89. *Steric Relations between Ionisation of Aralkyl Chlorides and Dissociation of Anilinium Ions. Part III.**

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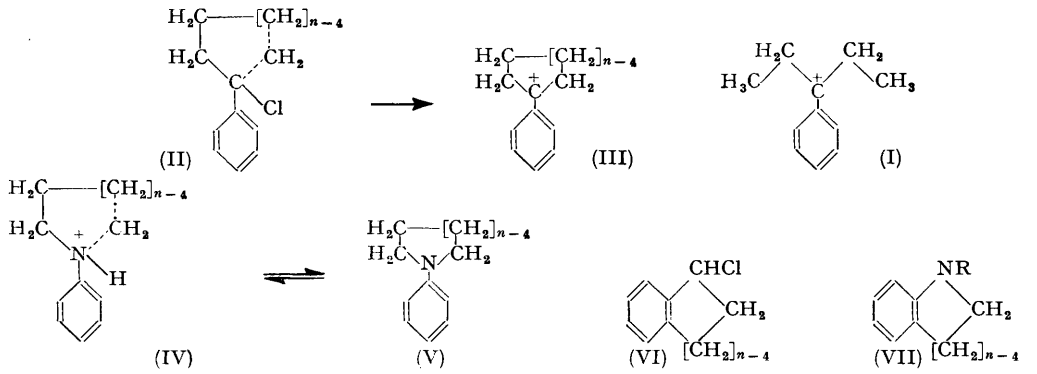
Rates of solvolysis of the chlorides $C_6H_5\cdot\overline{CCl\cdot[CH_2]_{n-1}}$ and their *o*-methyl derivatives in absolute ethanol, where *n* is 5, 6, and 7 severally, and the basic strengths of the corresponding amines $C_6H_5\cdot\overline{N\cdot[CH_2]_{n-1}}$ and their *o*-methyl derivatives in 50% aqueous ethanol have been measured. Reactivity of the chlorides *decreases* in the order $n = 5 > 7 > 6$ and, since this is the order of *increasing* basic strength of the amines, it is argued that this is the order of increasing steric hindrance of ionisation of the chlorides and of dissociation of the anilinium ions.

Reactivity of the chlorides $o\text{-}\overline{C_6H_4\cdot CHCl\cdot[CH_2]_{n-3}}$ *decreases* in the order $n = 5 > 6 > 7$, and our belief [1] that this is the order of increasing steric hindrance of ionisation of the chlorides is now further substantiated by the fact that this is the order of increasing basic strength of the corresponding amines $o\text{-}\overline{C_6H_4\cdot NH\cdot[CH_2]_{n-3}}$ and of their *N*-methyl derivatives.

In Part II,[2] ionisation of the chloride $Ph\cdot CR_2Cl$ and dissociation of the corresponding anilinium ion $Ph\cdot NR_2H^+$ were shown to be more hindered when R is ethyl than when it is a methyl group, and it was suggested that the ethyl group exerts the greater steric effect as a consequence of intramolecular steric interaction of its terminal methyl group and the benzene ring in the benzyl cation (I) and in the free amine $Ph\cdot NEt_2$. If this were so, then enclosure of the ethyl groups in a ring system, as in 1-phenyl*cyclo*pentyl chloride (II; $n = 5$) and 1-phenylpyrrolidine (V; $n = 5$) and the corresponding six- and seven-membered



ring systems (II and V; $n = 6$ and 7), should obviate this effect. The data assembled in Table 2, sets 1 and 2, show that it does: 3-phenyl-3-chloropentane ($Ph\cdot CEt_2Cl$) is the least reactive chloride while *N*-diethylaniline has the greatest basic strength.

Rates of ethanolysis of the 1-phenyl*cyclo*alkyl chlorides (II; $n = 5$, 6, and 7) and the *o*-methyl derivatives of the first two are given in Table 1; those of 2-phenyl-2-chloropropane and 3-phenyl-3-chloropentane are included for comparison; in general, increased reactivity is caused largely by diminution in activation energy (*E*).

