Comparative Mobility of Halogens in Reactions of Dihalobenzenes with Potassium Amide in Ammonia

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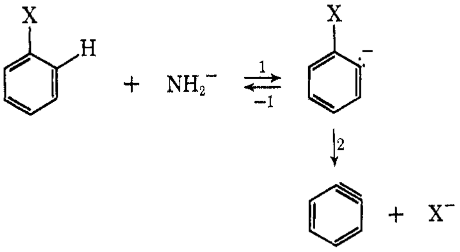
Dihalobenzenes in which the two halogens are unlike release two different halide ions, generally in unequal amounts, on reaction with KNH_2. From *m*-dihalobenzenes, the relative yields of halide ion are in the order I > Br > Cl, but *o*- and *p*-dihalobenzenes give more complex patterns because either of two steps in the aryne-forming reaction may be rate limiting. Under reaction conditions, haloanilines furnish little halide ion. When potassium anilide is the base, the heavier halogen is in all cases released preferentially.

Reactions of potassium amide
With halobenzenes in ammonia
Via benzyne intermediates occur.[3,4]
Bergstrom and associates[5] did report,
Based on two-component competition runs,
Bromobenzene the fastest to react,
By iodobenzene closely followed,
The chloro compound lagging far behind,
And fluorobenzene to be quite inert
At reflux (−33°).
Reactions with *para*-dihalobenzenes,
In which the halogens were not the same,
The same order of mobility revealed,
But differences in reactivity
Were somewhat less in magnitude.
The irregular mobility rank
Explanation finds in the mechanism
Whereby arynes are formed.[3,4] There are two steps:
Abstraction of the ortho proton
And then expulsion of the halogen
From the anion intermediate.
In Scheme I the mechanism is set forth.

SCHEME I



Here proton removal is favored, in rate
And in respect to equilibrium,
By high electronegativity
Of halogen.[6] But the expulsion step
Is faster in the opposite order.
According to the evidence, for both
Iodine and bromine step 1 limits rate.[3]
But on the other hand, the setting free
Of halogen determines total rate
For chlorine and fluorine atoms on the ring.
We have repeated the experiments
With dihalobenzenes of Bergstrom's group.
They are extended to the isomers
Meta and ortho, and to the action
Of potassium anilide reagent.
Throughout, halide ions have been determined
By potentiometric titration
In which end points for diverse halide ions
Are discrete, and easy to recognize.
Nitrogenous products were not assayed.

Results

Data for reactions of all nine mixed
Dihalobenzenes (excluding fluorine)
With four equivalents of amide base
Are set forth in Table I. Reactions
With the same base in deficiency
Appear, for six substrates, in Table II.
In Table I, more than one halide ion
Is set free from each dihalobenzene
Molecule. This suggests the possibility
That maybe haloanilines too react
With potassium amide. In Table III

TABLE I

REACTIONS OF DIHALOBENZENES WITH EXCESS POTASSIUM AMIDE IN AMMONIA[a]

Halogens present	Orientation	Registry no.	Halide ion yields, %[b]				Ratio[c]
			I^-	Br^-	Cl^-	Total	
Cl, Br	ortho	694-80-4		98.5	11	109.5[d]	90/10
	meta	108-37-2		101	7.5	108.5[d]	93/7
	para	106-39-8		95.5	8.0	103.5[e]	92/8
				97.5	8.0	105.5[d]	92/8
Br, I	ortho	583-55-1	71	83		154	46/54
			64	73.5		137.5	47/53
	meta	591-18-4	96	17.5		113.5	85/15
	para	589-87-7	50.5	70		120.5	42/58
Cl, I	ortho	615-41-8	93.5		42.5	136	69/31
			93.5		32.5	126	74/26
	meta	625-99-0	95.5		6.5	102	93/7
	para	637-87-6	96		14	110	87/13

[a] Reaction conditions: 0.02 mol of dihalobenzene with 0.08 mol of KNH_2; time 10 min, unless otherwise noted. [b] Reckoned on the basis of one halide ion per molecule of dihalobenzene; thus, the first experiment afforded 0.0197 mol of Br^- and 0.0022 mol of Cl^-. [c] Ratio of heavier halide ion to lighter halide ion. [d] 15 min. [e] 20 min.

