trated and distilled. Acetic anhydride, 0.5 g. (49%), b.p. 136–137°, and tri-*n*-butylphosphine oxide, 1.9 g. (86%), b.p. 123–125° (0.2 mm.), were obtained.

Reaction of Phenylmercuric Acetate with Tri-*n*-Butylphosphine and Acetic Acid.—A mixture of phenylmercuric acetate (6.7 g., 0.02 mole), tri-*n*-butylphosphine (4.0 g., 0.02 mole), and glacial acetic acid (1.3 g., 0.02 mole) was heated with stirring at 65° for 2 hr. Mercury (3.4 g., 86%) was separated and the filtrate was distilled. Benzene, 1.4 g. (90%), b.p. 80–82°, acetic anhydride,[5] 1.63 g. (82 × 2%), b.p. 70–72° (92 mm.), and tri-*n*-butylphosphine oxide, 3.8 g. (94%), b.p. 123–125° (0.2 mm.), were obtained.

Reaction of Diphenylmercury and Tri-*n*-Butylphosphine with Acetic Acid.—A solution of diphenylmercury (5.3 g., 0.015 mole), tri-*n*-butylphosphine (3.0 g., 0.015 mole), and glacial acetic acid (1.8 g., 0.03 mole) in 10 ml. of anhydrous benzene was refluxed for 2 hr. Then the liberated mercury (2.84 g., 94%) was filtered off and the filtrate was concentrated. The residue was distilled, giving acetic anhydride, 1.38 g. (80%), b.p. 134–136°, and tri-*n*-butylphosphine oxide, 2.6 g. (86%), b.p. 123–125° (0.2 mm.).

By a similar procedure, propionic, butyric, and benzoic anhydrides were obtained (see Table II).

Reaction of Diphenylmercury and Tri-*n*-Butylphosphine with Phthalic Acid.—A solution of diphenylmercury (5.3 g., 0.015 mole), tri-*n*-butylphosphine (3.0 g., 0.015 mole), and phthalic acid (2.5 g., 0.03 mole) in 10 ml. of anhydrous benzene was refluxed for 2 hr. Then a trace of liberated mercury was filtered off and the filtrate was cooled. The resulting white precipitate, 6.95 g., m.p. 128–133°, was filtered and the filtrate was concentrated *in vacuo*. An additional white precipitate, 2.35 g., m.p. 125–128°, was obtained. These were combined and recrystallized twice from benzene, m.p. 142–143°.

When 4.60 g. of these crystals was heated at 180° for 20 min., mercury, 0.90 g., was liberated and the residue solidified. This solid was washed with a small volume of dry ether and phthalic anhydride, 0.73 g., m.p. and m.m.p. 130–132°. From the filtrate, tri-*n*-butylphosphine oxide, 1.28 g., b.p. 123–135 (0.2 mm.), was obtained.

Reaction of Diphenylmercury and Tri-*n*-Butylphosphine with Phenyl Dihydrogen Phosphate.—A solution of diphenylmercury (3.5 g., 0.01 mole), tri-*n*-butylphosphine (2.0 g., 0.01 mole), and phenyl dihydrogen phosphate (3.4 g., 0.02 mole) in 15 ml. of anhydrous benzene was refluxed for 3 hr. After the liberated mercury, 1.70 g. (85%), was filtered off, a solution of barium chloride ($BaCl_2 \cdot H_2O$, 5 g.) in 20 ml. of water and pyridine (10 ml.) was added to the cold filtrate and allowed to stand in a refrigerator for about 30 min. The white precipitate was washed twice with acetone, dried, and then thoroughly washed with 50 ml. of water. The undissolved precipitate was filtered and dried *in vacuo* over phosphorus pentoxide, yielding 4.50 g. (86%) of barium diphenyl pyrophosphate, R_f 0.74 (n-PrOH:NH_3:H_2O = 6:3:1). From the filtrate, tri-*n*-butylphosphine oxide, 1.70 g. (78%), b.p. 121–122° (0.8 mm.), was obtained.

By a similar procedure, *sym*-di-*p*-chlorophenyl pyrophosphate and *sym*-di-*p*-nitrophenyl pyrophosphate were obtained.

