with dilute hydrochloric acid and the oily acid crystallized on standing to yield 216 mg. of partly active *l*-2,4-diethyl-3-propylpentanedioic acid, m.p. 93–94°, $[\alpha]^{20}D$ −2.4° (*c* 10); 95% ethanol used as solvent for all rotations measured.

Fractional crystallization of the crude *d*-acid monobrucine salt gave 929 mg. of the purified salt as rectangular prisms, m.p. 114–121°. Regeneration of the *d*-acid from this sample in the manner used above for the *l*-acid gave 180 mg. of partly active *d*-2,4-diethyl-3-propylpentanedioic acid, m.p. 85–93°, $[\alpha]^{20}D$ 5.4° (*c* 11), and a second crop, 71 mg., m.p. 86–91°, somewhat more active, $[\alpha]^{20}D$ 11.0° (*c* 5).

Dehydration of 5,7-Dihydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone.—A 41.9-g. (0.155 mole) sample of the lactone III was slowly distilled with a few crystals of iodine in a nitrogen atmosphere to yield 2.14 g. (0.119 mole) of water. The remaining residue was diluted with ether and washed with potassium hydroxide solution and water. After drying and distilling the ether, the following main fractions were obtained: (1) 3.5 g. of forerun, b.p. 60–134° (4.0 mm.); (2) 10.5 g. (27%) of crude C_{16}-unsaturated lactone mixture, b.p. 134–142° (4.0 mm.); (3) 1.0 g. of recovered III, b.p. 150–158° (1.3 mm.); and (4) 21 g. of residue. The crude lactone mixture was purified by extraction with *N* sodium hydroxide; b.p. 125–127° (0.5 mm.), $n^{25}D$ 1.4728; infrared bands at 3.37, 3.47, 5.64, 5.76, 6.84, 7.25m, 8.38, 8.85m, 9.25m, 10.40m and 11.1w μ.

Anal. Calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.03; H, 11.31.

On quantitative hydrogenation the unsaturated lactone mixture absorbed 1.0 mole-equivalent of hydrogen (platinum catalyst, one atm., 25°). On quantitative bromination (bromine in acetic acid), 0.68 mole-equivalent of bromine was absorbed. A Zerewitinoff determination showed 0.19 active hydrogen and 1.92 additional moles of methylmagnesium iodide reacted. Other acidic catalysts (sulfuric and phosphoric acids, aluminum oxide at 400°) were used to dehydrate III, but iodine distillation gave the best results.

A 4.83 g. (0.0192 mole) sample of the lactones in chloroform was ozonized using a slight excess of ozone. After removing the chloroform, the ozonide solution was decomposed with water, first at room temperature, then at reflux temperature while air was aspirated through the mixture. The exit vapors were passed through 2,4-dinitrophenylhydrazine reagent to yield 1.26 g. of precipitate, m.p. 85–150°. Fractional crystallization of this material gave (1) 0.74 g., m.p. 112–125°, and (2) 0.28 g., m.p. 135–140°. Recrystallization of the first fraction gave orange needles, m.p. 116–117°; melting point not depressed when mixed with an authentic sample of 2-butanone 2,4-dinitrophenylhydrazone, m.p. 117°. Several recrystallizations of the smaller second fraction gave orange platelets, m.p. 155–157°, identified as acetaldehyde 2,4-dinitrophenylhydrazone (mixture melting point with authentic sample, m.p. 157°, undepressed). Water-soluble, steam-volatile acidic material was isolated; 0.0108 equivalent total. By refluxing with mercuric oxide, 0.0036 equivalent of this acid was destroyed (formic acid, 19%).[3] The remainder of the acid, 0.072 equivalent (37.5%), gave Duclaux numbers, 8.5, 7.5 and 6.8 and a *p*-phenylphenacyl ester derivative, m.p. 106–114°, which could not be recrystallized to constant melting point. Acetic acid is believed to be the main constituent of this portion, with a small amount of higher molecular weight acid(s). Of the 1.26 g. of 2,4-dinitrophenylhydrazone derivative which precipitated, it is estimated from the above fractionation data that 0.0034 equivalent (18%) of 2-butanone and 0.015 equivalent of acetaldehyde (7.5%) were formed. Other ozonolysis products isolated were water insoluble and included 1.1 g. of a steam-volatile neutral oil, 0.37 g. of a neutral non-steam-volatile gum and 0.41 g. of an oily non-steam-volatile acid; none of these fractions could be crystallized, and they were not investigated further.[27]