The order of reactivity (II; $n = 5 > 7 > 6$) is probably caused by two mutually supporting steric effects. One arises from steric interaction of the aromatic and the alicyclic moieties: the five-membered ring of 1-phenyl*cyclo*pentyl cation (III; $n = 5$)

* Part II, preceding paper.
[1] Baddeley and Chadwick, *J.*, 1951, 368.
[2] Baddeley, Chadwick, and Taylor, preceding paper.

withdraws the α-methylene groups from the *ortho*-positions of the benzene ring and consequently the change of conformation which accompanies ionisation of the chloride (II) (the α-methylene groups are brought into the plane of the benzene ring) provides a smaller increase in steric interaction when n is 5 than when it is 6 or 7. The other steric effect is provided by change in conformation of the alicyclic moiety during the ionisation process: change in co-ordination number of a ring-carbon atom from four to three, as in (II ⟶ III), increases the number and degree of unfavourable conformations, *i.e.*, increases

TABLE 1. *Constants of the Arrhenius equation, $k = Ae^{-E/RT}$, for the formation of hydrogen chloride by ethanolysis of the chlorides.*

		$10^5k_{0\cdot0}$ (sec.$^{-1}$)	$10^5k_{25\cdot0}$ (sec.$^{-1}$)	E (kcal./mole)	$10^{-11}A$ (sec.$^{-1}$)
Ph·CMe$_2$Cl		1·47	34·7	21·4	15
Ph·CEt$_2$Cl		0·0282	1·15	25·3	47
Ph·CCl·[CH$_2$]$_{n-1}$	$n = 5$	108	1445 [a]	17·3	0·37
	$n = 6$	0·160	5·90	23·5	76
	$n = 7$	30·2	724 [b]	20·8	105
o-C$_6$H$_4$Me·CCl·[CH$_2$]$_{n-1}$	$n = 5$	470	—		
	$n = 6$	(1·27—0·89)	(40—24)		

[a] By calculation, using $10^5k_{10\cdot0} = 325$ sec.$^{-1}$. [b] By calculation, using $10^5k_{10\cdot0} = 116$ sec.$^{-1}$.

TABLE 2.

In ethanol

(1)		log $10^7k_{0\cdot0}$
Ph·CMe$_2$Cl		2·17
Ph·CEt$_2$Cl		0·45
Ph·CCl·[CH$_2$]$_{n-1}$	$n = 5$	4·03
	$n = 6$	1·20
	$n = 7$	3·48
o-C$_6$H$_4$Me·CCl·[CH$_2$]$_{n-1}$	$n = 5$	4·67
	$n = 6$	2·1 (*ca.*)

In 50% aqueous ethanol at 20°

(2)		pK_a
Ph·NMe$_2$		4·22
Ph·NEt$_2$		5·71
Ph·N·[CH$_2$]$_{n-1}$	$n = 5$	3·71
	$n = 6$	4·60
	$n = 7$	—
o-C$_6$H$_4$Me·N·[CH$_2$]$_{n-1}$	$n = 5$	4·88
	$n = 6$	5·20

(3)		pK_a
HN·[CH$_2$]$_{n-1}$	$n = 5$	10·37
	$n = 6$	10·14
	$n = 7$	10·30

(4)		pK_a
MeN·[CH$_2$]$_{n-1}$	$n = 5$	9·82
	$n = 6$	9·24
	$n = 7$	9·68

In 80% aqueous ethanol (c is a constant)

(5)		log $ck_{25\cdot0}$
Me·CCl·[CH$_2$]$_{n-1}$	$n = 5$	4·00
	$n = 6$	1·91
	$n = 7$	3·88

intramolecular steric interaction, when the atom is part of a six-membered ring, and has the opposite effect when the ring is five- and, to a less extent, when it is seven-membered.[3] Further, the plane of the benzene ring bisects the H–C–H angle of the α-methylene groups in the cation (III) when $n = 5$, whereas when $n = 6$ the equatorial C–H bonds of these groups are approximately in the plane of the benzene ring where they are best able to provide steric interaction. Similar, though in part smaller, changes in number and degree of unfavourable conformations affect ionisation of 1-methyl*cyclo*alkyl chlorides, and the rates of solvolysis of the 1-phenyl- and 1-methyl-*cyclo*alkyl chlorides (Table 2, sets 1 and 5 respectively) reveal this similarity.

