** but reduces that of **2** by 3.56 cal deg⁻¹ mol⁻¹. This entropy factor would reduce the proportion of **2** at equilibrium, as compared to **1**, by a factor of 6. On the other hand, **2** is definitely favored over **1** in regard to enthalpy. The two factors nearly offset each other, so as to afford nearly equal proportions of **1** and **2** at equilibrium.

Acid-catalyzed equilibration among trichlorobenzenes has been studied by Erykalov, *et al.*;¹⁷ for 200-230°, the equilibrium proportions reported are 73% 1,2,4, 24% 1,3,5, and 3% 1,2,3 isomer. In this case, the symmetry factor in favor of the 1,2,4, as compared to the 1,3,5 isomer is the same as with the tribromo-

benzenes, the enthalpy factor disfavoring the 1,2,4 isomer may be somewhat less, and the contribution of the enthalpy difference to the equilibrium constant is reduced because of the elevated temperature.

VII. Miscellaneous Experiments

1,2,3-Tribromobenzene. In DMF, 1,2,3-C₆H₃Br₃ (0.09 M) and *tert*-BuOK (0.20 M) reacted rapidly; there was appreciable isomerization within 50 sec. After 142 min, the products included 10% **1**, 10% **2**, 13% dibromobenzenes, 2.8% tetrabromobenzenes, and 52% bromide ion; also, 5.6% 1,2,3-tribromobenzene remained.

Triiodobenzenes. Both 1,2,4- and 1,3,5-triiodobenzene underwent facile isomerization and disproportionation on treatment with *tert*-BuOK in either DMF or HMPA. Salient results are set forth in Table V. It is to be noted that the reaction time for the experiments listed was in no case greater than 80 sec.

The general pattern of the results is similar to that in tribromobenzene reactions. Thus, *p*-diiodobenzene is formed in greater amount than its meta isomer, and the yield of diiodobenzenes is greater than that of tetraiodobenzenes. Again, it is presumed that the latter are preferentially consumed in further reactions. In HMPA, 1,2,4- and 1,3,5-triiodobenzenes are found in nearly equal amounts in the product mixture, regardless of which was the reactant; this suggests that equilibrium between them is attained. On the other hand, in DMF the reactant triiodobenzene predominates in the product mixture, indicating that equilibrium had not been achieved in both cases, if in either.

A striking result is that 1,3,5-triiodobenzene underwent isomerization with *tert*-BuOK even in DMF. This is remarkable because its tribromo analog, **2**, failed to isomerize under the same conditions, and because 1,2,4-triiodobenzene is much less reactive with potassium anilide in ammonia than is its tribromo analog, **1**. If the mechanism of isomerization is substantially that of Scheme II, isomerization of 1,3,5-triiodobenzene is probably initiated by formation of 1,2,3,5-tetraiodobenzene in the sense of Scheme V; *a priori*, one would expect capture of iodine by an aryl anion to occur more readily than that of bromine, but that the accumulation of three iodines in a 1,2,3 arrangement would be an energetic disadvantage. The reactivity pattern of triiodobenzenes remains rather puzzling.

In Table V, the tabulated yields of iodide ion (on the basis of 1 iodide ion/mol of C₆H₃I₃) and of aryl iodide total 107-117%. This is intelligible if, to some extent, more than one iodide ion were released per

(15) G. A. Olah, W. S. Tolgyesi, and R. E. A. Dear, *J. Org. Chem.*, **27**, 3455 (1962); G. J. P. Augustijn, E. C. Kooyman, and R. Louw, *Recl. Trav. Chim. Pays-Bas*, **82**, 965 (1963).

(16) G. N. Lewis, M. Randall, K. S. Pitzer, and L. Brewer, "Thermodynamics," 2nd ed, McGraw-Hill, New York, N. Y., 1961, p 428.

(17) Y. G. Erykalov, A. A. Spryskov, and V. K. Matyash, *Zh. Obshch. Khim.*, **34**, 237 (1964); *Chem. Abstr.*, **60**, 10571 (1964).

$C_6H_3I_3$ molecule. If di- or triiodobenzenes are formed, with release of iodide ion, and then undergo nucleophilic addition of *tert*-BuO⁻, an *o*-iodoaryl anion is likely to be an intermediate in the addition, and it may release a second iodide ion.

