oleacetamide).—1-Methyl-2-chloromethylbenzimidazole (1.8 g., 0.01 mole) in 40 cc. of acetone was mixed with 0.65 g. (0.01 mole) of potassium cyanide dissolved in the least amount of water. The mixture was gently refluxed for six hours, filtered and the filtrate evaporated. The residue was treated with water and filtered. The crude product was recrystallized from acetone-water, with the aid of Darco; yield. 80%; m. p. 239–240°.

Anal. Calcd. for $C_{10}H_{11}ON_3$: C, 63.47; H, 5.86; N, 22.21. Found: C, 63.24; H, 5.73; N, 22.08.

Summary

1. The following 2-α-chloroalkylbenzimidazoles have been prepared: 2-chloromethylbenzimidazole, 2-(α-chloroethyl)-benzimidazole, 2-(α-chloro-*n*-propyl)-benzimidazole (NC), 2-(α-chloroisopropyl)-benzimidazole (NC), 1-methyl-2-chloromethylbenzimidazole (NC), and 1-methyl-2-(α-chloroethyl)-benzimidazole (NC).

2. The labilizing effect of the benzimidazole nucleus on the chlorine atom in the above 2-α-chloroalkylbenzimidazoles has been studied. The results indicate that these halides are more active than the usual allyl halide type.

3. During the course of the investigation, the following new compounds were prepared: 2-ethoxymethylbenzimidazole, 2-(α-hydroxyisopropyl)-benzimidazole, 2-(α-hydroxy-*n*-propyl)-benzimidazole, 1-methyl-2-(α-hydroxyethyl)-benzimidazole, 2-iodomethylbenzimidazole, dibenzamido-(1,2-a,1′,2′-d)-piperazine, 2-(α-ethoxyisopropyl)-benzimidazole and 1-methyl-2-benzimidazoleacetamide.

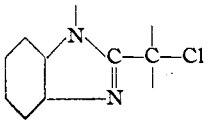
PHILADELPHIA, PA. RECEIVED MARCH 16, 1943

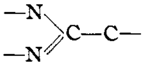
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Reaction of Some 2-(α-Chloroalkyl)-benzimidazoles with Potassium Iodide in Acetone Solution[1]

BY HERMAN SKOLNIK,[2] ALLAN R. DAY AND JOHN G. MILLER

The reaction of organic chlorides with potassium iodide in acetone solution, RCl + KI → RI + KCl, has been used frequently as a means of correlating the structures and reactivities of the chlorides.[3] This paper reports such a study applied to a series of 2-(α-chloroalkyl)-benzimidazoles whose preparation is described in a previous paper.[4] The series of six compounds was chosen to allow a thorough test of the labilizing influence of the benzimidazole grouping upon the chlorine atom situated as shown in the following skeleton common to the series



Despite unexpected complications met in the rate measurements, the results of this study show that the benzimidazole grouping in these compounds strongly enhances the reactivity of the chlorine, the  configuration in these compounds being the predominant activating structure discernible.

Experimental

Rate Measurements.—At the start of this work an attempt was made to follow the rates of reaction by measuring the fall in electrical conductance of the reaction system caused by the precipitation of the potassium chloride. This effort was abandoned because the specific rates measured in this way were very erratic, probably due to supersaturation.

The analytical method developed by Conant and co-workers[3a] was finally used. This method measures the extent of reaction by determining the amount of unreacted potassium iodide by titration with potassium iodate in cold hydrochloric acid solution. Chloroform is used as indicator, disappearance of color in the chloroform marking the end-point. Attempts to use other analytical methods failed. The procedure developed by Kolthoff, Laitinen and Lingane,[5] based on the iodoacetone method of Berg[6] employing

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(1) Presented at the Detroit Meeting of the American Chemical Society in April, 1943.

(2) Present address, Hercules Powder Company, Wilmington, Del.

(3) See, for example: (a) Conant and Kirner, THIS JOURNAL, **46**, 246 (1924); Conant and Hussey, *ibid.*, **47**, 476 (1925); Conant, Kirner and Hussey, *ibid.*, **47**, 488 (1925); (b) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, New York, N. Y., 1940, pp. 152–156, 208.

(4) Skolnik, Miller and Day, THIS JOURNAL, **65**, 1854 (1943).

