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RACEMIZATION AND RADIO-CHLORIDE EXCHANGE OF p-CHLOROBENZHYDRYL CHLORIDE IN ACETONE[1a]

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IT has been previously reported[2] from these Laboratories that first order racemization rate constants (k_α) of p-chlorobenzhydryl chloride are substantially greater than radio-chloride exchange (k_e) or solvolysis (k_t) rate constants in acetic acid[2a] (D = 6), acetone[2b] (D = 21), and even 80% aqueous acetone[2c] (D = 30). In all three solvents it is necessary to distinguish between ionization and dissociation and to consider explicitly the role of intermediate ion pairs.

In dry acetone, the poorest ionizing[3] of the above-mentioned solvents, we have found our former polarimetric rate constants[2b] to be in error, these being unaccountably high. It is thus necessary to revise our account of the competition between ionization and chloride displacement processes in this solvent. The new data show that either chloride displacement or ionization may be made dominant under suitable conditions in acetone. Ion pair return with racemization, but without radio-chloride exchange, which

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[2a] S. Winstein, J.S. Gall, M. Hojo and S. Smith, J.Amer.Chem.Soc. 82, 1010 (1960); [b] S. Winstein and J.S. Gall, Tetrahedron Letters No. 2, 31 (1960); [c] S. Winstein, M. Hojo and S. Smith, Ibid. No. 22, 12 (1960).

[3] S.G. Smith, A. Fainberg and S. Winstein, J.Amer.Chem.Soc. 83, 618 (1961).

accompanies ionization of p-chlorobenzhydryl chloride, is even more important than was formerly indicated.

In Table 1 are listed representative first order polarimetric and radio-chloride exchange rate constants for p-chlorobenzhydryl chloride in acetone at 75°. The anhydrous acetone solvent, b.p. 56.2°, was reagent grade material treated with Linde Molecular Sieve Type 4A and fractionated.[3] Radio-labeled tetrabutylammonium and lithium chlorides were employed for both polarimetric and exchange kinetic runs. Optically active p-chlorobenzhydryl chloride,[2c] analytically pure, from treatment of active alcohol with hydrogen chloride in pentane at -80°C, was most often used for both racemization and exchange measurements.

In several runs without added salts, active p-chlorobenzhydryl chloride was observed to racemize with satisfactory first order kinetics, the average k_α being[4] $(1.38 \pm 0.05) \times 10^{-6}$ sec^{-1} (Table 1). Racemization rate was increased only slightly by added tetrabutylammonium perchlorate (Bu_4NClO_4), but very greatly by added tetrabutylammonium chloride (Bu_4NCl). At the higher Bu_4NCl concentrations, the (k_α/k_e) ratio is not far from 2, the value first observed by Hughes and his coworkers[5] for several halides whose exchange in acetone occurs with Walden inversion. The (k_α/k_e) ratios and the kinetic form of the racemization and exchange reactions in the presence of substantial concentrations of Bu_4NCl are consistent with predominant attack by chloride ion on covalent RCl or on an intimate ion pair with retained configuration. Treating the exchange reaction as though

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[4] This racemization rate constant is approximately an order of magnitude smaller than the value previously reported.[2b] The former measurements were made with active chloride prepared from the alcohol with thionyl chloride in benzene. The exact cause of the previous high k_α values is not clear.

[5] E.D. Hughes, F. Juliusburger, S. Masterman, B. Topley and J. Weiss, J.Chem.Soc. 1525 (1935); 1173 (1936).

Table 1

Summary of Racemization and Radio-Chloride Exchange

Rates in Acetone at 75.0°

[RCl] 10^2 M	[Salt] 10^3 M	k Values (sec^{-1})		
		$10^6 k_\alpha$	$10^6 k_e$	(k_α/k_e)
9.32		1.34		
9.34		1.34		
9.34		1.45		
13.51	17.36[a]	1.95		
Bu_4NCl^*				
7.65	8.51	34.4	16.16	2.1
7.34	8.51	34.0	16.0	2.1
14.26	5.10	23.5	10.03	2.3
10.56	0.851	4.70		
5.64	0.851		2.14	2.2
6.38	0.166		0.42	(4.8)
$LiCl^*$				
9.15	11.59	3.46	0.830	4.2
7.78	5.80	2.70	0.473	5.7
5.68	1.39	1.82		
8.84	1.39		0.233	7.8
7.38	0.474		0.135	(11)
6.64	0.190	1.50		
9.86	0.190		0.702	21
9.47	0.095		0.053	25

[a] Bu_4NClO_4

it is due entirely to attack by dissociated chloride ion,[6] a satisfactory bimolecular exchange rate constant, k_{2e}, equal to ca. 3×10^{-3} l. $mole^{-1}$ sec^{-1}, is given by the data. At the lowest Bu_4NCl concentration investigated, the (k_α/k_e) ratio is substantially higher than 2, namely 4.8.