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[2] NOTE FROM EDITOR.—Although we are open to new styles and formats for scientific publication, we must admit to surprise upon receiving this paper. However, we find the paper to be novel in its chemistry, and readable in its verse. Because of the somewhat increased space requirements and possible difficulty to some of our nonpoetically inclined readers, manuscripts in this format face an uncertain future in this office. However, we take this opportunity to encourage readers and authors to examine carefully a new format represented by the articles on pages 3591–3646 and the *Editor's Notice* in the November 1970 issue of this journal.

[3] J. D. Roberts, D. A. Semenow, H. E. Simmons, Jr., and L. A. Carlsmith, *J. Amer. Chem. Soc.*, **78**, 601 (1956).

[4] J. F. Bunnett, *J. Chem. Educ.*, **38**, 278 (1961).

[5] F. W. Bergstrom, R. E. Wright, C. Chandler, and W. A. Gilkey, *J. Org. Chem.*, **1**, 170 (1936).

[6] J. Hine and P. B. Langford, *ibid.*, **27**, 4149 (1962).

TABLE II
REACTIONS OF DIHALOBENZENES WITH A DEFICIENCY OF POTASSIUM AMIDE IN AMMONIA[a]

Halogens present	Orientation	Halide ion yields, %[b]			
		I^-	Br^-, Cl^-	Total	Ratio[c]
Cl, Br	para		56.5	56.5	100/0[d]
Br, I	ortho	37	38	75	49/51
	meta	68	8	76	89/11
	para	23.5	37	60.5	39/61[e]
		26.5	41.5	68	39/61[e]
Cl, I	meta	63.5		63.5	100/0
2-Bromo-4-iodotoluene		46.5	27.5	74	63/37

[a] Reaction conditions: 0.02 mol of dihalobenzene or dihalotoluene with 0.03 mol of KNH_2, for 10 min. [b] Reckoned on the same basis as in Table I; yields based on KNH_2 (the limiting reagent) are 1.33 times greater than listed. [c] Ratio of heavier halide ion to lighter halide ion. [d] Bergstrom, *et al.*,[5] reported 89/11 and 85/15. [e] Bergstrom, *et al.*,[5] reported 32/68.

TABLE III
REACTIONS OF HALOANILINES WITH EXCESS POTASSIUM AMIDE IN AMMONIA[a]

Substituent	Halide ion yield, %	Substituent	Halide ion yield, %
m-Chloro	0.6	*p*-Bromo	3.0
p-Chloro[b]	0.6	*m*-Iodo	5.7
m-Bromo	2.6	*p*-Iodo	1.6

[a] Reaction conditions: 0.02 mol of haloaniline with 0.10 mol of KNH_2; time 10 min, unless otherwise noted. [b] 30 min.

TABLE IV
REACTIONS OF DIHALOBENZENES WITH EXCESS POTASSIUM ANILIDE IN AMMONIA[a]

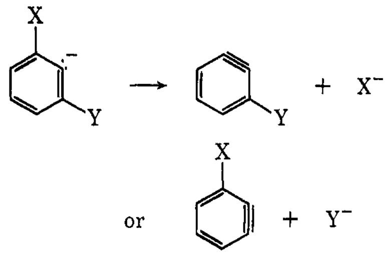
Halogens present	Orientation	Halide ion yields, %[b]			
		I^-	Br^-, Cl^-	Total	Ratio[c]
Cl, Br	para		11.5	11.5	100/0
Br, I	ortho	3.2	2.6	5.8	54/46
	meta	89	15	104	86/14
	para	36	5.5	41.5	87/13
Cl, I	meta	90.5		90.5	100/0

[a] Reaction conditions: 0.02 mol of dihalobenzene with 0.08 mol of potassium anilide and a slight excess (0.01 mol) of aniline; for 30 min. [b] Reckoned on the basis of one halide ion per molecule of dihalobenzene. [c] Ratio of heavier halide ion to lighter halide ion.

