ing the course of the dehydrogenation, some material collected on the cold finger. The remaining brown tar was sublimed and eventually 0.56 g. of crude product was collected, m.p. 107°. This was washed once with petroleum ether (b.p. 60–71°) to remove sulfur and, on drying, melted at 110–111°, yield 0.49 g.

Recrystallization from petroleum ether gave 0.40 g. of product, m.p. 113–113.5°, reported for 2-phenylbenzoic acid, 113–113.5°.[26] The melting point was not depressed when mixed with a sample of 2-phenylbenzoic acid prepared from 2-aminobiphenyl by a method similar to that used in converting *o*-toluidine to *o*-toluic acid *via* the nitrile.[27,28]

One-tenth of a gram of dehydrogenated VII was heated with 1 ml. of thionyl chloride for 10 minutes on a steam-bath cooled in ice, and then treated with 25 ml. of aqueous ammonia containing some ice. After standing 15 minutes, the solid material was collected and dried; yield 0.08 g. (80%), m.p. 173–174°. This melting point was not lowered by mixing with a known sample of 2-phenylbenzamide prepared from 2-phenylbenzonitrile by the method previously used.[20]

Acknowledgment.—All micro-analyses were performed by the Clark Microanalytical Laboratories, Urbana, Illinois. The authors are indebted to B. F. Goodrich Chemical Company for a generous sample of β-propiolactone, and to Mr. E. R. Hardwick, Jr., and Mr. H. L. Hill of our Laboratory, for a sample of *o*-phenylbenzoic acid and its amide.

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(26) M. Weger and K. Döring, *Ber.*, **36**, 888 (1903).

(27) H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, Second Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 514.

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

The Reaction of N-Methylpiperidine with Alkyl Durenecarboxylates

BY MELVIN S. NEWMAN AND HELEN A. LLOYD[1]

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A pronounced solvent effect on the position of equilibrium between *n*-methylpiperidine, methyl durenecarboxylate and *n*-dimethylpiperidinium durenecarboxylate has been discovered. Other aspects of the reaction between esters of durenecarboxylic acid and *n*-methylpiperidine are described.

The reaction of esters with *t*-amines has been known for some time but has received little attention. Since the discovery of the reaction,[2] only one study has appeared.[3] In this it was shown that the rate of reaction (1) was first order with respect to ester and amine and that the equation log k = $-1.81 - 0.81 \log K$, where K was the ionization constant of the acid RCOOH, was obeyed for aliphatic and aromatic acids, including *o*-substituted acids. More recently, the formation of quaternary salts from esters and *t*-amines has been postulated as a step in certain alkylations[4] and in the disproportionations observed in the reaction of benzyldimethylamine with methyl esters.[5]

$$\mathrm{RCOOCH_3 + N(CH_3)_3 \xrightarrow{k} R\,COON(CH_3)_4} \quad (1)$$

The reverse reaction, the decomposition of quaternary ammonium salts into esters and *t*-amines has been known even longer[6] and has been applied to the esterification of hindered acids.[7] When *d*-(+)-α-phenethyltrimethylammonium acetate was pyrolyzed, *l*-(−)-α-phenethyl acetate of 98–100% optical purity was isolated.[8] This shows that inversion had occurred and suggests an S_N2 type of mechanism. A related reaction, the thermal rearrangement of betaines into esters of amino-acids[2,9] has received some attention.

We became interested in the reactions of *t*-amines with esters because it seemed to offer the opportunity to study certain steric factors in a typical $\mathrm{S_N2}$ type reaction. The present study is a preliminary semiquantitative study of the reaction between N-methylpiperidine with alkyl durenecarboxylates. Durenecarboxylic acid was chosen as an easily prepared hindered acid which we desired in order to avoid complications that might arise from carbonyl addition side reactions. N-Methylpiperidine was chosen in preference to quinuclidine because of its greater ease of preparation and because the F-strain[10] in its reaction with esters should be low.