Dissociation of the conjugate acids of the amines listed in sets 3 and 4 of Table 2, unlike the ionisation of the chlorides of set 5, effects little change of conformation (the tetrahedral sp^3 distribution of the electrons of the nitrogen atom is common to the amines and their conjugate acids) and there is no cause for the basic strengths of these amines to vary inversely as the reactivities of the chlorides of set 5. In fact, d log k/d pK_a is positive and thereby affords evidence for an electronic effect whereby accession of electrons to the seat of reaction is greater in the five- than in the seven- and six-membered rings.

On the other hand, dissociation of the conjugate acids of the *N*-phenylamines of Table

[3] H. C. Brown and Borkowski, *J. Amer. Chem. Soc.*, 1952, **74**, 1894; *Ann. Reports*, 1954, **51**, 170.

2, set 2, is expected to involve conformational changes resembling those effected by ionisation of the 1-phenyl*cyclo*alkyl chlorides of set 1 : (*a*) The conjugate acids (IV), being comparatively free from mesomeric phenomena, will prefer those conformations in which the α-methylene groups avoid the plane of the benzene ring whereas these groups must lie near this plane in the amines if these are to enjoy maximum resonance stabilisation. (*b*) The nitrogen atoms of the conjugate acids have a tetrahedral distribution of bonds whereas the free amino-groups are considerably " flattened " by conjugation of nitrogen atom and phenyl group. The resemblance between the conformational changes involved in the two processes, dissociation and ionisation, results in 1-phenylpyrrolidine's having a smaller basic strength than has 1-phenylpiperidine while 1-phenyl*cyclo*pentyl chloride is more reactive than 1-phenyl*cyclo*hexyl chloride.

The 1-*o*-tolyl*cyclo*alkyl chlorides are more reactive than the corresponding 1-phenyl derivatives; the steric effect of the *o*-methyl group is apparently more than neutralised by electronic effects. The negative value of d ln k/d pK_a is evidence for steric hindrance in the reactions of the *o*-tolyl derivatives.

Similarity of conformational change also relates dissociation of the conjugate acids of the benzocyclamines (VII; R = H and Me) and ionisation of the chlorides (VI) where n is 5, 6, and 7 severally. The relevant data are listed in Table 3; those for the chlorides have previously been reported [1] and those for the bases are now provided. d ln k/d pK_a is negative and thereby indicates that both processes are sterically hindered by the conformational changes they incur when $n = 7$ and, to smaller extent, when $n = 6$; such hindrance is absent when $n = 5$ since little change in conformation is then involved.

Knowing the basic strengths of the benzocyclamines we are able to comment on the relative rates of hydrogen exchange between these bases and acidic reagent (see Table 4).

TABLE 3.

	pK_a	Relative [D$^+$]	Hydrogen exchange no.
Dimethylaniline	4·22	6·0	0·12
1-Methylindoline	3·69	20·4	1·58
Tetrahydro-1-methylquinoline	3·86	13·8	0·87
Tetrahydro-1-methylhomoquinoline	4·44	3·6	0·00

TABLE 4. *Relative reactivities of the chlorides in ethanol, and dissociation constants of the amines in* 50% *aqueous ethanol at* 20·0°.

	o-C_6H_4·CHCl·$[CH_2]_{n-3}$	*o*-C_6H_4·NH·$[CH_2]_{n-3}$	*o*-C_6H_4·NMe·$[CH_2]_{n-3}$
n	log $ck_{0·0}$	pK_a	pK_a
5	4·20	4·23	3·69
6	3·63	4·41	3·86
7	1·97	4·82	4·44

The rates, given [4] by dD/dt = k[D$^+$][Amine], decrease in the order $n = 5 > 6 \gg 7$, and W. G. Brown, Widiger, and Letang,[5] assuming that the values of k decrease correspondingly, explained the falls in rate in terms of steric hindrance of conjugation in the transition state; their explanation would be acceptable if the concentrations of the reactants were independent of the value of n, *i.e.*, if the basic strengths of these cyclamines were equal; they are not. Excess of the cyclamines was used and, as a consequence of the effect of the value of n on the magnitude of the conformational changes accompanying dissociation of the conjugate acids of (VII), the relative concentrations (or activities) of acid decreased in the order $n = 5 > 6 > 7$ and, at least in part, were the cause of the differences in the rates of exchange.