Trichlorobenzenes. Efforts were made to isomerize 1,2,4-trichlorobenzene by treatment with 0.2 *M tert*-BuOK in DMF, with or without 0.003 *M* 1,2,3-trichlorobenzene as cocatalyst. No isomerization occurred, but some chloride ion was liberated.

Attempt to Trap Aryl Radicals. In an experiment similar to that of Table IV, except that the initial concentration of **2** was 0.14 *M*, iodobenzene (0.14 *M*) was also present. The products obtained were similar to those reported in Table IV, both as to identity and proportions. There was no evidence for formation of new aryl iodides, and no liberation of iodide ion. Inasmuch as aryl radicals easily abstract iodine from iodobenzene,¹⁸ this constitutes evidence against the intermediacy of aryl radicals. This method of trapping aryl radicals has proven to be quite sensitive for reactions which do proceed *via* aryl radical intermediates.¹⁹

VIII. Assessment of Evidence as to Reaction Mechanism

Five different mechanisms, one of them in two closely related versions, have been considered in this and preceding papers.⁴⁻⁶ They are the following: (a) the aryne mechanism; (b) the 1,2-shift (in an *o*-halophenyl anion) mechanism; (c) the positive halogen transfer mechanism, in six-halogen and seven-halogen versions; (d) mechanisms involving transfer of positive halogen mediated by the catalyzing base (*e.g.*, involving *N*-haloaniline intermediates); and (e) radical mechanisms.

Strong evidence and arguments have been presented against mechanisms a, b, d, and e, and under certain conditions the only tenable mechanism of those considered is the seven-halogen version of the positive halogen transfer mechanism.

The case against the aryne mechanism is marshaled in an accompanying paper;^{5a} the mechanism fails on many counts, and moreover it is incompatible with the requirement of cocatalysis (Section III, this paper).

The 1,2-shift mechanism could not, in the very nature of things, account for disproportionation of halogens between aromatic rings; for isomerizations it is vitiated by the failure of **7** and **8** to interconvert on exposure to potassium anilide (section II) and for some reactions by the demonstrated need for cocatalysis (Sections III and IV).

Mechanisms involving mediation of positive halogen transfer by the catalyzing base are contraindicated by the fact that isomerization and disproportionation are catalyzed by both nitranion and oxyanion bases, which are apt to differ in their specific reactivity as nucleophiles attacking halogen, and by the likelihood that the conceivable *N*-haloaniline and *tert*-butyl hypoalite intermediates would undergo side reactions rather than transfer positive halogen efficiently. Moreover, such mechanisms could be reconciled with the require-

ment for cocatalysis only by the formulation of very elaborate mechanistic schemes.

Radical mechanisms are incompatible with the fact that iodine is not captured from iodobenzene during isomerization (section VII), nor do they accommodate the need of some reactions for cocatalysis. Furthermore, radical mechanisms of such high efficiency as we have observed for reactions in DMF and HMPA are improbable in solvents such as these which are good hydrogen atom donors to radicals.²⁰

The feasibility of mechanisms involving transfer of positive halogen from oligohalobenzene molecules to aryl anions, supporting experimental evidence, and the principle that such reactions are enormously favored when the aryl anion intermediates have halogen ortho to the anionic site were discussed in the preceding paper.^{5a} Such mechanisms find further support in the present work. The demonstrated requirement of some reactions for cocatalysis finds ready explanation in the seven-halogen version of the positive halogen transfer mechanism, and we have been unable to rationalize it on other grounds. This mechanism, in the seven-halogen version, is the only one of those considered which is compatible with all the evidence at hand. It remains possible, however, that the closely related six-halogen version may prevail under some circumstances.

Finally we add the universal proviso that the only mechanisms we have been able to reject are conceivable ones; perhaps one that is inconceivable to us at this writing will ultimately be found to give a better account of the facts.

Experimental Section

1-Chloro-2-fluoro-4-iodobenzene (7). From 2,6-dichloroaniline, 1-fluoro-2,6-dichlorobenzene, mp 34–36°, ²¹ was prepared in 40% yield by pyrolysis of the diazonium fluoroborate.²² To a solution of KNH₂ (from 7.13 g of potassium metal) in 500 ml of liquid ammonia, 5.0 g of this $C_6H_3Cl_2F$ was added in small portions. After 1 hr of reaction at reflux with stirring, the base was neutralized with NH₄NO₃, the ammonia was evaporated, and 3.0 g (66%) of 3-fluoro-4-chloroaniline, mp 60–62°, ²³ was isolated by conventional means. This amine was diazotized, with use of NaNO₂ and HCl in water, and the filtered diazonium solution was added to a hot (70°) solution of KI in water, and then allowed to react 1 hr with stirring; the **7** so formed was isolated by conventional means, with ultimate distillation at reduced pressure: bp 65–66° (1 Torr); *n*^{20D} 1.6071; yield 36%; the mass spectrum showed parent ions of *m/e* 256 and 258 in ratio of 3:1; the pmr spectrum was complex in the aromatic region.