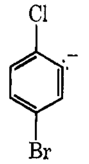
Are shown experiments which demonstrate
That haloanilines react but to
A slight degree under conditions such as used.
Tribromobenzene isomerizations
Are well catalyzed by potassium
Anilide in liquid ammonia.[7]
It was therefore of interest to see
The effect of this base on mobility.
Results are assembled in Table IV.

Discussion

In meta isomers, the hydrogen between
Two ortho halogens is more acidic than
The other hydrogens.[6] In consequence,
Halide expulsion to form arynes
Occurs predominantly from those anions
That are doubly ortho substituted.[8, 9]
Therefore either halide ion doth derive
From the very same anion, and which
Is preferentially expelled depends
Upon the intrinsic labilities
Of the two covalent bonds to halogen.



In Table I, data pertaining to
The meta isomers show clearly that
Carbon–iodine bonds more readily break
Than carbon–bromine bonds, and furthermore
That carbon–chlorine bonds are even more
Resistant. This is, of course, a familiar
Order of reactivity. Somewhat puzzling
Is that the heavier–lighter halide ratio
From *meta*-iodochlorobenzene
Is just the same as from *meta*-bromo-
Chlorobenzene. One would have expected
Almost exclusive iodine release
From the former compound. In Table II,
And likewise in examples found in Table IV,
The anticipated insignificance
Of chlorine release is however manifest.
Ortho and para isomers behave
Almost identically in Table I.
From the two bromoiodobenzenes,
Bromide release predominates in slight degree.
Clearly, the proton abstraction step (Scheme I)
Is for the most part rate determining.
From *ortho*- and *para*-bromochloro-
Benzenes, bromide ion is liberated
Some ten times faster than is chloride ion.
The two anions concerned are **1** and **2**.



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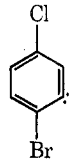
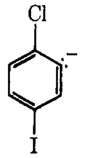


2

Doubtless **1** is formed more rapidly
But mostly to the parent molecule reverts.[8]
Anion **2** is not so quickly formed
But decomposes to a large extent[10]
With liberation of a bromide ion.
Remarkably, the *ortho*- and *para*-
Iodochlorobenzenes are less prone
Than corresponding bromochlorobenzenes
The heavier halogen to set free.
The reason surely is that iodine



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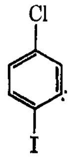

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(7) C. E. Moyer, Jr., and J. F. Bunnett, *J. Amer. Chem. Soc.*, **85**, 1891 (1963); J. F. Bunnett and G. Scorrano, *ibid.*, in press.
(8) J. A. Zoltewicz and J. F. Bunnett, *ibid.*, **87**, 2640 (1965).
(9) J. K. Kim, unpublished observations.
(10) M. Aufrere, unpublished observations.

But weakly aids formation of ion **4**;
Release of chlorine then from ion **3**,
Preferred over **4** in its free energy,
Creeps close to that of iodine less firmly bound.
para-Bromoiodobenzene demonstrates
An inversion of mobility
As the proton-seeking reagent is changed
From amide ion (in Table I or II)
To anilide (in Table IV). Release
Of iodine is preferred with anilide.
The same effect has three times been observed
With oligohalobenzenes, although
Interpretation is obscured somewhat
By disproportionations which occur
In several cases.[7,11] Isomerizations
Are improbable with the present substrate.
In the anilide–aniline milieu,
ortho-halophenyl anions revert
To parent molecules more frequently
Than they do with the amide base. Therefore,
Release of halide ion is determined
Relatively more by the lability
Of the carbon–halogen bonds concerned
Than by rates of abstraction of protons.
The haloanilines do not react
Extensively with excess amide ion,
As shown in Table III. In harmony
Appears the fact that yields of halide ion
With surplus amide ion slightly exceed
One ion from each dihalobenzene molecule
(Table I). However, *ortho*-iodo
Substrates afford much more halide ion
Than can be attributed to subsequent
Attack on the haloanilines that form.
An unexpected pathway of reaction,
Unclear in its details, is thus revealed.
This complication, our thanks to him,
Is under study by Jhong Kook Kim.

