

# REACTIONS OF TRIHALOGENOACETIC ACIDS—VIII<sup>†</sup>

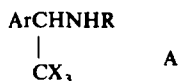
## ACCEPTOR AFFINITY OF $\alpha$ -(TRIHALOGENOMETHYL)AMINES FOR MINERAL ANIONS

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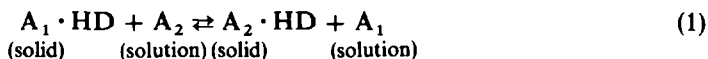
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**Abstract**—Exchange reaction  $A_1 \cdot HD + A_2 \rightleftharpoons A_2 \cdot HD + A_1$  between salts of radioactive  $\alpha$ -(trihalogenomethyl)amines with HCl, HNO<sub>3</sub> and HI ( $A_1^+ \cdot HD$ ) and free  $\alpha$ -(trihalogenomethyl)amines ( $A_2$ ) in hexadecane was investigated in order to establish relative affinities of  $A_1$  and  $A_2$  for these acids, depending on structures of the amines and character of the anion ( $D^-$ ). The aromatic derivatives of  $\alpha$ -(trihalogenomethyl)amines ( $A$ ) form complexes with electron-donors in organic solvents as well as solid, water-insoluble “salts-complexes” ( $A \cdot HD$ ) with proton-electron-donors HD (some mineral and carboxylic acids)<sup>1</sup>



Hydrolytic stability of the “salts-complexes”  $A \cdot HD$  (HD was HI, HNO<sub>3</sub>, CX<sub>3</sub>COOH and (COOH)<sub>2</sub>) as compared with the hydrochlorides ( $A \cdot HCl$ ), unstable in water, indicates an acceptor-donor interaction between the amine and the anion  $D^-$ . These acceptor properties of  $\alpha$ -(trihalogenomethyl)amines are ascribed to the presence of the CCl<sub>3</sub> or CBr<sub>3</sub> group, but, inability of the analogous aliphatic derivatives to form such salts stable in water suggests that the aromatic nucleus (Ar) is involved in acceptor-donor interaction in the solid complexes  $A \cdot HD$ .

IN THE present investigation, the rôle of the Ar radical in complexes  $A \cdot HD$  by means of the exchange reaction (1) in hexadecane has been described. This reaction



was used to compare relative affinities of the amines  $A_1$  and  $A_2$  for the acids of similar acidity but different electron-donating ability of the anion ( $D^-$ ). This method was used rather than a liquid-liquid system (solutions of the amines A in an organic solvent and in dilute HD) because an interaction of the amines A with proton-electron-donors HD in solution could be different from the interaction  $AH^+ \dots D^-$  in the solid state.

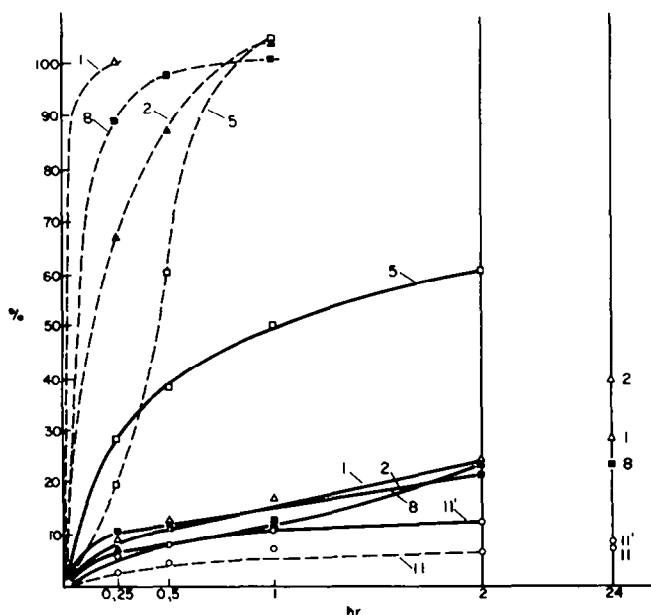
Radioactive amines  $A_1$  ( $A_1^+ \cdot HD$ ) labelled with C-14 in the CX<sub>3</sub> group were used. The amines A, used in experiments (given in Table 1), were of the two types—A'(R = n-butyl) and A'' (R = cyclohexyl). The acids (HD) used were HCl—with low anion affinity for A, HNO<sub>3</sub> and HI with high anion affinity. The results obtained for molar ratio  $A_1^+ \cdot HD : A_2 \sim 2:1$  are presented graphically in Figs 1–5 as per cents of the complete exchange between  $A_2$  and  $A_1$  (the inactive amines  $A_2$  completely replaced by active  $A_1^+$  in hexadecane solution). Points up to 2 hr correspond to stirring the mixture. The salts  $A_1 \cdot HD$  were practically insoluble in hexadecane.