(5) Kolthoff, Laitinen and Lingane, THIS JOURNAL, **59**, 429 (1937).

(6) Berg, *Z. anal. Chem.*, **69**, 369 (1926).

potassium permanganate, yielded poor results because the oxidant had a strong tendency to react with the organic iodide present. The same difficulty was encountered with the method of Lewis.[7] The method of Smith and Wilcox[8] using amaranth as internal indicator was investigated and found unsatisfactory. An original method was considered employing ferric iron as oxidant, and titrating the resultant ferrous iron with permanganate. This was discarded because of the slowness of the reaction.

In following the Conant procedure, each sample was put up in a separate ampoule. All reactions were run in a thermostat at 25 ± 0.01°. The specific rates, k, were calculated by means of the equation for bimolecular reactions such as studied here

$$k = \frac{2.303}{tb(n - 1)} \log_{10} \frac{n - z}{n(1 - z)}$$

where b was the initial molarity of potassium iodide, z the fraction of the iodide which has reacted in t hours, and n the molecular proportion of organic chloride to potassium iodide. Where equivalent concentrations of chloride and iodide were used, k was calculated by the alternate bimolecular formula

$$k = \frac{z}{tb(1 - z)}.$$

The values of k calculated by these equations were in excellent agreement for any run in which the initial concentrations were fixed, as is seen from the data in Table I, which shows a sample run.

TABLE I

THE RATE OF REACTION OF 2-CHLOROMETHYLBENZIMIDAZOLE AND POTASSIUM IODIDE IN ACETONE AT 25°

Initial molarity of potassium iodide, 0.01997; of 2-chloromethylbenzimidazole, 0.009987; initial titer of potassium iodide, 20.09 ml.; $n = 0.500$.

Time, minutes	Titer	z	k
5	17.95	0.1065	152.3
10	16.45	.1812	150.3
15	15.40	.2334	145.5
20	14.45	.2807	148.7
25	13.70	.3181	151.0
30	13.20	.3430	147.9
35	12.75	.3654	147.3

Mean k = 149.0 liter mole^{-1} hour^{-1}; probable error, ±0.60.

The probable error of the mean value of k obtained for this run is typical of the mean specific rates listed in this paper, more than two-thirds showing probable errors lower than 1% and only one-tenth errors greater than 2%, no error being greater than 4%. As noted in the tables, most of the specific rates are such mean values, only a few being values for single samples. Five-sixths of the runs included samples which reacted well over the half-time of the reactions. Separate tests showed that the reaction proceeds to completion. The organic iodides were quite stable unless heated or kept in prolonged contact with water.

Chemicals.—The 2-(α-chloroalkyl)-benzimidazoles were prepared and purified as described in the previous paper.[4] Allyl chloride, benzyl chloride, benzene and nitrobenzene were purified by distillation. To prepare the acetone, a pure grade conforming to A. C. S. specifications was refluxed from four to eight hours with lime and potassium permanganate, and distilled through a Vigreux column. The portion boiling at 56.5 to 57.0° was collected in a receiver protected from moisture in the atmosphere. The potassium iodide and potassium iodate were of analytical grade, dried carefully at 110°.

Results

Table II presents the specific rates of the reactions of the 2-(α-chloroalkyl)-benzimidazoles and of benzyl and allyl chlorides with potassium iodide in pure dry acetone at different initial concentrations and molecular ratios of chloride to iodide. The low solubility of the benzimidazoles in acetone was an important factor in the choice of the concentrations used.

TABLE II

THE BIMOLECULAR SPECIFIC RATES IN PURE ACETONE

KI molarity	RCl molarity	Total molarity	k
2-Chloromethylbenzimidazole			
0.02034	0.10169	0.12203	29.76
.02042	.05105	.07147	58.96
.02017	.02017	.04034	97.44
.02015	.01000	.03015	148.9
.01997	.009987	.02996	149.0
.02715	.00500	.03215	233.6
.007659	.00500	.01266	274.1
.01470	.00500	.01970	338.8
.01916	.00500	.02416	389.5
1-Methyl-2-chloromethylbenzimidazole			
.01997	.01997	.03994	250.0
.009987	.02497	.03496	907.5
.01997	.009987	.02996	2506
2-(α-Chloroethyl)-benzimidazole			
.01987	.04967	.06954	44.12
.01997	.01997	.03994	91.50
.01974	.009868	.02961	137.3
.01000	.02500	.03500	163.7

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[7] Lewis, *Ind. Eng. Chem., Anal. Ed.*, **8**, 199 (1936).