Reaction of Diphenylmercury and Tri-*n*-Butylphosphine with *p*-Toluenesulfonic Acid.—Diphenylmercury (3.5 g., 0.01 mole), tri-*n*-butylphosphine (2.0 g., 0.01 mole), and *p*-toluenesulfonic acid (3.4 g., 0.02 mole) were dissolved in 15 ml. of anhydrous benzene and refluxed for 3 hr. Then the liberated mercury, 1.86 g. (93%), was filtered off and the filtrate was evaporated *in vacuo*. On addition of 0.9 g. (0.01 mole) of aniline to the residue, a white precipitate deposited. It was filtered off and washed with a small volume of water and dried *in vacuo*; 1.88 g. (76%) of *p*-toluenesulfonyl anilide, m.p. and m.m.p. 100–102°, was obtained. From the filtrate, tri-*n*-butylphosphine oxide, 1.92 g. (88%), b.p. 120–122° (0.2 mm.), was isolated.

Acknowledgment.—The authors wish to express their hearty thanks to Mr. Hirohiko Nambu for his kind advice during the course of this experiment.

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[5] Acetic anhydride, derived from two sources, can not be determined separately; consequently, it is assumed that equal volumes are obtained from them.

Mechanisms of Hydrolysis of Several Atom-Bridged Bicyclic Anhydrides, N-Methylimides, and Lactones

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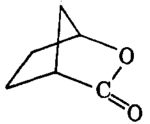
Several atom-bridged bicyclic carbonyl compounds were synthesized. The saponification or hydrolysis rates of these and related compounds were determined. Ground state strains were assessed by determining the position of the monomer–polymer equilibrium. The rates were interpreted using a postulate of Bruice and Pandit about the location of the transition states. Because these cage structures reacted readily in most cases, a configuration of the transition state wherein the hydroxyl ion is colinear with the carbonyl oxygen was rejected.

Interest in the mechanisms of hydrolysis and saponification reactions[1] prompted determination of the rates of these reactions for several atom-bridged bicyclic compounds prepared earlier[2] and for several new ones.

Results

Preparation of Compounds.—Ethyl 3-hydroxycyclopentanecarboxylate was prepared according to Vaughan[3] and Toki.[4] When heated with a trace of litharge,[2] ethanol was eliminated and the lactone, 2-oxabicyclo[2.2.1]heptan-3-one (**1**), distilled as a waxy solid.[5] 2-Oxabicyclo[3.2.1]octan-3-one (**2**) was prepared by Baeyer–Villiger oxidation of norcamphor.[6,7] 3-Oxabicyclo[3.2.1]octane-2,4-dione (**3**)[8] and 3-oxabicyclo[3.2.2]nonane-2,4-dione (**4**)[9] were prepared from corresponding dicarboxylic acids by literature procedures. N-Methyl-3-azabicyclo[3.2.1]octane-2,4-dione (**5**) and N-methyl-3-azabicyclo[3.3.1]nonane-2,4-dione (**6**) were prepared by treating *cis*-cyclopentane-1,3-dicarboxylic acid and *cis*,-



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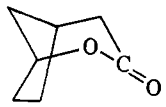

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[2] H. K. Hall, Jr., *ibid.*, **80**, 6412 (1958).

[3] H. A. Vaughan, Jr., Ph.D. thesis, Columbia University, 1955; *Chem. Abstr.*, **51**, 16314 (1957).

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[5] The same lactone has been reported by D. S. Noyce and J. Fessenden, *J. Org. Chem.*, **24**, 715 (1959).

[6] A. Rassat and G. Ourisson, *Bull. soc. chim. France*, 1133 (1959).

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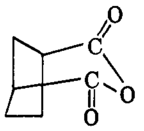
TABLE I