7-Acetoxy-5-hydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone.—A solution of 70.7 g. (0.0262 mole) of the lactone III in 150 ml. of acetic anhydride was treated with one drop of concentrated sulfuric acid and allowed to stand 15 hr. at room temperature, then heated on the steam-bath for 8 hr. After standing overnight and then treating with 2 g. of barium hydroxide, the material was distilled *in vacuo* to remove acetic acid and acetic anhydride. The residue was then filtered and the filtrate distilled twice to yield 63 g. (77%) of the colorless acetate, b.p. 158–162° (0.5 mm.), $n^{25}D$ 1.4662. By slowly distilling the acetate through a glass tube packed with glass wool (450°), low yields (10–20%) of unsaturated lactone were obtained.

Anal. Calcd. for $C_{18}H_{32}O_4$: C, 69.19; H, 10.33. Found: C, 69.57; H, 10.65.

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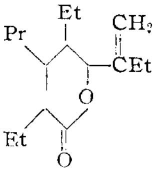
(27) The above data suggest the unsaturated lactone mixture to consist mainly of the isomers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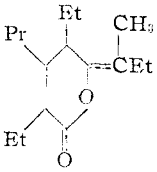
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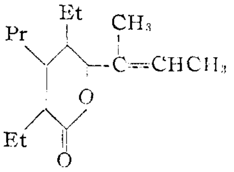
XIX

NEW BRUNSWICK, N. J.

[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Steric Effects in Hydrolysis of Hindered Amides and Nitriles[1]

BY LIN TSAI,[2] T. MIWA[3] AND MELVIN S. NEWMAN[4]

RECEIVED JANUARY 29, 1957

The relative extent of alkaline hydrolysis in ethylene glycol at 190–192° of seven hindered aliphatic amides has been determined. The results are reasonably well correlated by the Rule of Six. Alkaline hydrolysis of hindered aromatic amides leads to the formation of nitriles. The acidic hydrolysis of hindered aliphatic nitriles to amides and the conversion of these amides to acids by sulfuric acid–sodium nitrite treatment is described.

Perhaps the most inclusive study of steric hindrance to carbonyl addition reactions in the aliphatic series is that involving the acid-catalyzed esterification. In this work the effect of structure on the rate of esterification with methanol of 26 saturated aliphatic acids was reported and discussed in terms of the Rule of Six and other variables.[5] However, the rates of esterification of highly sterically hindered acids could not be measured because the side reaction between the catalyst, hydrogen chloride and methanol became too important a factor when longer times and higher temperatures were needed for esterification. For example, diisopropylacetic acid esterified too slowly to measure under the general conditions used for the other acids. Accord-

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[2] Post-doctoral fellow, 1954–1955.

[3] Research assistant, 1953–1954.

[4] To whom inquiries should be sent.

[5] K. L. Loening, A. B. Garrett and M. S. Newman, THIS JOURNAL, **74**, 3929 (1952).

ingly, we became interested in other reactions which might be studied quantitatively to yield information on highly hindered acid derivatives. We here report our observations on hydrolysis of highly hindered amides, both aliphatic and aromatic, and of hindered nitriles.

Because of experimental difficulties we were unable to devise a simple accurate procedure to measure the rate constants of alkaline hydrolysis of hindered amides. Experiments in which reactants were sealed in small stainless steel bombs equipped with closures using lead or gold gaskets failed because of leaks which developed erratically at the 190–210° temperatures needed for hydrolysis.[6] Accordingly, we turned to hydrolysis in ethylene glycol–alkali mixtures at atmospheric pressure. The extent of hydrolysis was estimated by titration of the ammonia evolved. The results are listed in Table I.