Our interpretation of the effect of ring size on the properties of these cyclamines and the analogous cyclic ketones (VII; >CO in place of >NR) was given in a letter [6] and in a paper : [1] Heddon and W. G. Brown,[7] referring only to the letter, say " Nor do they explain why their interpretation of the amine spectra, based upon the steric requirements for

[4] Ingold, Raisin, and Wilson, *J.*, 1936, 1637; Best and Wilson, *J.*, 1938, 28.
[5] W. G. Brown, Widinger, and Letang, *J. Amer. Chem. Soc.*, 1939, **61**, 2597.
[6] Baddeley, Chadwick, and Rawlinson, *Nature*, 1949, **164**, 833.
[7] Heddon and W. G. Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 3744.

hyperconjugation, should not apply equally to the analogous cyclic ketones" and, discussing the absorption spectra of the cyclic ketones, "it appears unnecessary to invoke hyperconjugation, and its dependence upon the orientation of the methylene groups, as these authors have done;" and "Nor is the present series a suitable one for the demonstration of such minor effects since, by varying the ring size, the orientation of the ortho methylene groups cannot be altered without also affecting the orientation of the carbonyl group." It is clear that they believe that we consider the effect of ring size on conjugation in these systems to be determined in some unspecified way by hyperconjugation; we wish to place it on record that their belief is mistaken. Further, in the last paragraph of their discussion they write: "the B-band intensities for $n = 2$ and 3 are substantially higher than, and at $n = 4$ approximately equal to, the intensity of the corresponding transition in acetophenone. This situation is perhaps the basis for the statement of Baddeley, Chadwick and Rawlinson to the effect that it is the compounds with five- and six-membered rings, not the seven-, that are abnormal." Their surmise is wrong, as our letter [6] and our paper [1] in the *Journal* show.

Experimental

Materials.—Chlorides. When 1-phenyl*cyclo*hexyl and 1-phenyl*cyclo*heptyl chloride were obtained from the corresponding alcohols in solution in light petroleum (5 g. in 25 c.c.) by passing in dry hydrogen chloride for 3 hr., their solvolyses gave velocity coefficients which decreased as reaction proceeded; the chlorides were obviously impure and preparation had apparently involved partial isomerisation. This difficulty was overcome by passing hydrogen chloride into *dilute* solutions (5 g. in 500 c.c.) of the alcohols in light petroleum and by having present finely powdered anhydrous calcium chloride (10 g.). The structures of the chlorides were established by hydrolysis and identification of the resulting alcohols. Similar attempts to obtain pure 1-*o*-tolyl*cyclo*hexyl chloride from the corresponding *cyclo*hexanol or from 1-*o*-tolyl*cyclo*hexene failed. The 1-*o*-tolyl*cyclo*hexyl cation, if only as part of an ion pair, is a likely intermediate in the preparation of the chloride, and ready isomeration of the cation can reasonably be attributed to steric hindrance of conjugation and consequent loss of resonance stabilisation.

1-Phenyl- and 1-*o*-tolyl-*cyclo*pentyl chloride were prepared by passing dry hydrogen chloride through 1-phenyl- and 1-*o*-tolyl-*cyclo*pentene at 0° and subsequently removing hydrogen chloride by a stream of dry nitrogen; they contained only 80—90% of the calculated amount of chlorine. 1-*Phenyl*cyclo*hexyl chloride* was prepared from 1-phenyl*cyclo*hexanol: dry hydrogen chloride was passed for 3 hr. through a mixture of this alcohol (5 g.), anhydrous calcium chloride (10 g.), and light petroleum (500 c.c.). The mixture was filtered and calcium chloride was added to the filtrate. After an hour the calcium chloride was separated by filtration and the solvent by evaporation under reduced pressure. The residue contained Cl, 18·2% ($C_{12}H_{15}Cl$ requires Cl, 18·5%). 1-*o*-Tolyl*cyclo*hexyl chloride (together with isomeric material) and 1-phenyl*cyclo*heptyl chloride were similarly obtained and contained 95% and 98% respectively of the calculated amount of chlorine.

1-Phenyl*cyclo*hexyl chloride (2·0 g.) was hydrolysed in 50% aqueous acetone (50 c.c.), the acetone was removed under reduced pressure, the residue was extracted with ether, and the extracts were dried (Na_2SO_4); evaporation of the ether left 1-phenyl*cyclo*hexanol (1·7 g.), m. p. 58—59°, m. p. and mixed m. p. 61—62°, after one recrystallisation from ligroin. Similarly, 1-phenyl*cyclo*heptanol (1·6 g.), m. p. 21—23°, m. p. and mixed m. p. 24—25°, after one recrystallisation from light petroleum, was obtained from 1-phenyl*cyclo*heptyl chloride (2·0 g.).