[8] Smith and Wilcox, *ibid.*, **14**, 49 (1942).

TABLE II (*Concluded*)

KI molarity	RCl molarity	Total molarity	*k*
1-Methyl-2-(α-chloroethyl)-benzimidazole			
0.01916	0.03832	0.05748	43.06
.01939	.02909	.04848	59.39
.021127	.021127	.04225	194.0
.01000	.02500	.03500	541.3
.02112	.01056	.03168	708.6
.01907	.00477	.02384	825.9
2-(α-Chloro-*n*-propyl)-benzimidazole			
.02115	.03000	.05115	45.55
.01907	.01600	.03507	134.3
.02115	.01600	.03715	176.7
.02113	.02113	.04226	204.6
.01000	.02500	.03500	205.5
.01804	.04000	.05804	261.0
.02113	.01056	.03169	335.9
2-(α-Chloroisopropyl)-benzimidazole			
.02113	.02113	.04226	235.4
.01000	.02500	.03500	869.7
.02113	.01056	.03169	1533
Allyl chloride			
.0203	.1015	.1218	1.14
.021127	.021127	.04125	10.11
Benzyl chloride			
.02614	.1600	.1861	2.07
.04506	.2319	.2770	2.14
.04193	.2096	.2515	2.25^a
.03333	.1666	.1999	2.26^a
.02119	.2119	.2331	2.44
.03229	.0765	.1088	2.62
.02042	.1021	.1225	2.95
.03541	.0604	.09581	3.86
.02500	.1250	.1500	3.92^a
.05889	.05889	.1178	4.06^a
.03928	.0786	.1179	4.69^a
.02000	.1000	.1200	5.09^a
.01667	.0833	.1000	6.49^a
.01429	.0715	.08579	7.75^a
.02944	.0883	.1174	8.86^a
.01250	.0625	.0750	9.13^a
.01963	.0982	.1178	9.46^a
.02356	.0942	.1178	9.51^a
.00444	.0222	.02664	42.15^a

[a] These *k* values were determined by measurement of one sample only.

When the effect of change in initial concentrations upon the specific rates for the benzimidazoles was noticed, allyl and benzyl chlorides were studied because a search of the literature showed that no thorough test for the possible existence of this effect had been made by others studying this reaction. It is seen that here, too, the specific rates are sensitive to change in the initial concentration of the potassium iodide and of the organic chloride.

Although the behavior is irregular, the values of *k* generally increase as the total molarity is lowered, the effect being most pronounced in dilute solution. It is to be noted that in the case of benzyl chloride the *k* values are relatively insensitive to concentration change when the total molarity is greater than 0.125.

Following these results, it was decided to test the effect of addition of varying amounts of different solvents to the reaction system. Water, nitrobenzene, and benzene were used. The results of these experiments are shown in Table III. In these experiments no decomposition of the organic iodide was observed.

TABLE III

THE EFFECT OF ADDITION OF WATER, NITROBENZENE AND BENZENE

KI molarity	RCl molarity	H_2O weight per cent.	*k*
Water (using benzyl chloride)			
0.04539	0.2320	0.09	1.89
.04635	.2319	.09	1.87^a
.04891	.1419	.91	1.73^a
.04857	.1409	1.79	1.54^a
.04570	.2286	1.87	1.46
.04651	.1550	1.94	1.60^a
.04055	.2028	15.90	0.891
.04643	.2319	21.90	0.847
Water (using 2-chloromethylbenzimidazole)			
.02000	.01000	0.50	139.6
.02000	.01000	1.52	81.5
.02000	.01000	6.24	48.05
.02000	.01000	12.28	37.40
.02000	.01000	23.76	37.25
.02000	.01000	34.82	36.03
		Nitrobenzene, wt. %	
Nitrobenzene (using benzyl chloride)			
.03753	.06359	4.31	2.45
Nitrobenzene (using 2-chloromethylbenzimidazole)			
.02022	.01000	0.62	114.6
.02022	.01000	1.85	69.13
.02022	.01000	7.47	37.71
.02022	.01000	14.58	26.55
.02026	.01000	27.74	21.36
		Benzene, wt. %	
Benzene (using 2-chloromethylbenzimidazole)			
.02026	.01000	0.44	198.0
.02026	.01000	1.33	226.3
.02015	.01000	5.55	231.6
.02015	.01000	11.04	228.3

[a] Single sample values.