RATES OF SAPONIFICATION AND HYDROLYSIS IN WATER AT 25.0°

Acyl derivative	Ground state strain by polymerization criterion	Ref.	Initial concn., $M \times 10^3$, of acyl derivative	$k_1 \times 10^3$ [d]	k_2 [e]	Ref.
Anhydrides						
Glutaric anhydride	0	[f]		2.80	11	
3-Oxabicyclo[3.2.1]octane-2,4-dione (**3**)	0	[c]	35.8	1.41[a]		[c]
			35.8	0.414[b]		[c]
3-Oxabicyclo[3.2.2]nonane-2,4-dione (**4**)	+	[g]	39.0	Insol.[a]		[c]
			39.0	0.381[b]		[c]
N-Methylimides						
N-Methylglutarimide	0	[c]			1.81	[f]
N-Methyl-3-azabicyclo[3.2.1]octane-2,4-dione (**5**)	0	[c]	5.14	8.51	1.65	[c]
			10.0	14.5	1.45	[c]
			19.4	30.1	1.55	[c]
N-Methyl-3-azabicyclo[3.3.1]nonane-2,4-dione (**6**)	0	[g]	12.0	8.97	0.75	[c]
Lactones						
γ-Butyrolactone	0	[g]			0.81	[f]
δ-Valerolactone	+	[g]			13.8	[f]
6-Oxabicyclo[3.2.1]octane-7-one (**7**)	+	[g]			0.36	[f]
2-Oxabicyclo[2.2.1]heptane-3-one (**1**)	+	[c]	15.5	3.80	.25	[c]
			35.6	9.00	.25	[c]
2-Oxabicyclo[2.2.2]octane-3-one (**8**)	+	[g]			.027	[f]
2-Oxabicyclo[3.2.1]octane-3-one (**2**)	0	[c]	13.2	0.0576	.0044	[c]
			79.7	.340	.0043	[c]

[a] Solvent 20% acetone–80% water by weight. [b] Solvent 40% acetone–60% water by weight. [c] Present work. [d] First-order rate constant in sec.$^{-1}$ for solvolysis in initially neutral water or pseudo first-order rate constant for disappearance of hydroxide ion[1]. [e] Second-order rate constant in l. mole^{-1} sec.$^{-1}$ for bimolecular saponification by hydroxide ion. [f] Ref. 1. [g] Ref. 2.

trans-cyclohexane-1,3-dicarboxylic acid, respectively, with methylamine and distilling the reaction mixtures.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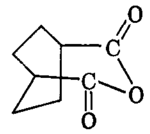
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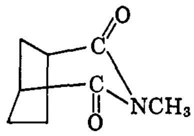
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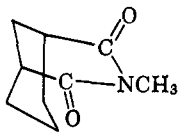
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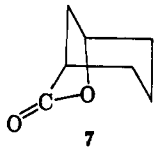
Polymerizations and Rate Measurements.—The ability of these atom-bridged bicyclic compounds to polymerize *via* ring-opening was established by the methods described earlier.[2] The results are presented in Table I. The saponification rates of the esters and N-methylimides were determined as described earlier.[1,10]

Discussion

Ground State Strains.—Ground state strains were assessed by ring-opening polymerizations since heat of combustion data for these compounds are lacking. As described earlier,[2] polymerization of a cyclic monomer is an equilibrium process. Destabilizing factors, mainly nonbonded hydrogen interactions or angle strain, favor the formation of polymer, which is usually unstrained.

The strained bicycloheptane system in 2-oxabicyclo[2.2.1]heptan-3-one (**1**) favors polymerization. The bicyclo[3.2.1]octane system is marginal. None of the new compounds **2**, **3**, or **5** belonging to this class polymerized, although 6-oxabicyclo[3.2.1]octan-7-one (**7**) does so.[2]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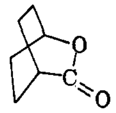
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3-Oxabicyclo[3.2.2]nonane-2,4-dione (**4**) polymerized as expected to relieve the strained boat form of the cyclohexane ring. The strainless two-chair form of N-methyl-3-azabicyclo[3.3.1]nonane-2,4-dione (**6**) did not polymerize, also as predicted.

Configuration of the Transition State.—Earlier work[1] suggested that the hydroxyl ion and carbonyl oxygen group might be at a 180° angle in the transition state. Such a transition state would not be possible for compounds **1**, **3**, **4**, and **5** of the present study, yet they are quite reactive. Accordingly, the suggestion of a 180° transition state can be dropped[11] and the results can be discussed in terms of the 90° transition state suggested by Bender.[12]

Additionally, we shall use the postulate of Bruice and Pandit,[13] who suggest that the carbonyl group in anhydride hydrolysis is mostly sp^2 hybridized (the transition state is close to reactants), in N-methylimide saponification is intermediate in hybridization, and in lactone saponification is mostly sp^3 hybridized (the transition state possesses a fairly strong bond between the hydroxide ion and the lactone). Their proposal was based on the relative reactivities of six- and five-membered rings.

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(10) J. Koskikallio, *Ann. Acad. Sci. Fennicae, Ser. A*, **57**, 1 (1954).

(11) The same conclusion was claimed recently for phthalamic acid by Zerner and Bender [*J. Am. Chem. Soc.*, **83**, 2267 (1961)], but their criterion, based on k D_2O/k H_2O ratios, was apparently not decisive [M. L. Bender, E. J. Pollack, and M. C. Neveu, *ibid.*, **84**, 595 (1962)].