TABLE I

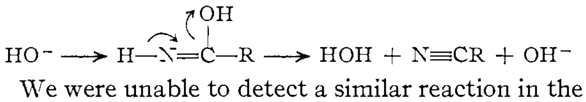
ALKALINE HYDROLYSIS OF HINDERED AMIDES IN ETHYLENE GLYCOL AT 190–192°

	Amide	% NH_3 in 48 hr.	Six no.
1	$(C_2H_5)_3CCONH_2$	50.4	9
2	$(CH_3)_3CC(CH_3)_2CONH_2$	34.5	9
3	$[(CH_3)_2CH]_2CHCONH_2$	16.7	12
4	$[(CH_3)_3C](C_2H_5)CHCONH_2$	12.5	12
5	$[(CH_3)_3C][(CH_3)_2CH]CHCONH_2$	3.0	15
6	$[(CH_3)_2CH]_2(CH_3)CCONH_2$	2.4	12
7	$[(CH_3)_2CH]_2(C_2H_5)CCONH_2$	2.2	15

The over-all results are roughly what one would expect by application of the Rule of Six. In amides 6 and 7 we seem to be approaching a limit in steric hindrance, as the change from a methyl to an ethyl group in the α-position makes little difference, whereas in the acid series a similar change often makes a considerable difference (acids 12 and 24 in Table I).[5] We attach no significance to the small differences in ammonia obtained for amides 5, 6 and 7.

Turning to aromatic amides, we found that attempts to follow the alkaline hydrolysis in the ethylene glycol–alkali system used for the aliphatic mixtures revealed the presence of nitriles corresponding to the starting amides. Blank experiments in ethylene glycol alone (190–195°) showed that no nitrile was formed. Alkali is necessary for nitrile formation. We believe that this finding represents the first case of alkaline dehydration of an amide to a nitrile in solution.[7]

The transformation is pictured as a base-catalyzed elimination reaction of the enol form of the amide.



$$HO^- \longrightarrow H{-}N{=}\overset{OH}{C}{-}R \longrightarrow HOH + N{\equiv}CR + OH^-$$

We were unable to detect a similar reaction in the alkaline hydrolyses of the hindered aliphatic amides mentioned above. Our results in the aromatic series are summarized in Table II.

TABLE II

ALKALINE TREATMENT OF HINDERED AROMATIC AMIDES IN ETHYLENE GLYCOL AT 195–197°

Amides	Moles of amide	NaOH–ethylene glycol (0.27 molal), g.	% nitrile (in 12 hr.)	% NH_3
Mesitamide	3.1×10^{-3}	100	56	0.6
2,3,5,6-Tetramethylbenzamide	2.9×10^{-3}	100	62	Trace
2,4,6-Triisopropylbenzamide	2.0×10^{-2}	650	58	0.7

In addition to the studies on alkaline hydrolysis of hindered amides, which was shown to be impractical on a kinetic basis, we have also studied the acid-catalyzed conversion of hindered amides to acids by nitrous acid.

In our study of acid hydrolysis of hindered aliphatic nitriles,[8] the nitrile was dissolved in an excess of strong sulfuric acid and held at specified temperatures for various times. The amide formed and nitrile unreacted were determined. The results of these experiments are summarized in Table III. Here again the increase in steric hindrance parallels the increase in six number. Since nitriles are in general somewhat less subject to steric hindrance than are amides, it is not surprising to find that nitriles of six number of 12 (nitriles 2 and 3, Table III) are hydrolyzed fairly well under rather drastic conditions. However, when the six number rises to 15 and 18 (nitriles 4 and 5, Table III), hydrolysis is extremely difficult and, from a practical point of view, unattainable under the prevailing conditions. Other attempts at higher and lower temperatures were even more unpromising.

In our study of the conversion of hindered amides to acids, we turned to treatment with nitrous acid in strong sulfuric acid solution, as previous work in the literature indicated that this procedure worked fairly well for moderately hindered amides.[9] Our results are summarized in Table IV. Although we did not include very highly hindered amides in this work (because we were unable to get sufficient quantities by hydrolysis of the required nitriles), we include the studies on the moderately hindered amides because this work shows that treatment with nitrous acid in strong sulfuric affords an excellent procedure for conversion to acids.

Experimental[10]

Mesitamide.—Mesitylene was brominated[11] to bromomesitylene which was converted to the Grignard reagent and carbonated to form the acid.[12] Treatment of the acid with thionyl chloride followed by ammonia furnished the amide. Recrystallization from benzene gave pure mesitamide, m.p. 192.0–193.5° (reported[13] m.p. 187–188°).

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[6] Many of these experiments were performed by Dr. H. S. Eleuterio, post-doctoral fellow, 1953–1954.