1-Chloro-2-fluoro-5-iodobenzene (8). 1-Chloro-2-fluoro-5-nitrobenzene, mp 41–42°, ²⁴ was obtained by chlorination of *p*-fluoronitrobenzene with dry Cl₂ and anhydrous FeCl₃ at 130°. It was reduced to 3-chloro-4-fluoroaniline, mp 44–45°, ^{23,24} by means of iron powder and NH₄Cl in aqueous methanol. By diazotization and treatment with KI, as described above, this amine was converted to **8** in 44% yield; the **8** had bp 57–58° (1 Torr), *n*^{20D} 1.6063, and a mass spectrum with parent ions of *m/e* 256 and 258 in ratio of 3:1.

Reactions with Potassium Anilide in Ammonia-Ether. In general, the apparatus and procedures were as described by Bunnett and Moyer.⁵ The requisite amount of anhydrous diethyl ether was placed in the reaction flask before any ammonia was condensed in

(20) (a) Cf. E. Hayon, T. Iyata, N. N. Lichtin, and M. Simic, *J. Amer. Chem. Soc.*, **92**, 3898 (1970); (b) David Cook, unpublished observations.

(21) A. Pavlath and G. Olah, *Acta Chim. Acad. Sci. Hung.*, **10**, 227 (1956); *Chem. Abstr.*, **51**, 8666 (1957).

(22) A. Roe, *Org. React.*, **5**, 193 (1949).

(23) C. K. Ingold and C. N. N. Vass, *J. Chem. Soc.*, 417 (1928).

(24) I. J. Rinkes, *Chem. Weekbl.*, **11**, 952 (1914); *Chem. Abstr.*, **10**, 194 (1916).

(18) J. F. Bunnett and C. C. Wamser, *J. Amer. Chem. Soc.*, **88**, 5534 (1966); D. L. Brydon and J. I. G. Cadogan, *J. Chem. Soc. C*, 819 (1968).

(19) L. Friedman and J. F. Chlebowski, *J. Org. Chem.*, **33**, 1633 (1968); T. J. Broxton, unpublished observations.

it, and ammonia was condensed until the flask was filled to a predetermined mark. The aniline and trihalobenzene were added, in that order, each dissolved in a small amount of ether, after the KNH_2 solution had been prepared. In Table I, $[\text{C}_6\text{H}_5\text{NH}_2]$ refers to molecular aniline in excess of that which reacted with KNH_2 to form potassium anilide.

Reaction of 1-Chloro-2-fluoro-5-iodobenzene (8) with Potassium Anilide in the Presence of 1-Iodo-2,4,6-trichlorobenzene (15). Reaction of **8** (0.02 M), **15** (0.02 M), and potassium anilide (0.02 M) in 91% ammonia–9% ether medium also containing 0.02 M aniline, for 120 min, afforded a grand mixture of products; the glpc tracing showed nine prominent peaks, plus some minor ones. In order of elution these were 1,3,5-trichlorobenzene (46%), **7** (12.4%), **8** (14.3%), unreacted **15** (1.8%), and four different chlorofluorodiodobenzenes (totaling 10.8%). (Yields of trichloro products are based on **15**, and of chlorofluoro products on **8**.) The ninth peak was unidentified. The first four peaks were identified by the match of infrared and pmr spectra of eluted samples with those of authentic materials. The four chlorofluorodiodobenzenes were separately identified as to composition by their mass spectra; in the absence of authentic samples of probable isomers, the infrared and pmr spectra of individual fractions, which were obtained, were of no use for assignment of orientation.