(12) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).

(13) T. C. Bruice and U. K. Pandit, *J. Am. Chem. Soc.*, **82**, 5858 (1960).

Hydrolysis of Anhydrides.—The strained bicyclic anhydride **4** hydrolyzes at the same rate as the unstrained anhydride **3** and as monocyclic or acyclic anhydrides. The ground state strain in **4** is, therefore, still present in the transition state. Since the latter resembles the reactants, the anhydride ring is not opening to provide relief of strain and enhancement of rate.

Saponification of N-Methylimides.—The particular compounds studied, **5** and **6**, were not strained. The transition state for these reactions is further along the reaction coordinate, but the hydroxyl group is still not firmly bonded or close enough to undergo steric crowding by the bridges. Accordingly, these compounds saponify at equal rates to each other and to monocyclic and acyclic N-methylimides.

Saponification of Lactones.—Here considerable bond formation between hydroxide ion and the reactant is present in the transition state. Steric crowding between the hydrated hydroxyl ion and the reactant will be more important for these compounds. We may ask whether the ring is being broken as the hydroxyl ion attacks the carbonyl group.[14] Strained lactones should saponify faster than unstrained ones if this were true. The strained compounds **1** and **7** saponify at rates similar to those of model compounds, while the strained lactone **8** saponifies quite slowly. Moreover, the unstrained lactone **2** reacts much more slowly than any of the others. Therefore, no significant cleavage of the ring has occurred at the transition state for the saponification of the lactones. The same conclusion can be reached by considering the fact that the saponification rates of the strained propiolactone and the unstrained γ-butyrolactone are equal.[1] The markedly lower reactivity of lactones **2** and **8** can be ascribed to drastic steric interference between the hydroxyl ion and the ethylene bridges of these molecules.

Experimental

2-Oxabicyclo[2.2.1]heptan-3-one (**1**).—Cyclopentanone-3-carboxylic acid was prepared according to literature procedures.[3,4] During the distillation of the product, it was difficult to maintain the vacuum, owing to slight decomposition in the boiler, and it was necessary to continue the distillation over several hours while gradually increasing the bath temperature in order to distil all of the acid. The product, obtained in 58.7% yield, melted at 54.0–60.5° (lit.[4] m.p. 64–65°) and was sufficiently pure for conversion to the ester. Ethyl cyclopentanone-3-carboxylate was prepared according to Toki[4] except that the reaction was terminated after 18 hr. Hydrogenation was carried out in ethanol over Raney nickel at 80°.

A mixture of 13.1 g. (0.0828 mole) of ethyl 3-hydroxycyclopentanecarboxylate and 0.16 g. of red Pb_3O_4 was held at 190–200° for 1 hr. under 150-mm. pressure. Ethanol, b.p. 42–47° (150 mm.), 4 ml., distilled. Pressure was reduced to 0.3 mm. and the lactone distilled slowly over a 3-hr. period, b.p. up to 80°. The product, a mixture of liquid and solid, weighed 4.5 g. It was crystallized from a mixture of 12 ml. of ether and 6 ml. of hexane at −80°, filtered onto a Dry Ice-chilled Allihn sintered glass funnel under nitrogen, and spun in a centrifuge until it attained room temperature.[15] There was obtained 2.44 g. (26.3%) of nicely crystalline, hygroscopic, 2-oxabicyclo[2.2.1]heptan-3-one (**1**), m.p. 51.0–56.0° (sealed cap.). The analytical sample had m.p. 56.5–60.5° (lit.[5] m.p. 53.7–54.5°). Its infrared spectrum was consistent with the assigned structure, in particular showing carbonyl absorption at 1775 cm.$^{-1}$, which is characteristic of five-membered lactones.

Anal. Calcd. for $C_6H_8O_2$: C, 64.0; H, 7.0. Found: C, 64.3; H, 7.2.

2-Oxabicyclo[3.2.1]octan-3-one 2.—The procedure was that of Sauers,[16] starting from norcamphor. The lactone had b.p. 81° (0.20 mm.), m.p. 58.5–60.5° (sealed cap.) (lit.[6,7] m.p. 64°), 66.2% yield.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.6; H, 8.0. Found: C, 66.9; H, 8.1.

The infrared spectrum was consistent with the assigned structure, the carbonyl absorption occurring at 1742 cm.$^{-1}$.