[7] The conversion of benzamide to benzonitrile has previously been accomplished by fusion with lime. See (a) F. Wohler, *Ann.*, **192**, 362 (1878); (b) R. Anschütz and G. Schultz, *ibid.*, **196**, 48 (1879). We have checked this by converting mesitamide to mesitonitrile.

[8] The preparation of the hindered nitriles will be described in a forthcoming publication.

[9] (a) C. Schuerch, Jr., and E. Huntress, THIS JOURNAL, **70**, 2824 (1948); (b) N. Sperber, D. Papa and E. Schwenk, *ibid.*, 3091 and references contained therein.

[10] Analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. All melting points are corrected.

[11] L. I. Smith, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 95.

[12] D. M. Bowen, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 553.

[13] H. L. Wheeler, *Am. Chem. J.*, **23**, 468 (1900).

TABLE III

ACIDIC HYDROLYSIS OF HINDERED NITRILES IN SULFURIC ACID

	Nitrile, $R_1R_2R_3CCN$			H_2SO_4				Amides		
	R_1	R_2	R_3	%	g./g. nitrile	Time, hr.	Temp., °C.	Yield, %	Pure sample m.p., °C.	Rec. nitriles, %
1	C_2H_5	C_2H_5	C_2H_5	75	1.7	0.5	140	93	110.6–111.4	..
2	$(CH_3)_2CH$	$(CH_3)_2CH$	H	75	1.7	0.5	140	83	147.2–149.4	..
3	$(CH_3)_2CH$	$(CH_3)_2CH$	CH_3	75	1.7	0.6	140	66[a]	57.8–58.8[b]	..
4	$(CH_3)_2CH$	$(CH_3)_2CH$	C_2H_5	85	5.4	18	100	25[a]	95.8–96.4[c]	32
				95	14	45	50	10[a]		75
				95	10	70	65	15[a]		57
5	$(CH_3)_2CH$	$(CH_3)_2CH$	$(CH_3)_2CH$	95	10	168	70	Trace		79
6	$(CH_3)_3C$	CH_3	CH_3	[d]	2.1	1	140	63[e]	203.5–204.5[f]	..

[a] Based on crude product. [b] *Anal.* Calcd. for $C_9H_{19}NO$: C, 68.3; H, 11.5; N, 8.9. Found: C, 68.5; H, 11.5; N, 8.9. [c] *Anal.* Calcd. for $C_{10}H_{21}NO$: C, 70.1; H, 12.4; N, 8.2. Found: C, 70.3; H, 12.3; N, 8.1. [d] In this experiment 23.9 g. of nitrile was heated in 30 ml. of 85% sulfuric acid and 10 ml. of acetic acid. [e] The corresponding acid, m.p. 195.0–196.0°, was also obtained in 20% yield. [f] *Anal.* Calcd. for $C_8H_{17}NO$: C, 67.1; H, 12.0; N, 9.8. Found: C, 66.8; H, 11.8; N, 9.6.

TABLE IV

CONVERSION OF HINDERED AMIDES TO ACIDS

	Amide, $R_1R_2R_3CCONH_2$						
	R_1	R_2	R_3	75% H_2SO_4 g./g. nitrile or amide	$NaNO_2$, mole/mole nitrile or amide	Yield, %	Acid Pure sample m.p., °C.
1	C_2H_5	C_2H_5	C_2H_5	3.2	1.4	90[a]	38.9–39.5[b]
2	$(CH_3)_2CH$	$(CH_3)_2CH$	H	1.7	1.5	93[a]	20.0[c]
3	$(CH_3)_2CH$	$(CH_3)_2CH$	CH_3	2.4	2.3	88	49.5–50.2[d]
4	$(CH_3)_2CH$	$(CH_3)_2CH$	C_2H_5	2.4	4.8	71	56.4–57.0[e]
5	$(CH_3)_3C$	CH_3	CH_3	[f]	1.9	63[a]	198.5–199.0[g]
6	$(CH_3)_3C$	$(CH_3)_2CH$	H	2.7	1.4	76	B.p. 224[h]