<sup>†</sup> Part VII<sup>1</sup>.

TABLE I. FORMULAS OF THE AMINES  $\text{ArCH}(\text{CCl}_3)\text{NHR}$  (A)

No.	Ar	R	Type
I	$\text{C}_6\text{H}_5$	$n\text{-C}_4\text{H}_9$	A'
II	$4\text{-F-C}_6\text{H}_4$	$n\text{-C}_4\text{H}_9$	A'
III	$4\text{-Cl-C}_6\text{H}_4$	$n\text{-C}_4\text{H}_9$	A'
IV	$4\text{-CH}_3\text{O-C}_6\text{H}_4$	$n\text{-C}_4\text{H}_9$	A'
V	$2,4\text{-(CH}_3\text{O)}_2\text{-C}_6\text{H}_3$	$n\text{-C}_4\text{H}_9$	A'
VI	$3,4\text{-(CH}_3\text{O)}_2\text{-C}_6\text{H}_3$	$n\text{-C}_4\text{H}_9$	A'
VII	$2,3\text{-(CH}_3\text{O)}_2\text{-C}_6\text{H}_3$	$n\text{-C}_4\text{H}_9$	A'
VIII	$2\text{-CH}_3\text{-C}_6\text{H}_4$	$n\text{-C}_4\text{H}_9$	A'
IX	$\alpha\text{-naphthyl}$	$n\text{-C}_4\text{H}_9$	A'
X	$\beta\text{-naphthyl}$	$n\text{-C}_4\text{H}_9$	A'
XI	$\text{C}_6\text{H}_5$	cyclohexyl	A''
XII	$4\text{-CH}_3\text{O-C}_6\text{H}_4$	cyclohexyl	A''
XIII	$2,3\text{-(CH}_3\text{O)}_2\text{-C}_6\text{H}_3$	cyclohexyl	A''
XIV	$2,4\text{-(CH}_3\text{O)}_2\text{-C}_6\text{H}_3$	cyclohexyl	A''
XV	$2\text{-CH}_3\text{-C}_6\text{H}_4$	cyclohexyl	A''

The amines of A' type had a higher affinity for HCl (proton affinity) than the amines A'' irrespective of the substituents on the Ar radical, but affinity of both A' and A'' for  $\text{HNO}_3$  and HI (anion affinity) was determined by the substituents. All the amines A' (except IX) shown in Figs 1 and 1a replaced XII (A'') in  $\text{XII} \cdot \text{HCl}$  but not in  $\text{XII} \cdot \text{HNO}_3$  except V and VI which gave over 50% exchange with  $\text{XII} \cdot \text{HNO}_3$ . The amine XI (A'', unsubstituted) did not replace XII either in the hydrochloride or in the nitrate. The amine IV (analogous to XII but of A' type) was replaced by V and

FIG. 1  $\text{XII}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{XII}^*\text{HD}$ : —  $\text{HNO}_3$ , ---  $\text{HClA}_2$ : 1, II, V, VIII, XI.