Addition of water or nitrobenzene lowers the value of *k*, small amounts of these substances having relatively greater effect than large amounts. Addition of benzene, on the other hand, raises the value of *k*.

Discussion

The effect of the concentration of the reactants upon the specific rate of the reactions studied in this paper was unanticipated. Van Duin[9] suggested the possible presence of such an effect, but the magnitude was such as to be considered negligible. Indeed, at the outset of the present study, the literature dealing with this reaction indicated no concentration effect. This situation probably resulted because the concentrations used by the workers in this field have been relatively high, lying in the range in which the specific rates vary little with concentration.

Since the reaction is apparently one between a neutral molecule and an ion, little salt effect is to be expected. This is also suggested by the fact that although potassium chloride leaves the system as the reaction progresses, the specific rates are not affected by this lowering of the ionic strength. Indeed, Conant showed that the use of lithium iodide instead of potassium iodide causes no change in the values of the specific rates, although lithium chloride is soluble and thereby maintains a constant ionic strength in the medium.

The effect of the organic chloride concentration may be due in part to increase in the dielectric constant of the medium with increase in concentration of the organic chloride. In general, the greater the dielectric constant of the medium, the lower the specific rate of such reactions. When nitrobenzene or water is added to acetone the dielectric constant increases[10] since these substances have higher dielectric constants than acetone. It was noted that addition of nitrobenzene or water decreased the rate of reaction. Furthermore, addition of benzene which has a lower dielectric constant than acetone increased the specific rate. Unfortunately, this explanation of the organic chloride concentration effect encounters the difficulty that benzyl and allyl chlorides probably lower rather than raise the dielectric constant of acetone solutions.

It is interesting that complex concentration effects have been noted in the study of the displacement reaction between organic iodides and iodide ion in acetone solution.[11] The effect of change in dielectric constant has been found the same as that noticed in this work.

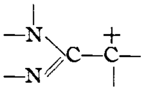
It is possible that the effects discussed here as concentration effects are due partly to the solvent, acetone. If the acetone interferes with the titration procedure its effect will be greatest in the dilute solutions. Careful search of the literature has revealed no mention of such interference and the constancy of the specific rates obtained in each run is argument against its presence in this work. Further investigation of the problem is in progress in this Laboratory.

Despite the unanticipated complications met in this study, the results obtained are of considerable interest to the original project. It has been demonstrated that the benzimidazole grouping is a highly activating one. Thus, no discernible decrease in the high reactivity results from substitution of alkyl groups for α-hydrogen although such substitution usually decreases the rate of reactions of this type.[3b]

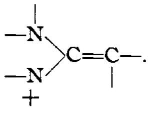
Branch and Calvin[12] have treated the effect of resonance in the group B in a nucleophilic displacement reaction such as studied in this paper.

$$\mathrm{A{:}B} + \mathrm{{:}C} \longrightarrow \mathrm{A{:}} + \mathrm{B{:}C}$$

They point out that the greater the resonance in B itself as compared to A:B the lower the energy of the transition state in which A: and :C are both weakly attached to B, and hence the more rapid the reaction. Thus, any structural features in B which stabilize the free group by resonance will tend to increase the reactivity of A:B in these displacement reactions. This explains the high reactivity of compounds such as the benzimidazoles in which the chlorine is attached to a carbon alpha to a double bond. In the case of the benzimidazoles, the transition state is probably stabilized by resonance between such structures as



and



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Summary

1. The reaction of 2-(α-chloroalkyl)-benzimidazoles with potassium iodide in acetone solution is a bimolecular nucleophilic displacement reaction which proceeds readily to completion. The specific rate in dilute solution is markedly affected by the concentration of the reactants and is

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[9] Van Duin, THIS JOURNAL, 47, 585 (1925); Conant, Kirner and Hussey, *ibid.*, 47, 587 (1925).

[10] Graffunder and Heymann, *Z. Physik*, 72, 744 (1931).

[11] Bergmann, Polanyi and Szabo, *Z. physik. Chem.*, B20, 161 (1933); Hughes, Juliusburger, Masterman, Topley and Weiss, *J. Chem. Soc.* 1525 (1935).