In this work we have observed a number of interesting facts listed below.

(1) The reaction between methyl durenecarboxylate and N-methylpiperidine to form N-dimethylpiperidinium durenecarboxylate is reversible.

$$\mathrm{2,3,5,6\text{-}(CH_3)_4C_6HCOOCH_3 + CH_3N(CH_2)_5 \rightleftarrows 2,3,5,6\text{-}(CH_3)_4C_6HCOO^-(CH_3)_2\overset{+}{N}(CH_2)_5} \quad (2)$$

(2) Solvents have a profound effect on the position of this equilibrium at 140°: alcoholic solvents favor a position far to the right; non-hydroxylic solvents, such as benzene, nitrobenzene and dioxane, favor a position far to the left.

(3) The rate of reaction to the right in the case of various alkyl esters falls off in the order $\mathrm{CH_3 >> C_2H_5 > CH_3CH_2CH_2– > (CH_3)_2CH–}$.

(4) The *t*-butyl ester is thermally unstable at 140° and its decomposition into durenecarboxylic acid is not affected by amine.

(5) The rate of the salt forming reaction in meth-

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(1) Taken from the Ph.D. Thesis of H. A. Lloyd, The Ohio State University, 1951.

(2) R. Willstätter, *Ber.*, **35**, 584 (1902); R. Willstätter and W. Kahn, *ibid.*, **35**, 2757 (1902).

(3) L. P. Hammett and H. L. Pfluger, THIS JOURNAL, **55**, 4079 (1933).

(4) H. R. Snyder, E. L. Eliel and R. E. Carnhan, *ibid.*, **72**, 2958 (1950).

(5) E. L. Eliel, Abstr. of Papers, 118th Meeting, ACS, Chicago, Sept., 1950.

(6) A. T. Lawson and N. Collie, *J. Chem. Soc.*, **53**, 631 (1888).

(7) V. Prelog and M. Piantanida, *Z. physiol. Chem.*, **244**, 56 (1936), and R. C. Fuson, J. Corson and E. C. Horning, THIS JOURNAL, **61**, 1290 (1939).

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(9) V. Prelog, *Coll. trav. chem. Tchech.*, **2**, 712 (1930); R. Kuhn and F. Giral, *Ber.*, **68**, 387 (1935).

(10) H. C. Brown and N. R. Eldred, THIS JOURNAL, **71**, 445 (1949).

anol is not affected by adding N-dimethylpiperidinium ion or methoxide ion, although in the latter case a different reaction involving displacement of the durenecarboxylate ion by methoxide ion enters the picture.

Other points are discussed in the Experimental part. We are not continuing this work.

Experimental

Bromodurene.—A solution of 500 g. of durene[11] in 875 cc. of chloroform containing a small amount of dissolved iodine was brominated at 0–5° by the addition during three hours of 600 g. of bromine in 375 cc. of chloroform. After one more hour at room temperature the solution was washed with dilute alkali and dried. The solvent was removed and the crude bromide was refluxed for two hours with a solution prepared by dissolving 30 g. of sodium in 600 cc. of 95% alcohol. The crystals which separated on cooling were collected, partly dried, stirred with concentrated sulfuric acid, collected, and eventually distilled to yield 600 g. (75%) of pure bromodurene,[12] b.p. 111–113° at 6 mm., m.p. 60–61°.

Durenecarboxylic Acid.—A solution of 5 g. of bromodurene and 7 g. of ethyl bromide in 300 cc. of ether was added to 65 g. of magnesium turnings all at once. The reaction started immediately and was maintained for two hours by the slow addition of a solution of 261 g. (total 1.25 moles) of bromodurene and 130 g. (total 1.25 moles) of ethyl bromide in 1250 cc. of ether. After refluxing a further two hours the cooled mixture was poured rapidly on a large excess of powdered Dry Ice in a large beaker with stirring. The yield of good acid, m.p. 176–177°, was 170 g. (76.5%). The acid chloride, b.p. 124–125° at 10 mm., m.p. 59–60°, was prepared in 97% yield using pure thionyl chloride (reflux for three hours).