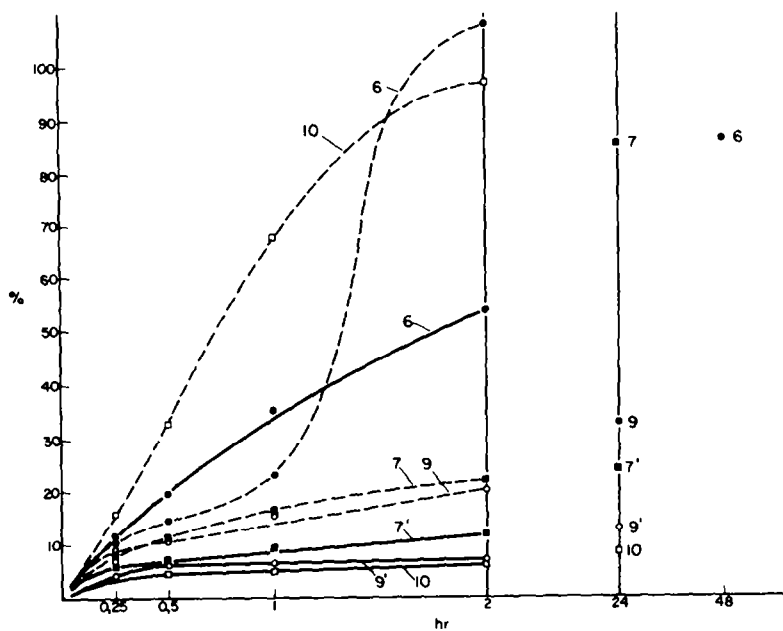


FIG. 1a  $\text{XII}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{XII}^*\text{HD}$ : —  $\text{HNO}_3$ ; - - -  $\text{HCl}$   $\text{A}_2$ : VI, VII, IX, X.

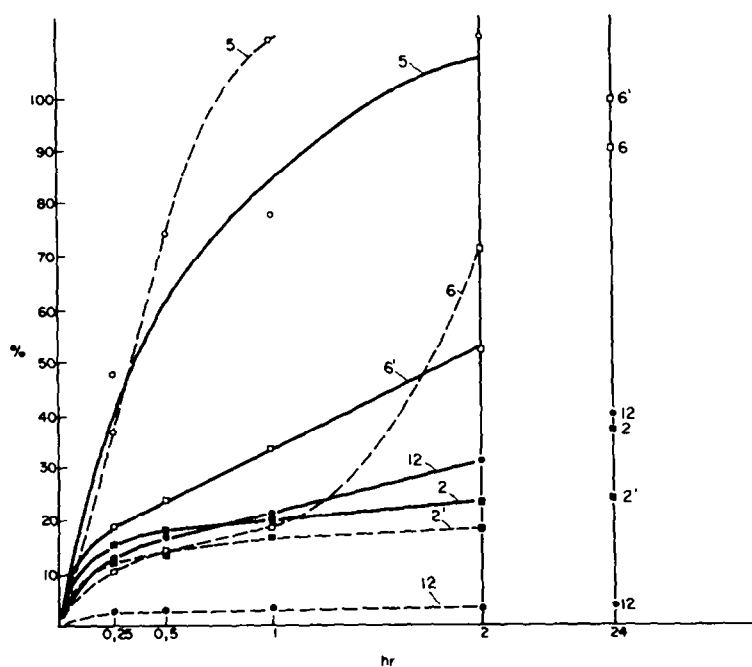


FIG. 2  $\text{IV}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{IV}^*\text{HD}$ : —  $\text{HNO}_3$ ; - - -  $\text{HCl}$   $\text{A}_2$ : II, V, VI, XII.