Addition of *cyclo*hexanone to phenylmagnesium bromide and decomposition of the product with 10% ammonium chloride solution gave 1-phenyl*cyclo*hexanol,[8] b. p. 109—110°/0·4 mm. with slight decomposition, and m. p. 61—62° after recrystallisation from ligroin. 1-Phenyl-*cyclo*heptanol,[9] b. p. 119—120°/0·4 mm. with slight decomposition, and m. p. 24—25° after recrystallisation from light petroleum, was similarly obtained from *cyclo*heptanone. This ketone, b. p. 179—180°/760 mm., was separated from the product of reaction of *cyclo*hexanone with diazomethane [10] as its semicarbazone, m. p. 163—164°. 1-*o*-Tolyl*cyclo*hexanol, b. p. 150—151°/15 mm., was obtained from *o*-tolylmagnesium bromide and *cyclo*hexanone.[11]

[8] Sabatier and Mailhe, *Ann. Chim.* (*France*), 1907, **10**, 546.
[9] Pines, Edeleanu, and Ipatieff, *J. Amer. Chem. Soc.*, 1945, **67**, 2195.
[10] Kohler, Tischler, Potter, and Thompson, *ibid.*, 1939, **61**, 1057.
[11] Sherwood, Short, and Stansfield, *J.*, 1932, 1833.

1-Phenyl*cyclo*pentene (16 g.), b. p. 107—108°/12 mm. (from metallic sodium), m. p. 22—23°, was afforded by stirring 1-phenyl*cyclo*pentanol (20 g.) with 90% formic acid (100 c.c.) for an hour at room temperature. The olefin formed an upper layer which was separated and washed successively with water, dilute aqueous sodium carbonate, and water. 1-Phenyl*cyclo*hexene,[8] b. p. 128—129°/19 mm., 1-phenyl*cyclo*heptene,[9] b. p. 115—116°/10 mm., 1-*o*-*tolyl*cyclo*pentene*, b. p. 116—117°/30 mm. (Found: C, 90·8; H, 8·8. $C_{12}H_{14}$ requires C, 91·1; H 8·9%), and 1-*o*-tolyl*cyclo*hexene,[11] b. p. 136—137°/25 mm., were similarly obtained. Their ultraviolet absorption spectra are given in Table 5.

TABLE 5.

	$\lambda_{max.}$ (Å)	ε		$\lambda_{max.}$ (Å)	ε
1-Phenyl*cyclo*pentene	2540	12,600	1-*o*-Tolyl*cyclo*pentene	2480	9800
1-Phenyl*cyclo*hexene	2480	11,100	1-*o*-Tolyl*cyclo*hexene	2450 *	4000
1-Phenyl*cyclo*heptene	2470	11,500			

* No maximum between 2100 and 3000 Å.

Determination of Rates of Ethanolysis of the Chlorides.—The sampling method described by Hughes, Ingold, and Taher [12] was used. The ethanol was purified in the manner described by Lund and Bjerrum [13] and the chlorides were used immediately after removal of the solvent in which they were prepared. Distillation of the chlorides under reduced pressure caused considerable decomposition and gave distillates containing much less halogen than was required. Before and after distillation each chloride gave rate constants which did not differ by more than the usual experimental error (*ca.* 3%). A flask, fitted with ground-in stopper, was charged with absolute ethanol (150 c.c.) and placed in a thermostat at a selected temperature. After 30 min., sufficient chloride to provide an approximately 0·05M-solution was added and the solution was vigorously shaken. At selected intervals of time samples (10 c.c.) were pipetted into ice-cold acetone (100 c.c.) and titrated with 0·05N-sodium hydroxide with lacmoid as indicator. Solvolysis was allowed to proceed to completion. The rate coefficients were derived from the equation $k = (1/t) \ln (T_\infty - T_0)/(T_\infty - T_t)$, in which the symbols have their usual significance. Each reaction was duplicated at two different temperatures. The parameters of the Arrhenius equation are listed in Table 1.