[a] Figures represent over-all yield from corresponding nitriles which were hydrolyzed by 75% H_2SO_4 to give the crude amides which were treated directly with specified amount of sodium nitrite. [b] C. Schuerch, Jr., and E. H. Huntress, THIS JOURNAL, **70,** 2824 (1948). [c] F. C. B. Marshall, *J. Chem. Soc.*, 2754 (1930). [d] *Anal.* Calcd. for $C_9H_{18}O_2$: C, 68.3; H, 11.5; neut. equiv., 158.2. Found: C, 68.5; H, 11.5; neut. equiv., 158.5. [e] *Anal.* Calcd. for $C_{10}H_{20}O_2$: C, 69.8; H, 11.7. Found: C, 69.7; H, 11.7. [f] In this experiment, 9.5 g. of the nitrile was heated at 150° in 20.1 g. of 75% sulfuric acid and 8.5 g. of acetic acid for 1.5 hr. After the reaction mixture was cooled, 10 g. of sodium nitrile was added. [g] A. Byers and W. S. Hickinbottom, *J. Chem. Soc.*, 1334 (1948). [h] A. A. Sacks and J. G. Aston, THIS JOURNAL, **73,** 3902 (1951), reported the following physical constants for this acid: b.p. 122.5–123.8° (22 mm.), $n^{20}D$ 1.4343.

2,3,5,6-Tetramethylbenzamide (m.p. 187–188°, reported[14] m.p. 178°) was obtained in a similar manner from durene.

Anal. Calcd. for $C_{11}H_{15}ON$: N, 7.9. Found: N, 7.9.

2,4,6-Triisopropylbenzamide (m.p. 216.5–219.5°, reported[15] m.p. 218.7–219.3°) was similarly prepared from 1,3,5-triisopropylbenzene.

***t*-Butylethylacetamide.**—A mixture of 50.4 g. of *t*-butylethylacetic acid[16] (m.p. 76–78°) and 50 g. of thionyl chloride was allowed to stand overnight at room temperature and then heated at 90° for 4 hr. The reaction mixture was distilled twice through a fractionation column to give 51.8 g. (91%) of pure *t*-butylethylacetyl chloride, b.p. 67–69° at 25 mm. The acid chloride was poured into an ethereal solution of ammonia to give the crude amide which was recrystallized from a mixture of benzene–Skellysolve B (petroleum ether, b.p. 65–69°) to furnish 44.8 g. (98%) of *t*-butylethylacetamide, m.p. 136.6–137.2°.[17]

Anal. Calcd. for $C_8H_{17}ON$: C, 67.1; H, 11.9; N, 9.8. Found: C, 67.2; H, 12.2; N, 9.8.

***t*-Butylisopropylacetonitrile and *t*-Butylisopropylacetamide.**—To a solution of sodium ethoxide (prepared from 23 g. of sodium in about 400 ml. of absolute ethanol) was introduced 169 g. of ethyl *t*-butylcyanoacetate[18] and 190 g. of isopropyl iodide. The mixture was heated under reflux for 15 hr. The solvent was removed by distillation under reduced pressure. The residue was taken up in 200 ml. of water and extracted several times with benzene–ether mixture. The combined extracts were successively washed with sodium hydrosulfite, sodium hydroxide and saturated sodium chloride solutions and dried over magnesium sulfate. After removal of the solvent under reduced pressure, the residual liquid was fractionated at 18 mm. pressure to afford 64.5 g. (38%) of unchanged ethyl *t*-butylcyanoacetate, b.p. 110–113°, and 89.0 g. (42%) of ethyl *t*-butylisopropylcyanoacetate, b.p. 128–132°.

A mixture of ethyl *t*-butylisopropylcyanoacetate (75 g.) and 150 g. of potassium hydroxide was fused and distilled. The distillate was again fused with 100 g. of potassium hydroxide and distilled. Fractionation of the distillate afforded 22.2 g. (45%) of *t*-butylisopropylacetonitrile, b.p. 178–181°.

Anal. Calcd. for $C_9H_{17}N$: C, 77.6; H, 12.3; N, 10.1. Found: C, 77.0; H, 12.8; N, 10.2.

The residue from the potassium hydroxide fusion on taking up in water furnished 12.9 g. (23%) of an insoluble solid which was recrystallized from benzene–Skellysolve B to give pure *t*-butylisopropylacetamide, m.p. 124.8–125.6°.

Anal. Calcd. for $C_9H_{19}ON$: C, 68.7; H, 12.2; N, 8.9. Found: C, 68.8; H, 12.0; N, 8.9.