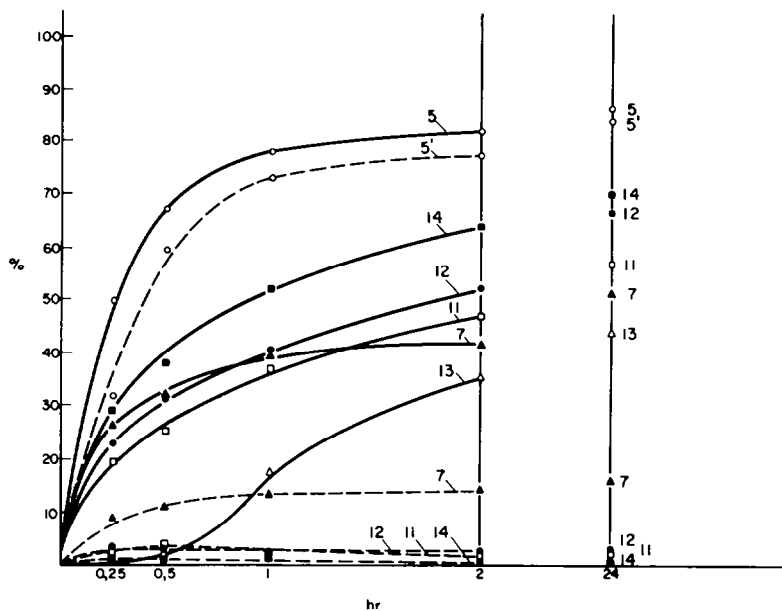


FIG. 3  $\text{III}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{III}^*\text{HD}$ : —  $\text{HNO}_3$ ; - - -  $\text{HCl A}_2$ : V, VII, XI, XII, XIII, XIV.

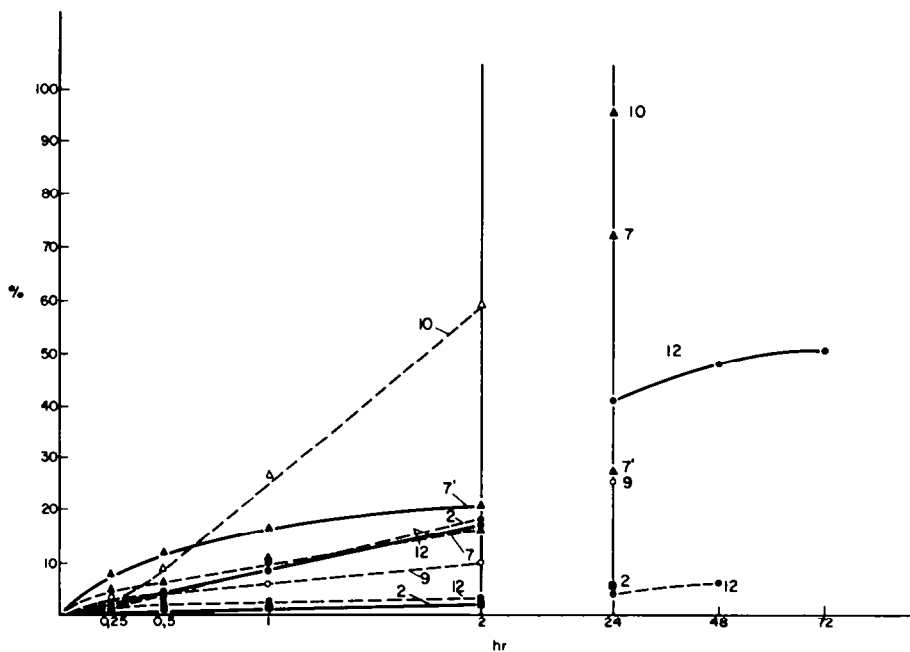


FIG. 4  $\text{XI}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{XI}^*\text{HD}$ : —  $\text{HNO}_3$ ; - - -  $\text{HCl A}_2$ : II, VII, IX, X, XII.

