contains water of crystallization which is lost on more vigorous treatment.[12] Recrystallization of this compound must be performed with care.[13]

Anal. Calcd. for $C_8H_6O_2N_2 + 2H_2O$: C, 48.50; H, 5.01; N, 14.14. Found: C, 48.70; H, 5.32; N, 14.01.

For isotope experiments, III is heated to its m.p. and yields carbon dioxide and benzimidazole.[14] The carbon dioxide originates from the methyl carbon atom of the acetic acid molecule while the benzimidazole nucleus contains the carboxyl carbon atom.[15] It has been possible to perform the entire degradation starting with 11 mg. of 2-methylbenzimidazole, although in this case difficulty was experienced in isolating the pure benzimidazole.

Degradation of 2-(α-Hydroxyethyl)-benzimidazole (V).—The lactobenzimidazole isolated as described above is oxidized with potassium permanganate to III. A solution of 2.90 g. of potassium permanganate in 100 ml. of boiling water is added *all at once* to a boiling solution of 810 mg. of V and 200 mg. of sodium carbonate in 50 ml. of water. The mixture is boiled for 3 minutes and is placed on the steam-bath for 30 minutes. After the addition of small amounts of ethanol and Norit A, filtration, and adjustment to *p*H 6 with acetic acid, the colorless solution is placed in the refrigerator. After 2 days, 675 mg. of colorless needles is deposited, m.p. 174°. In other experiments, oxidation of 102 mg. and 41 mg. of V yielded 72 and 25 mg. of III, respectively. Decomposition of III as described above yields carbon dioxide (C-2 of lactic acid) and benzimidazole (contains C-1 of lactic acid).

The methyl carbon atom of lactic acid is obtained by treating V with sodium hypoiodite under the standard conditions[16] used for hydroxyethyl groups. The reaction is performed at 60° for 30 minutes and 54 mg. of V yields 22 mg. of iodoform, m.p. 117–119°. The iodoform is purified before combustion.

Isotope Experiments.—The validity of the degradation procedures was tested by degradation of benzimidazole derivatives of isotopic acetic and lactic acids. Standard techniques[6] were used to prepare 1-C^{14}-acetic acid. Group A streptococcus grown[1] in the presence of 1-C^{14}-glucose was used to produce 2-C^{14}-acetic acid and 3-C^{14}-lactic acid.[17] It is clear that in the case of the biosynthetic acids, it is possible that carbon atoms other than those indicated may contain isotope. Under these conditions, radioactivity will be obtained during the course of the degradation procedure where none is predicted. It is to be noted, however, that interpretation is always made that such results are due to the errors of the method (mixing of carbon atoms, etc.) rather than to isotope impurity of the starting material. The error of the method, as determined by these techniques, must therefore be considered the maximum error. All samples were plated as barium carbonate after combustion according to an accepted technique.[18] The activities reported have all been corrected to "infinite thickness" and are reported as counts per minute. Counting was performed using a windowless counter and "Q" gas. Table I gives the results obtained with isotopic acetic acid and Table II—with lactic acid.

The results obtained indicate that the *maximum* possible contamination of the methyl carbon atom by the carboxyl carbon atom in the case of the synthetic acetic acid is less than 0.02%, on the assumption that 1 count per minute above background is detectable. When biosynthetic acetic acid is used, and the assumption made that all of the isotope in the acid is present in the methyl carbon atom, it is possible to set an upper limit for mixing of carbon atoms during the degradation procedure at 0.37%. Calculations of this type (Table II) for the lactic acid derivatives indicate that the possible errors are of the same order of magnitude as those obtained with acetic acid. Within this range, therefore, the degradation procedure is considered valid.