Experimental Section

Materials.—All dihalobenzenes were used as supplied by Eastman Kodak Co., except *m*-bromoiodobenzene which was distilled [bp 72.5–73.5° (1 Torr)] to remove a colored impurity. *p*-Bromo- and *p*-chloroanilines (from Eastman Kodak) and *m*-chloro-, *m*-iodo-, and *p*-iodoanilines (from Aldrich Chemical Co.) were used without further purification. 2-Bromo-4-iodotoluene, bp 96.5–97.0° (1 Torr), was synthesized by standard methods from a sample of 3-bromo-4-methylacetanilide which had been prepared by Dr. T. Okamoto.

Reaction Procedure.—Reactions were carried out substantially as described by Bunnett and Moyer.[11] In all cases, 500 ml of liquid ammonia was used, the dihalobenzene or halobenzene was added in solution in diethyl ether, and the addition funnel was rinsed with ether, the total volume of ether used being 70 ml. Reaction mixtures were usually dark red-brown in color. After the times listed in the tables, an excess of crushed ammonium nitrate was added, the ammonia was allowed to evaporate, and the residue was transferred to a separatory funnel with alternate washings of water and ether. The (alkaline) water layer was separated, and the ether layer was washed with water. The combined aqueous layers were adjusted to pH 3–4 by addition of dilute nitric acid, warmed briefly to expel dissolved ether, and diluted to the mark in a volumetric flask. Aliquots were titrated potentiometrically with silver nitrate, a radiometer titrator–titrigraph being used.

For reactions with dihalobenzenes in excess (Table II), the apparatus and procedure of Bunnett and Hrutfiord[12] were used without modification.

Registry No.—2-Bromo-4-iodotoluene, 26670-89-3; potassium amide, 17242-52-3.

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[11] J. F. Bunnett and C. E. Moyer, Jr., *J. Amer. Chem. Soc.*, in press.

[12] J. F. Bunnett and B. F. Hrutfiord, *ibid.*, **83**, 1691 (1961).

The Reactions of *in situ* *n*-Propylmagnesium, -cadmium, and -zinc Reagents with 4-*tert*-Butylcyclohexanone. Addition *vs.* Reduction and the Stereochemistry of Each

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The stereochemistry of both addition and reduction products of 4-*tert*-butylcyclohexanone with *n*-propylmagnesium, -cadmium, and -zinc reagents has been determined. Reactivity among Cd and Zn reagents varies over a wide range with a change in metal and halide ion, factors which also affect addition–reduction and the stereochemistry of both reactions. Cd reagents exhibit the greatest preference for addition over reduction. The Zn reagent leads to the nonthermodynamic reduction product (axial alcohol) in two instances.

In view of the striking tendency of methylcadmium and methylzinc reagents to add to 4-*tert*-butylcyclohexanone (**1**) from the axial side,[2] we undertook an investigation of the addition of *n*-propyl organometallics to the same ketone. The reaction of *n*-PrM (M = Mg, Cd, Zn) with **1** offered the opportunity to determine both the relative importance of addition and reduction with the various reagents as well as the stereochemistry of both processes (Scheme I).

After our experiments had been completed, preliminary results by Abenhaim[3] were published, including some experiments on the addition and reduction, with the stereochemistry of addition (only) reported for these same propyl reagents with 4-*tert*-butylcyclohexanone. Although no experimental details were described, the organometallic reagents employed by Abenhaim were presumably those containing bromide ion exclusively. His results are somewhat misleading inasmuch as he reported neither the yield of alcohol products nor the stereochemistry of reduction.

We should like to report our detailed study of the

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[1] (a) National Science Foundation Trainee, 1966–1969; (b) National Defense Education Act Fellow, 1966–1969.

[2] P. R. Jones, E. J. Goller, and W. J. Kauffman, *J. Org. Chem.*, **34**, 3566 (1968).

[3] M. Abenhaim, *C. R. Acad. Sci., Ser. C*, **267**, 1426 (1968).