Alkaline Hydrolysis of Hindered Aliphatic Amides.—The solvent used in these experiments was ethylene glycol (b.p. 196–198°) which was purified by refluxing with 2 g. of sodium (per liter of solvent) for several hours and distilling.

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(14) V. Meyer and L. Wohler, *Ber.*, **29**, 2571 (1896).

(15) A. Newton, THIS JOURNAL, **65**, 2441 (1943).

(16) We wish to thank Dow Chemical Co. for a generous gift of this acid.

(17) W. A. Mosher and J. C. Cox, Jr., THIS JOURNAL, **72**, 3701 (1950), reported this amide as melting at 115–116°. In order to check the identity of our amide, m. p. 137°, we alkylated 25 g. of *t*-butylacetonitrile with sodium amide (from 6 g. of sodium in 400 ml. of ammonia) and 29 g. of ethyl bromide for 20 hours, to yield 12.2 g. of *t*-butylethylacetonitrile, b. p. 170–175°, and 5.0 g. of *t*-butyldiethylacetonitrile, b. p. 198–200°. A redistilled sample of *t*-butylethylacetonitrile, b. p. 174–175°, was analyzed (Calcd. for $C_8H_{15}N$: C, 76.7; H, 12.1; N, 11.2. Found: C, 76.7; H, 12.2; N, 11.3) and hydrolyzed by heating 2 g. with 3.4 g. of 75% sulfuric acid for 1.5 hours, at 140–150° to yield 1.6 g. of amide, m. p. 135–136°, undepressed by mixing with a sample of the amide of *t*-butylethylacetic acid, m. p. 136–137°, made from the acid obtained from the Dow Co.

(18) S. Widequist, *Arch. Keim.* **2**, 322 (1950).

A solution of sodium hydroxide in ethylene glycol was prepared by mixing an appropriate amount of carbonate-free 40% sodium hydroxide solution with ethylene glycol. The concentration of sodium hydroxide in the solution was determined by titration of weighed aliquots, after diluting 10-fold with distilled water, against standard sulfuric acid using phenolphthalein as indicator.

The hydrolysis of the amide was carried out in a 3-necked flask equipped with a reflux condenser, a thermometer and an inlet for nitrogen gas which was bubbled slowly through the reaction mixture. The outlet of the reflux condenser was led into a known volume of standard sulfuric acid solution which served as an absorption system for ammonia. The reaction flask was heated by a heating mantle and the temperature was controlled by a Thermocap relay.[19]

A weighed amount of a 0.5 molal solution of sodium hydroxide in ethylene glycol was placed in the reaction flask. The temperature of the system was brought rapidly to 190–192°, and a weighed amount of amide ($^{1}/_{20}$ of the molar concentration of sodium hydroxide in the solution) was introduced.

The condenser and the absorption system was immediately connected to the reaction flask. Ammonia evolved during the course of the reaction was entrained by the stream of nitrogen and absorbed in the standard sulfuric acid solution. After 48 hr. the reaction was stopped and the amount of ammonia from the hydrolysis was estimated by titration of the excess acid against standard sodium hydroxide solution using as indicator screened methylene blue–methyl red. The results are shown in Table I.

Reaction of Hindered Aromatic Amides with Sodium Hydroxide in Ethylene Glycol.—A procedure similar to that described for the hydrolysis of aliphatic amides was employed. After the formation of nitrile was observed in preliminary experiments, the apparatus was modified by replacing the reflux condenser by a distilling condenser. The nitrile formed during the course of the reaction was removed from the reaction mixture by co-distillation with ethylene glycol. The reaction was carried out for 12 hr. during which about 10% of the reaction mixture was distilled. The amount of ammonia evolved was determined by titration. The nitrile was isolated from the distillate.

Mesitonitrile (m.p. 50°, reported[20] m.p. 53°) was purified by sublimation at 40° and 0.1 mm. pressure. The infrared spectrum (chloroform solution) showed an intense band at 4.6 μ (2170 cm.$^{-1}$) due to the nitrile function.[21] In one experiment, an intimate mixture of 0.30 g. of mesitamide and 2.8 g. of powdered sodium hydroxide was heated at 290–310° under 20 mm. pressure for 0.5 hr. Mesitonitrile (m.p. 49°) was obtained in 86% yield.