TABLE I

DEGRADATION OF ISOTOPIC 2-METHYLBENZIMIDAZOLE

Starting material		$CH_3C^{14}O_2H$[a]	$C^{14}H_3C^{?}O_2H$[b]
Benzimidazole (C-1 of acetic acid)	c.p.m.	601	5
	× 7[c]	4207	35
CO_2 (C-2 of acetic acid), c.p.m.		0	9485
Max. possible contamination of C-2 by C-1	c.p.m. ratio	0–1/4207	
	%	0.02	
Max. possible contamination of C-1 by C-2	c.p.m. ratio		35/9485
	%		0.37

[a] Synthetic acetate; the isolated 2-methylbenzimidazole activity was 551. [b] Bacterial product[1] after metabolism of 1-C^{14}-glucose. The isolated 2-methylbenzimidazole activity was 1,280 (× 8 = 10,240). [c] The benzimidazole activity is multiplied by 7 to correct for the dilution of C-1 of acetic acid by the carbon atoms in the benzene ring. The value 4207 compares satisfactorily with 4408 (551 × 8)—the corrected activity of the synthetic 2-methylbenzimidazole.

TABLE II

DEGRADATION OF ISOTOPIC 2-(α-HYDROXYETHYL)-BENZIMIDAZOLE

Starting material		$CH_3C^{14}HOHCO_2H$[a]	$C^{14}H_3C^{?}HOHC^{?}O_2H$[b]
Benzimidazole (C-1 of lactic acid)	c.p.m.	0	2
	× 7[c]	0	14
CO_2 (C-2 of lactic acid), c.p.m.		339	9
CHI_3 (C-3 of lactic acid), c.p.m.		0	13,200
Max. possible contamination of C-3 or C-1 by C-2	c.p.m. ratio	0–1/339	
	%	0.3	
C-1 or C-2 by C-3	c.p.m. ratio		14/13,200
	%		0.11

[a] Synthetic lactic acid. The activity of the lactobenzimidazole was 38 c.p.m. [b] Bacterial product[1] obtained after metabolism of 1-C^{14}-glucose. The isolated lactobenzimidazole activity was 1,437 c.p.m. (× 9 = 12,930). [c] The benzimidazole activity is multiplied by 7 to correct for dilution of C-1 of lactic acid by the carbon atoms in the benzene ring. The activity of C-2 of the synthetic lacto-benzimidazole (339) compares satisfactorily with the corrected activity of the whole molecule, 342 (38 × 9).

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Activities of Aqueous Magnesium and Barium Acetate Solutions at 25°

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The measurements reported here were made in 1947 as part of a proposed study (since abandoned

from lack of time) of a number of bivalent metal acetates in aqueous solution.

Experimental

Barium acetate of analytical reagent quality was made into a stock solution which was analyzed by evaporating suitable portions with excess sulfuric acid and weighing the dry barium sulfate. Magnesium acetate was prepared by dissolving the calculated amount of pure MgO (calcined at 900°) in an acetic acid solution of known concentration. These solutions were equilibrated against sodium chloride solutions in an isopiestic vapor pressure apparatus of the usual pattern.[1] The molalities of the pairs of isopiestic solutions are given in Table I. Table II gives the molal-scale osmotic coefficients $\phi = -55.51/3m \ln (p/p_0)$ and activity coefficients γ. There is some difficulty in estimating the value to be assigned to γ at 0.1 m owing to the form of the osmotic coefficient curves; ϕ evidently has a minimum somewhere below the experimental range and then turns sharply upward to reach the value unity at zero concentration. The value $\gamma_{0.1m} = 0.450$ has been rather arbitrarily assigned to both salts from a comparison with some other 2:1 electrolytes; the remaining values are correct relative to these, but the absolute values could well be as much as 5% different.