Alkyl Durenecarboxylates.—The following alkyl durenecarboxylates were prepared in over 90% yields by heating a mixture of acid chloride, corresponding alcohol, and pyridine for a short time. The esters were recrystallized from methanol and were dried *in vacuo* over phosphorus pentoxide. The corrected melting points follow: methyl,[13] 58.2–59.0°; ethyl, 78.6–79.4°; propyl, 46.2–47.0°; isopropyl, 104.6–105.6°; isobutyl, 54.0–54.8°; *t*-butyl, 94.2–95.0°.

Anal.[14] Calcd. for $C_{13}H_{18}O_2$: C, 75.6; H, 8.8. Found: C, 75.5; H, 9.1. Calcd. for $C_{14}H_{20}O_2$: C, 76.3; H, 9.1. Found: propyl, C, 76.2; H, 9.3; isopropyl, C, 76.3; H, 9.2. Calcd. for $C_{15}H_{22}O_2$: C, 76.8; H, 9.4. Found: isobutyl, C, 76.7; H, 9.6; *t*-butyl, C, 76.7; H, 9.5.

N-Methylpiperidine.—Piperidine (170 g.) was added slowly to 270 g. of 87% formic acid with cooling. To this solution was added 190 g. of 35% aqueous formaldehyde and the mixture was refluxed for ten hours. After acidifying with hydrochloric acid the excess formic acid and formaldehyde were evaporated on the steam-bath. The residue was made alkaline and the base steamed out, dried over solid potassium hydroxide and rectified to yield 165 g. (83%) of N-methylpiperidine,[15] b.p. 106–106.5°. The base was stored over barium oxide.

Dimethylpiperidinium Durenecarboxylate.—A mixture of 7.2 g. of dimethylpiperidinium iodide and 8.5 g. of silver durenecarboxylate was heated in refluxing benzene for two hours with frequent shaking. The benzene was decanted and the residue washed with dry ether. The residue was then extracted with several portions of dry methanol. There remained undissolved 6.9 g. (98%) of silver iodide. On removal of the methanol there remained a pale yellow viscous oil, 8.3 g. (95%), which crystallized after standing for a few days over phosphorus pentoxide. This salt was hygroscopic and was used without further purification.

General Description of Runs.—The ester, weighed to 0.001 g., was put by means of a small funnel into a Pyrex ampoule which when sealed had a volume of about 10 cc. N-Methylpiperidine, solvent and other additives were added through the same funnel. The ampoule was then cooled at −80°, sealed, allowed to come to room temperature, and well shaken. The reactions were carried out by placing the ampoules in a double-walled Pyrex tube about two inches in diameter which was connected at the bottom to a boiler flask and at the top to a reflux condenser (a modified Abderhalden drier). The temperature was controlled by the boiling of suitable liquids: xylene, *ca.* 140°; tetrachloroethane, *ca.* 160°; and ethyl oxalate, *ca.* 180°. After heating for the desired time a tube would be cooled, opened, and the contents taken into ether. After shaking with a slight excess of hydrochloric acid to remove amine and free the acid, the acidic material was extracted with sodium bicarbonate solution until acidification produced no turbidity. The combined alkaline extracts were re-extracted with ether and acidified. The acid which separated was collected, washed and dried to constant weight over phosphorus pentoxide. The ether layer and extracts containing ester were washed with saturated sodium chloride solution and then filtered through a layer of sodium sulfate. After removal of all solvent and drying to constant weight the amount of ester could be determined. The experiments were performed with enough care that over 90% of the starting material was accounted for in every case. Almost all experiments were checked by running duplicates. Unless otherwise stated all experiments involved 2×10^{-3} mole of ester, 0.5 cc. (4×10^{-3} mole) of N-methylpiperidine, and 4 cc. of dry methanol.