Attempted Preparation of 3-Oxabicyclo[3.2.1]octan-2-one.—Hydrogenolysis of 25 g. of *cis*-cyclopentane-1,3-dicarboxylic anhydride in dioxane over copper chromite at 200° gave 13.6 g. of *cis*-cyclopentane-1,3-dimethanol, b.p. 117° (0.55 mm.), $n^{25}\text{D}$ 1.4842.

Anal. Calcd. for $C_7H_{12}O_2$: C, 64.6; H, 10.8. Found: C, 63.8, 64.1; H, 10.5, 10.8.

The infrared spectrum was consistent with this formulation showing strong hydroxyl absorption but no carbonyl absorption.

3-Oxabicyclo[3.2.1]octane-2,4-dione (**3**).—This anhydride melted at 160.5–163.0° (lit.[8] m.p. 160–161.5°).

3-Oxabicyclo[3.2.2]nonane-2,4-dione (**4**).—A mixture[9] of 70 g. (0.406 mole) of *cis,trans*-1,4-cyclohexanedicarboxylic acid and 225 g. of acetic anhydride was refluxed for 5 hr. Acetic acid and acetic anhydride were removed by distillation. The resulting solid polyanhydride depolymerized smoothly when heated with a pale blue flame at 1–3 mm., head temperature 210°, to give 56.3 g. of solid distillate. Recrystallization from benzene–hexane containing a little acetone gave 28.8 g. (46.1%) of white crystals of the desired anhydride, m.p. 160–168°, on a heated bar (lit.[9] m.p. 150–160°) (polymerization occurs during the determination).

N-Methyl-3-azabicyclo[3.2.1]octane-2,4-dione (**5**).—The procedure was that of Grogan and Rice.[17] The imide (38.9% yield) had m.p. 43.5–47.0°.

Anal. Calcd. for $C_8H_{11}O_2N$: N, 9.14. Found: N, 9.04.

N-Methyl-3-azabicyclo[3.3.1]nonane-2,4-dione (**6**).—This imide has been prepared previously.[2]

Kinetics Methods.—The rates of hydrolysis of the lactone and imides were determined by the pH method previously described.[1] The anhydride rates were determined by the aniline titration method.[10] Because saponification and hydrolysis rate constants are very sensitive to solvent composition,[10,18,19] the rates were determined generally using water alone at 25° as the solvent. Only in the cases of the two bicyclic anhydrides was acetone added to form a homogeneous solution.

Polymerizations.—These were performed as previously described.[2] The lactones were sealed in glass tubes with traces of litharge or tetraisopropyl titanate and heated at 150° for 48 hr. 3-Oxabicyclo[3.2.1]octane-2,4-dione was heated similarly with water at 170°. Under these conditions 2-oxabicyclo[2.2.1]heptan-3-one became a rather viscous sirup on cooling. This was extracted twice with ether to remove most of the unreacted lactone. The remaining polymer, *ca.* 50% yield, had a molecular weight of 1100 (isopiestic in chloroform). Its infrared spectrum was consistent with the polyester structure and a little unchanged lactone was present also.

Acknowledgment.—The author is indebted to Mrs. Nancy Abbadini for excellent technical assistance, to Mr. I. D. Plank and his associates for the microanalyses, to Dr. Caryl Sly for the hydrogenations, to Professor J. Meinwald for information about the oxidation of norcamphor, and to Dr. D. R. Wilson for helpful criticism.

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(14) M. L. Bender, H. Matsui, R. J. Thomas, and S. W. Tobey, *J. Am. Chem. Soc.*, **83**, 4193 (1961), have shown that no tetrahedral intermediate is detectable in lactone saponification.

(15) S. I. Miller and R. M. Noyes, *J. Am. Chem. Soc.*, **73**, 2377 (1951).

(16) R. R. Sauers, *ibid.*, **81**, 975 (1959).

(17) C. H. Grogan and L. M. Rice, *J. Org. Chem.*, **22**, 1223 (1957).

(18) E. Tommila and M. P. O. Ilömaki, *Acta Chem. Scand.*, **6**, 1246 (1952), and other articles in this series.

(19) For example, Huisgen and Ott[20] showed that the saponification rate ratio *k* butyrolactone/*k* aliphatic ester was 1.8 × 10^2 in dioxane–water at 0°, whereas data obtained in water at 25°, give the same ratio *k* butyrolactone/*k* ethyl acetate as 7.3.

(20) R. Huisgen and H. Ott, *Tetrahedron*, **6**, 253 (1959).