Amines.—1-Phenylpyrrolidine, b. p. 124—126°/16 mm. (picrate,[14] m. p. 116°), was obtained in 62% yield by reduction of *N*-phenylsuccinimide with lithium aluminium hydride, and 1-phenylpiperidine, b. p. 116—118°/12 mm. (picrate,[15] m. p. 148°), was similarly obtained in 62% yield from *N*-phenylglutarimide. 1-*o*-Tolylpyrrolidine, b. p. 116—118°/10 mm. [*picrate*, m. p. 138° (Found: N, 14·2. $C_{17}H_{18}O_7N_4$ requires N, 14·4%)], and 1-*o*-tolylpiperidine, b. p. 115—116°/10 mm. [*picrate*, m. p. 150° (Found: N, 13·8. $C_{18}H_{20}O_7N_4$ requires N, 13·9%)], were similarly obtained. 1-Methylpyrrolidine, b. p. 77°, was obtained by reduction ($LiAlH_4$) of *N*-methylsuccinimide, and 1-methylpiperidine in the manner described by Clarke, Gillespie, and Weisshaus.[16] 1-Methylaza*cyclo*heptane, b. p. 146° [picrate, m. p. 202° (Found: N, 17·4. Calc. for $C_{13}H_{18}O_7N_4$: N, 17·6%)], was given by reduction ($LiAlH_4$) of *N*-methyl-ε-hexanolactam, the product of methylation of ε-hexanolactam by Hepp's method.[17] Indoline, b. p. 101—102°/13 mm. (picrate,[18] m. p. 175°), was obtained by demethylation of its *N*-methyl derivative [19] (picrate, m. p. 166°), by hydriodic acid and phosphorus. 1 : 2 : 3 : 4-Trtrahydroquinoline, b. p. 248—250°, was afforded by hydrolysis of its benzoyl derivative,[20] m. p. 75°, and its *N*-methyl derivative (picrate, m. p. 144°) by reduction [21] of quinoline methiodide by tin and hydrochloric acid. Tetrahydrohomoquinoline, b. p. 119—121°/11 mm., m. p. 33° (picrate,[22] m. p. 182°), was obtained by reduction ($LiAlH_4$) of homohydrocarbostyril, the product of Beckmann rearrangement of the toluene-*p*-sulphonate of α-tetralone oxime: the sulphonate and the equivalent amount of sodium acetate were dissolved in warm glacial acetic acid, and water was

[12] Hughes, Ingold, and Taher, *J.*, 1940, 949.
[13] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.
[14] Craig and Hixon, *J. Amer. Chem. Soc.*, 1930, **52**, 807.
[15] von Braun, *Ber.*, 1907, **40**, 3920.
[16] Clarke, Gillespie, and Weisshaus, *J. Amer. Chem. Soc.*, 1933, **55**, 4571.
[17] Hepp, *Ber.*, 1877, **10**, 328.
[18] von Braun and Sobecki, *Ber.*, 1911, **44**, 2159.
[19] Koizumi, Komaki, and Titan, *Bull. Chem. Soc. Japan*, 1938 **17**, 645; Wenzing, *Annalen*, 1887, **239**, 239.
[20] von Braun and Stendorff, *Ber.*, 1904, **37**, 4726.
[21] Decker, *Ber.*, 1903, **36**, 2569.
[22] von Braun and Bartsch, *Ber.*, 1912, **45**, 3376.

added until the mixture was turbid; as reaction proceeded the turbidity disappeared and more water was gradually added. The required compound, m. p. 139—140°, separated when the mixture was cooled. Its *N*-methyl derivative was afforded by addition of methyl iodide to the sodio-derivative in toluene and gave tetrahydro-1-methylhomoquinoline, b. p. 116—117°/15 mm. (picrate,[23] m. p. 140°), by reduction ($LiAlH_4$).

Determination of Basic Strengths.—The procedure was similar to that described by Davis and Addis.[24] Solutions of the amines in 50% (by volume) aqueous ethanol at 20·0° were titrated electrometrically with a standard solution of hydrogen chloride in the solvent. The amines were purified *via* their picrates and were redistilled before use. The values of pK_a are accurate within $\pm 0{\cdot}05$ unit.

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[23] von Braun and Seemann, *Ber.*, 1922, **55**, 3824.
[24] Davis and Addis, *J.*, 1937, 1622.