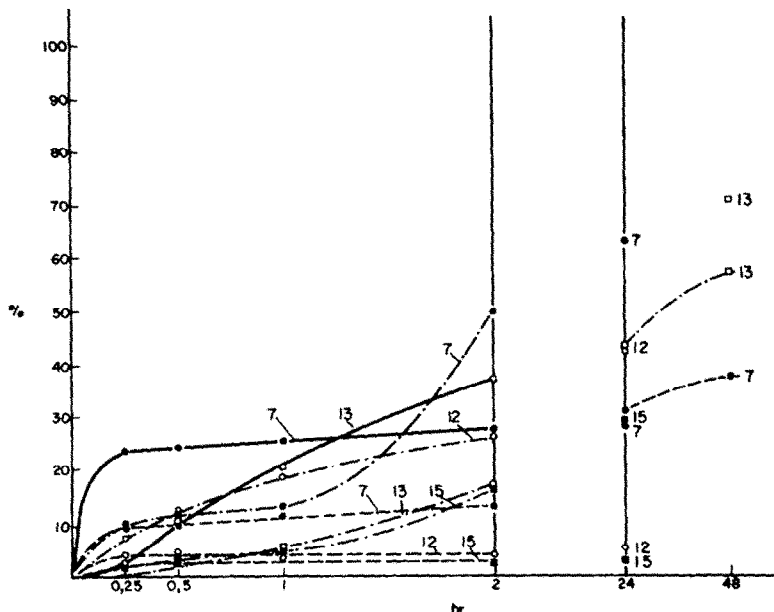


FIG. 5  $\text{II}^*\text{HD} + \text{A}_2 \rightleftharpoons \text{A}_2\text{HD} + \text{II}^* \text{HD}$ : —  $\text{HNO}_3$  ----  $\text{HCl}$  .....  $\text{HI}$   $\text{A}_2$ : VII, XII, XIII, XV.

VI only (Fig. 2); it was not replaced by XII in the hydrochloride but it was replaced (40%) in the nitrate. Amines XI–XIV ( $\text{A}_2'$ ) did not replace III ( $\text{A}_1'$ ) in  $\text{III} \cdot \text{HCl}$  but did in  $\text{III} \cdot \text{HNO}_3$  (Fig. 3); II ( $\text{A}_2'$ ) replaced XI ( $\text{A}_1'$ ) in the hydrochloride but not in the nitrate (Fig. 4); XIII ( $\text{A}_2'$ ) did not replace II ( $\text{A}_1'$ ) in  $\text{II} \cdot \text{HCl}$  but it did in  $\text{II} \cdot \text{HNO}_3$  and  $\text{II} \cdot \text{HI}$  (Fig. 5). The exchange of  $\text{II} \cdot \text{HI}$  with XII was considerable (Fig. 5), though the amine II had a higher affinity for  $\text{HCl}$  than the amine XII (Figs 1 and 5).

These results indicate that  $\text{OMe}$  groups increase the affinity of the amines A for  $\text{HNO}_3$  and  $\text{HI}$ , whereas chlorine and fluorine act in the reverse: the amines XII–XIV ( $\text{A}''$ ) with  $\text{OMe}$  groups in  $\text{Ar}$  replaced more basic  $\text{A}'$  with *para*-F and *para*-Cl (Figs 3 and 5); unsubstituted XI ( $\text{A}''$ ) replaced more basic III ( $\text{A}'$ ) with *para*-Cl (Fig. 3); the amine II ( $\text{A}'$ ) with *para*-F did not replace unsubstituted XI ( $\text{A}''$ ) in  $\text{XI} \cdot \text{HNO}_3$  (Fig. 4).

The affinity of the amine VII with two  $\text{OMe}$  groups in 2,3 positions of  $\text{Ar}$  was lowered for  $\text{HNO}_3$  (Figs 1a, 4 and 5) but it was "normal" for  $\text{HI}$  (Fig. 5).