Reactions with *tert*-BuOK in DMF or HMPA. DMF was purified by treating it with anhydrous CuSO_4 (which complexes both water

and dimethylamine) and ultimately by distilling it from a fresh sample of anhydrous CuSO_4 . *tert*-BuOK was obtained as a dry, powdery solid from MSA Research Corp., Evans City, Pa. Solutions of *tert*-BuOK in DMF or HMPA were prepared in a drybox; aliquots were removed and titrated with standard hydrochloric acid to determine the base concentration. Reactions were initiated by combining a portion of a solution of *tert*-BuOK in DMF or HMPA with a solution of an aryl halide or aryl halides in the same solvent. Reactions were performed at room temperature (about 25°) under a nitrogen atmosphere; great care was taken to prevent access of atmospheric moisture to the reaction mixtures. After a measured period of time, the reaction mixture was poured into water, a measured amount of an internal standard for glpc purposes (usually diphenyl ether) was added, the mixture was extracted with ether, the ether solution was dried over Drierite and evaporated to a small volume, and the residue was analyzed by glpc. In general, a 2.44-m column packed with 5% SE 30 silicone rubber and 5% Bentone 34 on Chromosorb P was used for the glpc work. In many experiments, the halide ion content of the aqueous layer was determined by potentiometric titration against AgNO_3 . No aryl *tert*-butyl ethers were detected as products.

Unless otherwise stated, the identities of products and recovered reactants were established by the match of their glpc retention times and the infrared spectra of eluted samples with those of authentic samples.

Bromine Scrambling Accompanying Base-Catalyzed Isomerization of 1,2,4-Tribromobenzene¹

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Contribution from the University of California, Santa Cruz, California 95060, and The Urey Radiochemical Laboratory, University of Auckland, Auckland, New Zealand. Received February 12, 1970

Abstract: 1,2,4-Tribromobenzene radiolabeled in the 1 position (**1b**) undergoes partial isomerization to 1,3,5-tribromobenzene (**2b**) during 15-min exposure to potassium anilide and aniline in liquid ammonia. Product **2b** and recovered 1,2,4-tribromobenzene are equal in molar radioactivity to each other and to the **1b** introduced. In the recovered 1,2,4-tribromobenzene, the radiolabel is equally distributed among the three bromine positions. For the bromine scrambling, a mechanism is proposed the key step of which is positive bromine transfer from 1,2,4,5-tetrabromobenzene to 2,4,5-tribromophenyl anion, forming products identical with the reactants except for possible differences in the location of the radiolabel.

Although 1,2,4-triiodobenzene, on treatment with potassium anilide in ammonia, undergoes isomerization to 1,3,5-triiodobenzene at a very slow rate,³ redistribution of the radiolabel of 2-radiolabeled-1,2,4-triiodobenzene occurs more rapidly.⁴ Under conditions which effect only 5% isomerization, the radiolabel is statistically redistributed among the 1, 2, and 4 positions.⁴

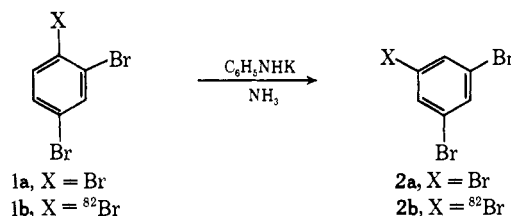
Isomerization of 1,2,4-tribromobenzene (**1a**) to 1,3,5-tribromobenzene (**2a**) occurs readily in the potassium anilide–ammonia system.³ We now report that conditions which bring about substantial isomerization of **1a** to **2a** also cause full redistribution of the radiolabel of 1,2,4-tribromobenzene-1-⁸²Br (**1b**).

(1) Research supported in part by the National Science Foundation.

(2) (a) University of Auckland; preliminary experiments were performed at Santa Cruz, and the radiochemical experiments at Auckland; (b) to whom inquiries should be addressed, at Santa Cruz.

(3) C. E. Moyer, Jr., and J. F. Bunnett, *J. Amer. Chem. Soc.*, **85**, 1891 (1963); J. F. Bunnett and C. E. Moyer, Jr., **93**, 1183 (1971).

(4) J. F. Bunnett and D. J. McLennan, *ibid.*, **90**, 2190 (1968).



In experiments of this type, it is essential to devise a way to degrade the 1,2,4-trihalobenzene in such a way as to remove halogens selectively from at least two of the three positions they occupy. One of the degradation reactions used in the experiment with radiolabeled 1,2,4-triiodobenzene,⁴ namely, radical-induced deiodination in alkaline methanol,⁵ cannot be used for degradation of **1a** because debromination does not occur under the conditions employed.

(5) J. F. Bunnett and C. C. Wamser, *ibid.*, **89**, 6712 (1967).