TABLE I

MOLALITIES OF ISOPIESTIC SOLUTIONS AT 25°

m_1 = molality of acetate solution, m_2 = molality of sodium chloride solution

m_1	m_2	m_1	m_2	m_1	m_2
Barium acetate					
0.1073	0.1384	0.6496	0.8926	1.870	2.454
.1510	.1964	1.087	1.493	2.062	2.649
.1902	.2500	1.283	1.755	2.822	3.332
.2593	.3434	1.464	1.973	3.474	3.812
.5045	.6880	1.667	2.220		
Magnesium acetate					
0.1431	0.1847	0.8053	1.337	2.205	3.173
.2013	.2597	.9605	1.355	2.748	3.994
.2503	.3245	1.053	1.443	3.300	4.794
.3799	.4930	1.259	1.740	4.149	5.984
.4286	.5588	1.728	2.439		

TABLE II

OSMOTIC AND ACTIVITY COEFFICIENTS OF BARIUM AND MAGNESIUM ACETATES AT 25°

	$BaAc_2$		$MgAc_2$	
m	ϕ	γ	ϕ	γ
0.1	0.800	(0.450)	(0.797)	(0.450)
.2	.807	.395	.793	.389
.3	.817	.370	.795	.359
.5	.841	.347	.807	.328
.7	.857	.335	.826	.314
1.0	.873	.325	.861	.307
1.2	.881	.320	.886	.308
1.4	.884	.315	.910	.310
1.6	.885	.311	.935	.315
1.8	.884	.306	.961	.321
2.0	.878	.301	.987	.329
2.5	.856	.286	1.049	.351
3.0	.832	.271	1.109	.378
3.5	.804	.256	1.159	.406
4.0			1.207	.436

The relative positions of the osmotic coefficient curves are noteworthy. At low concentrations that for barium acetate is slightly the higher, in contrast to the nitrates and halides where the magnesium salts have the higher osmotic coefficients. A similar reversal has been remarked with the alkali metal acetates.[2] Potassium acetate for example, has a higher osmotic coefficient than lithium acetate, though that of potassium chloride is lower than that of lithium chloride. This effect has been tentatively explained by Robinson and Harned[2] in terms of a "localized hydrolysis" resulting from interaction of a proton from the hydration sheath of the Li^+ ion with the acetate ion, the effect being most marked with the most strongly hydrated cation. A similar effect would appear to be operating in the present case. Above 1 M however the position is different; the osmotic coefficient of magnesium acetate continues to rise, while that of barium acetate passes through a maximum. It seems likely that here we have the effect of Bjerrum ion association dominating the osmotic coefficients; the heavily hydrated magnesium ion is larger than the less hydrated barium ion, and hence shows less tendency to form ion pairs. The behavior of these two salts thus provides a striking example of the complexities which may be encountered in moderately concentrated electrolytes, and which can be qualitatively explained by considerations of ion–ion and ion–solvent interactions.

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The Configurations of the 3-Bromocyclohexanecarboxylic Acids[1]

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The configurations of the 3-bromocyclohexanecarboxylic acids were originally assigned by Perkin[3] on the basis of their mode of formation. The reaction of the lactone I with aqueous hydrobromic acid at room temperature yields a bromo acid, m.p. 65°, which was named *cis*-3-bromocyclohexanecarboxylic acid. Either *cis*- or *trans*-3-hydroxycyclohexanecarboxylic acid (III and IV) reacts with aqueous hydrobromic acid at 100° to yield a mixture from which a higher melting acid, m.p. 167–168°, is isolated and is labeled *trans*.[3] However, current theory suggests that these conversions are displacement reactions which proceed with the inversion of the configuration of the carbon atom under attack, although inversion may be accompanied by varying degrees of racemization.[4] Consequently the designated configurations of the 3-bromo acids are probably inverted. The more probable configurational relationships are diagrammed below.

Furthermore, a neutralized alcoholic solution of the bromo acid, m.p. 67–68°, decomposes in a few minutes at the reflux temperature to yield the lactone I, whereas the higher melting acid is stable under the same conditions.[5] Only the latter acid forms a stable benzylammonium salt. These phenomena clearly demonstrate the participation of the carboxylate group in the decomposition of the salt of the lower melting bromo acid and therefore, in this acid, the carboxylate group must be *trans* to the bromo group, a configuration which permits the carboxylate group to displace the latter in a

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