Thus, a decisive influence of the structure of  $\text{Ar}$  radicals in the amines A of both  $\text{A}'$  and  $\text{A}''$  type on their affinity for proton-electron-donors  $\text{HI}$  and  $\text{HNO}_3$  was established. This influence confirms the hypothesis<sup>1</sup> that the nucleus  $\text{Ar}$  is involved in the acceptor-donor interaction with the anion in "salts-complexes"  $\text{A} \cdot \text{HD}$ . At the same time, the affinity of the amines A for  $\text{HNO}_3$  and  $\text{HI}$  (i.e. for  $\text{NO}_3^-$  and  $\text{I}^-$  anions) is increased by electron-donating substituents ( $\text{OMe}$  groups) and decreased by electron-attracting ones (fluorine and chlorine). This proves that acceptor ability of the nucleus cannot be caused by an inductive effect of the  $\text{CX}_3$  group on the  $\pi$ -electron system because this would be opposed to the influence of substituents, but an intramolecular steric interaction between nucleus (electron-donor) and a

halogen of the  $CX_3$  group (electron-acceptor) as shown in Fig. 6 is possible. Such interaction should lead to polarization of the  $\pi$ -electrons of the nucleus in a direction perpendicular to its plane (a coplanar interaction is not possible—Fig. 7), i.e.  $\pi$ -electrons should be found more frequently in the “halogen-side” of nucleus than on the “free-side”. Thus, the “free-side” becomes positively charged and able to interact with electron-donors. The influence of substituents can now be understood: electron-donating groups increase electron density in the nucleus and consequently increase the ability of the  $\pi$ -electrons to be polarized by the X atom. The electron-attracting

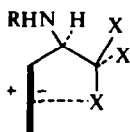


FIG. 6

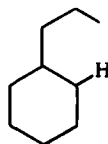


FIG. 7

substituents act in reverse. In this interaction<sup>†</sup> one halogen of the  $CX_3$  group should participate since one X is able to approach the nucleus and to overlap its  $\pi$ -orbital; besides, the Ar—C bond should be “bent” (Fig. 6).

The anion affinity of the amines A depends on the steric structure of both the Ar ring and the  $D^-$  anion: The amine VII with two OMe groups in 2,3 positions differs from other amines A in its affinity for  $HNO_3$  but not for HI. Also the amine XV with the *ortho*-Me in Ar showed a higher affinity for HI than for  $HNO_3$ . This is further evidence for the interaction between Ar and  $D^-$ . Apparently, due to location of the substituents in Ar, a steric hindrance appears in regard to  $NO_3^-$  but not in regard to the smaller I.

The decreased basicity (affinity for HCl) of the amines of the A'' type as compared with A' suggests that their conformation favours the steric interaction between X and electrons of the nitrogen<sup>1</sup> (Fig. 6). Lowered basicity of the amine VII (Figs 3 and 5) may be due to the same reason. The difference in affinity for HCl (an analogous difference in affinity for  $HNO_3$  has been found) between  $\alpha$ - and  $\beta$ -naphthyl derivatives IX and X (Fig. 1a) requires a detailed explanation.

Ability of other amines A to form hydrophobic salts-complexes with various weak acids will be described in a subsequent publication.

## EXPERIMENTAL

**Materials.**  $\alpha$ -(Trihalogenomethyl)amines A were prepared from trichloroacetic acid and the corresponding imines in benzene or toluene.<sup>3</sup> The derivatives I, XI, XII and XV have been described.<sup>3</sup> Analytical data of the amines II, and IV–X are given in Table 2. Data concerning the amines III, XIII and XIV will be given elsewhere. Radioactive amines II\*, III\*, IV\*, XI\* and XII\* were prepared by using radioactive trichloroacetic acid 2- $C^{14}$  in reaction with the imines (the active acid from Amersham was diluted with the inactive acid). The active hydrochlorides ( $A_1^+ \cdot HCl$ ) were obtained by adding an ether soln of HCl to an ether soln of  $A_1^+$ ; nitrates ( $A_1^+ \cdot HNO_3$ ) by extraction of  $A_1^+$  from ether with 1N  $HNO_3$  and the hydro-