2,3,5,6-Tetramethylbenzonitrile (m.p. 73–74°, reported[22] m.p. 76–77°) was purified by sublimation at 50° and 0.08 mm. pressure. The infrared spectrum (chloroform solution) showed an intense band at 4.6 μ (2170 cm.$^{-1}$).

2,4,6-Triisopropylbenzonitrile was purified by chromatography of the crude substance in redistilled Skellysolve F (petroleum ether, b.p. 35–55°) over activated alumina. The solvent was removed under reduced pressure at room temperature. The residue was distilled to afford a pure sample of the nitrile, b.p. 264–268° at 740 mm., $n^{20}\text{D}$ 1.5089 (lit.[15] $n^{20}\text{D}$ 1.5093). Physical properties and the infrared spectrum of this nitrile were identical with those of a sample of the nitrile obtained by the dehydration of 2,4,6-triisopropylbenzamide by means of thionyl chloride in benzene solution. The results are summarized in Table II.

Acidic Hydrolysis of Hindered Aliphatic Nitriles.—A mixture of the nitrile[8] and sulfuric acid of known concentrations was heated at a specific temperature. After a certain period of heating, the reaction mixture was poured into a large excess of ice-water, and the mixture was worked up by the usual method of extraction. The extent of hydrolysis of the nitrile was indicated by the yield of the amide and the amount of recovered nitrile. The conditions and results of these experiments are summarized in Table III.

Conversion of Aliphatic Amides to Acids.—The amides were treated with a mixture of sodium nitrite and sulfuric acid according to procedures described in the literature.[9] The conditions and results are shown in Table IV.

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[19] Niagara Electronic Laboratories, Andover, N. Y. This instrument controlled the supply of electrical power to the heating system. The change of electric capacity necessary for the operation of this type of relay was effected by the movement of the mercury thread in the thermometer to which the relay lead was connected.

[20] R. Scholl and F. Kacer, *Ber.*, **36**, 331 (1903).

[21] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954.

[22] O. Jacobsen, *Ber.*, **22**, 1224 (1889).

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis and Solvolysis of the 2-Halo-1,4-endoxocyclohexanes[1]

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A kinetic study of the hydrolysis of *exo*-2-chloro-1,4-endoxocyclohexane has shown it to be less reactive than *exo*-norbornyl chloride by a factor of approximately 2000. Its relative inertness is considered to result from the inductive effect of the oxygen bridge, enhanced by its geometric situation. Solvolysis of *endo*-2-chloro-1,4-endoxocyclohexane was slower than that of its *exo* isomer by a factor of 160 (at 140°). This factor is of the same order of magnitude as the corresponding factor in the solvolysis of norbornyl derivatives suggesting that the anchimeric acceleration of ionization of the *exo*-2 substituent is not greatly affected by substitution of an oxygen bridge for the methylene bridge of the norbornyl derivatives. In every case the solvolysis product was that expected to result from rearrangement, 3-formylcyclopentanol. The structures of these chloro ethers, which were obtained from the photochlorination of 1,4-endoxocyclohexane, were confirmed by dipole moment studies. *exo*-2-Bromo-1,4-endoxocyclohexane, isolated from the N-bromosuccinimide bromination of the parent ether, showed a reactivity 30-fold greater than its chloro analog. An interesting side product (16%) isolated from this bromination reaction was β-bromopropionyl isocyanate.

Introduction

A large amount of work of a quantitative nature has been performed on the solvolytic reactions of the various norbornyl derivatives.[3] In the frame of understanding created by this work we have examined the chemical consequences of the replace-

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[3] (a) J. D. Roberts, W. Bennett and R. Armstrong, THIS JOURNAL, **72**, 3329 (1950); (b) J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954); (c) S. Winstein and D. Trifan, *ibid.*, **71**, 2953 (1949); (d) S. Winstein and D. Trifan, *ibid.*, **74**, 1147, 1154 (1952); (e) S. Winstein, B. Morse, E. Grunwald, H. Jones, J. Corse, D. Trifan and H. Marshall, *ibid.*, **74**, 1127 (1952); (f) S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, *Chem. and Ind.*, 664 (1954); (g) J. D. Roberts and C. C. Lee, THIS JOURNAL, **73**, 5009 (1951); (h) J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954); (i) P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3184 (1939); (j) W. von E. Doering and E. F. Schoenewaldt, *ibid.*, **73**, 2333 (1951); (k) S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955); (l) S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).