[12] Branch and Calvin, "The Theory of Organic Chemistry" Prentice-Hall, Inc., New York, N. Y., 1941, pp. 434-438.

lowered by increase in the dielectric constant of the medium.

2. The benzimidazoles studied are very reactive. The reactivity is apparently due to the benzimidazole grouping, being little affected by the alkyl groups attached to the carbon atom bearing the chlorine.

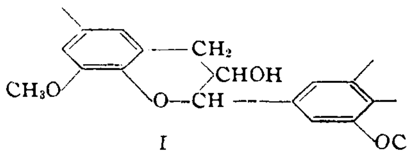
PHILADELPHIA, PA. RECEIVED MARCH 16, 1943

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, McGILL UNIVERSITY]

Studies on Lignin and Related Compounds. LXXII. The Ultraviolet Absorption Spectra of Compounds Related to Lignin

BY R. F. PATTERSON AND HAROLD HIBBERT

The use of ultraviolet absorption spectroscopy for the examination of lignins and related compounds is by no means a new approach to the study of lignin structure. Herzog and Hillmer[1] were the first investigators in this field. From the absorption spectra of a large number of lignins and simple compounds they concluded that lignin is derived from units consisting of partly or wholly etherified di- or trihydroxy phenols having side chains of about three carbon atoms containing neither carbonyl nor unsaturated linkages in conjugation with the benzene ring. They also noted a consistent difference in the position of the absorption maxima for lignins isolated from hardwoods and softwoods. Hägglund and Klingstedt[2] and Stamm, Semb and Harris[3] have also reported a difference between the curves of hardwood and softwood lignins, the latter workers placing the absorption maximum at 2740–2760 Å. for hardwoods and at 2800–2870 Å. for softwoods. Other absorption curves for lignins, reported by Goslawski and Marchlewski,[4] include those of methanol, ethanol, isobutylcarbinol and alkali lignins in ethanol and alkali solution. Maxima range from 2795 to 2835 Å. and the different curves have the same general shape in spite of the different extraction methods used. Glading[5] has recently determined the absorption spectra of spruce "native" lignin, lignins isolated by the use of phenol, glycol, thiophenol, alkali, etc., and various lignin derivatives, all of which show the same characteristic absorption band at approximately 2800 Å. This author also reports the absorption curves for benzalacetophenone, piperonalacetophenone, 2-hydroxychalcone, flavanone, quercetin, guaiacol and benzalacetone and by comparison with these known compounds he concludes that the spectrum of "native" lignin can be explained by the assumption that each building unit (mol. wt. 840) contains two pyran rings such as that present in I. The absorption spectrum of flavanone, on which this argument is largely based, has a maximum at 2530 Å. and it is assumed by Glading that polymerization to a compound having a molecular weight as great as that of lignin would produce a bathochromic shift of the absorption band to 2800 Å., this conception being based on the fact that a shift to longer wave lengths is observed when isoeugenol is polymerized to the dimer. This assumption does not seem to be justified by recent work on styrene[6] in which it was found that a shift of the absorption bands to *shorter* wave lengths occurred on polymerization.



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All of these investigators used amorphous lignins—water-insoluble materials of relatively high molecular weight—and in most cases a direct comparison has been made with simple monomolecular model substances. Herzog and Hillmer[1] compared their lignin curves with those of such compounds as eugenol, isoeugenol and isosafrole which are compounds related to those isolated as degradation products of lignin. Glading has used a different approach by tentatively accepting one of Freudenberg's suggested lignin formulas and comparing it with the most closely related compounds available.

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(1) Herzog and Hillmer, *Z. physiol. Chem.*, **168**, 117 (1927).

(2) Hägglund and Klingstedt, *Svensk. Kem. Tid.*, **41**, 185 (1929); *Z. physik. Chem.*, **152**, 295 (1931).

(3) Stamm, Semb and Harris, *J. Phys. Chem.*, **36**, 1574 (1932).

(4) Goslawski and Marchlewski, *Bull. intern. acad. polon. sci., Classe sci. math. nat.*, **1934A**, p. 261.

(5) Glading, *Paper Trade J.*, **111**, 288 (1940).

(6) Owens, *Ind. Eng. Chem.*, **11**, 643 (1939).