<sup>†</sup> The acceptor-donor interaction in the amines A is indicated also by the spectroscopic data: substituents in aromatic ring Ar influence IR absorption of the halogens in  $CX_3$  group<sup>2</sup>; the second aromatic band in UV is in the amines. A distinctly changed and bathochromically shifted as compared with the amines of the type  $ArCH_2N(CH_2)_3$  similarly substituted (in preparation).

TABLE 2. ANALYTICAL DATA OF SOME A · HCl

Amine	Found			Formula of A · HCl	Requires		
	C	H	N		C	H	N
II	43.4	4.85	4.5	C <sub>12</sub> H <sub>16</sub> NFCl <sub>4</sub>	43.0	4.75	4.2
IV	45.05	5.7	4.4	C <sub>13</sub> H <sub>19</sub> ONCl <sub>4</sub>	44.95	5.5	4.05
V	44.55	5.45	4.2	C <sub>14</sub> H <sub>21</sub> O <sub>2</sub> NCl <sub>4</sub>	44.55	5.55	3.7
VI	44.75	5.55	4.2	C <sub>14</sub> H <sub>21</sub> O <sub>2</sub> NCl <sub>4</sub>	44.55	5.55	3.7
VII	44.85	5.5	4.2	C <sub>14</sub> H <sub>21</sub> O <sub>2</sub> NCl <sub>4</sub>	44.55	5.55	3.7
VIII	47.4	5.65	4.5	C <sub>13</sub> H <sub>19</sub> NCl <sub>4</sub>	47.15	5.75	4.25
IX	51.95	5.3	4.1	C <sub>16</sub> H <sub>19</sub> NCl <sub>4</sub>	52.3	5.15	3.8
X	52.6	5.25	4.2	C <sub>16</sub> H <sub>19</sub> NCl <sub>4</sub>	52.3	5.15	3.8

iodide II\* · HI by adding II\* · HCl in ethanol to a water soln of NaI (the ppt formed was washed with dil HCl and ether).<sup>1</sup>

#### Investigation of the exchange A<sub>1</sub>\* · HD + A<sub>2</sub>

The active salt A<sub>1</sub>\* · HD (100 mg) was added to a soln of inactive amine A<sub>2</sub> (50 mg) in hexadecane (5 ml) and the mixture was stirred by means of a magnetic stirrer. Stirring was stopped after 0.25, 0.5, 1 and 2 hr, about 50 mg of the hexadecane phase was taken, weighed and activity of the sample was measured. After 2 hr, the mixture was left without stirring for a further 22 hr, then it was stirred for 10 min and activity was measured as above. In some experiments activity was measured again after 24 hr. Activity measurement was performed using a scintillation-counter SE-2. As scintillator PBD + POPOP in toluene (7 g + 0.1 g per litre) was used. Specific activity of the free amines A<sub>1</sub>\* was determined (about 5 · 10<sup>4</sup> imp/min per 50 mg soln of 50 mg A<sub>1</sub>\* in 5 ml hexadecane) and activities of the samples taken during exchange experiments were expressed in per cents of the complete exchange (activity of the hexadecane phase corresponding to amounts of A<sub>1</sub>\* equimolar to A<sub>2</sub>). Solubility of A<sub>1</sub>\* · HD in hexadecane alone was measured by mixing 100 mg A<sub>1</sub>\* · HD with 5 ml hexadecane; the mixture was stirred for 30 min and activity of the liquid phase was determined as above and for most A<sub>1</sub>\* · HD was below the activity corresponding to 5% exchange with A<sub>2</sub>.

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