Addition of the much less dissociated lithium chloride instead of the tetrabutylammonium salt gives much smaller accelerations of racemization rate. Also, even at the highest LiCl concentrations, the (k_α/k_e) ratios are well above 2, being 4-6 at 0.01-0.005 M salt. As salt concentration is lowered, (k_α/k_e) rises, the value being 25 at ca. 1×10^{-4} M. Estimating chloride ion concentrations from the known dissociation constant for lithium chloride,[6] calculated exchange rates due to the chloride ion displacement process may be obtained with the aid of the k_{2e} value of 3×10^{-3} l. $mole^{-1}$ sec^{-1}. These calculated displacement rates approximate the observed exchange rates even at the lowest salt concentration. Therefore, even at 10^{-4} M salt, most of the exchange reaction may be ascribed to chloride ion displacement. On this basis, the (k_α/k_e) ratio would be much larger than 25, probably at least 10^2, if chloride displacement were not contributing.

The general available evidence suggests that the racemization without exchange involves ionization. For example, the racemization rates display an appropriate solvent sensitivity,[3] the solvent sequence of k_α values at 25° being: 80% acetone, ca. $2 \times 10^4 \simeq$ AcOH, ca. $2 \times 10^4 >$ Me_2CO, 1. Thus, ion pairs from ionization of p-chlorobenzhydryl chloride in acetone lose configuration and return to racemic chloride much more often than they dissociate or exchange their anion partner with external chloride ion.

There is a variety of very recent evidence for benzhydryl derivatives in both hydroxylic and non-hydroxylic solvents demonstrating that racemiza-

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[6] S. Winstein, L.G. Savedoff, S. Smith, I.D.R. Stevens and J.S. Gall, Tetrahedron Letters No. 9, 24 (1960).

tions and isomerizations by way of ion pairs can be much more rapid than accompanying exchanges or solvolyses. Thus, for p-chlorobenzhydryl chloride, (k_α/k_t) is ca. 30 in acetic acid[2a,7] and ca. 3 in 80% acetone.[2c] For $C_6H_5CHClC_6D_5$ and $C_6H_5CDClC_6D_5$, Pocker[8] has recently found that (k_α/k_t) is ca. 3 in 80% acetone, while (k_α/k_e) is ca. 20 and 100 in $MeNO_2$ and liquid SO_2, respectively. He has also ascribed his results to ion pairs which lose their configuration and return to racemic chloride rather than dissociate, solvolyze or exchange anion partners. Isomerization of benzhydryl thiocyanates to isothiocyanates has been reported by Iliceto[9] to occur in acetonitrile more rapidly than exchange with labeled thiocyanate ion. Also, isomerization of benzhydryl thionbenzoates to thiolbenzoates has been observed by Dr. S. Smith[10] to proceed much more rapidly than solvolysis in solvolyzing solvents. Further, O^{18}-labeled benzhydryl p-nitrobenzoate has been found by Professor H. Goering[11] to undergo oxygen scrambling more rapidly than solvolysis in aqueous acetone. The rates of the various racemizations and isomerizations being measured by the different investigators all represent characteristic, but not identical, fractions of the rates of ionization of the various substrates under the prevailing conditions.

It is interesting to contrast the high (k_α/k_e) ratio for p-chlorobenzhydryl chloride in the presence of low LiCl concentrations with the value observed with low concentrations of $HgCl_2$ in acetone.[7] In the presence of this electrophilic catalyst, k_α and k_e are both increased

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[7] A. Ledwith and M. Hojo, unpublished work.

[8] Y. Pocker, Proc.Chem.Soc. 140 (1961).

[9a] A. Iliceto, A. Fava and U. Mazzucato, Tetrahedron Letters No. 11, 27 (1960); [b] A. Iliceto, A. Fava, O. Rossetto and U. Mazzucato, J.Amer. Chem.Soc. in press; [c] A. Iliceto, private communication.

[10] S.G. Smith, private communication.

[11] H. Goering, private communication.

enormously and are linear in $HgCl_2$ concentration. At all salt concentrations investigated at 25°, the (k_α/k_e) ratio is (1.50 ± 0.03). This exact 3:2 ratio of racemization to exchange is in line with an ionization of RCl to $\overset{\oplus}{R}\overset{\ominus}{H}gCl_3$ and regeneration of RCl from an $\overset{\oplus}{R}\overset{\ominus}{H}gCl_3$ pair which has become racemic and has three equivalent chlorine atoms, but is still so constituted that two chlorine atoms are from the original labeled $HgCl_2$ and one is from the RCl. Thus, the $\overset{\ominus}{Hg}Cl_3$ group which donates chloride ion to regenerate covalent RCl has not exchanged chloride with other labeled $HgCl_2$ molecules.