Solvent Effect.—Experiments at 140° for 48 hours with typical charges in the following solvents returned the methyl ester quantitatively: dioxane, acetone, benzene. In chloroform a trace (< 1%) of durenecarboxylic acid (hereinafter abbreviated to acid) was obtained and in carbon tetrachloride tarry materials were formed. In nitrobenzene 5% of acid was obtained in 48 hours and 8% in 97 hours. When no solvent was used only a trace of acid was obtained after 120 hours. In methanol, a 91% yield of acid was obtained. Accordingly a series of typical reactions involving methyl durenecarboxylate at 140° for 50 hours in various alcohols was studied. In each case pure methyl ester (no ester interchange was ever noted), sufficient to bring the material accounted for to over 90%, was recovered in addition to the following yields of acid: methanol, 90%; ethanol, 79%; 1-propanol, 70%; 2-propanol, 48.5%; 1-butanol, 62%; *t*-butyl alcohol, 8%; 1-pentanol, 48.5%; diisobutylcarbinol, 5.4%; and 2-methyl-1-pentanol, 19%. From these experiments, it is impossible to state whether the low conversion to acid is a result of a different point of equilibrium or a slower rate of attainment of equilibrium. No further work to clarify this point was done.

In one experiment, which involved heating a solution of 10 g. of methyl durenecarboxylate and 15 cc. of N-methylpiperidine in 100 cc. of dry 1-butanol in a sealed tube at 150° (furnace) for 48 hours, no butyl methyl ether could be detected on distillation of the reaction mixture through a column. The yield of durenecarboxylic acid was 65%. In a similar half-scale experiment 2 g. of butyl methyl ether (b.p. 69–70°, prepared from sodium butoxide and methyl iodide) was added to the charge and 1.7 g. was recovered by rectification through the same column. Since this proves that butyl methyl ether could be detected if formed, these experiments show that there is insufficient *n*-butoxide ion (formed from reaction (3)[16]) to form butyl methyl ether by a nucleophilic attack on the methyl ester carbon. Such a reaction, therefore, is not involved to any important extent in the formation of carboxylate ion (and thence, acid). Presumably, a similar situation exists with the other alcohols although we have not established this point.

$$[R_3N + C_4H_9OH \rightleftarrows R_3NH^+ + C_4H_9O^-] \qquad (3)$$

The effect of concentration of methanol on the rate of reaction was examined by determining the amount of acid formed after heating for six hours at 140° the usual equivalent quantities of methyl ester and amine with varying amounts of methanol. Expressing the concentration as moles of ester per liter of solution the results were as follows: no solvent, 0; 4 moles/l., 54%; 2, 59%; 0.5, 40%; and 0.25, 29%. Thus, with the 4 molar solution, the reaction medium was still not most favorable for reaction; with the 2 molar solution the medium was more favorable; as more

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[11] Purified by recrystallization from alcohol of a sample generously supplied by the Esso Laboratories, Elizabeth, New Jersey.

[12] Compare R. Willstätter and H. Kubli, *Ber.*, **42**, 4151 (1909).

[13] O. Jacobsen, *ibid.*, **22**, 1223 (1889), gives 59°.

[14] All microanalyses by Mrs. E. Klotz.

[15] H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, This Journal, **55**, 4576 (1933).

[16] J. R. Schaefgen, M. S. Newman and F. H. Verhoek, *ibid.*, **66**, 1847 (1944).

dilute solutions were involved, the usual drop in yield expected because of the dilution effect became apparent.

Effect of Variation of Alkyl Component of Ester.—This variable was studied by heating the methyl, ethyl, propyl, isopropyl, isobutyl and *t*-butyl esters of durenecarboxylic acid with amine in methanol. Blank experiments in which the amine was omitted were also carried out. The results are summarized in Table I. It can be seen that the esters fall in the order to be expected if the similarity to the Menschutkin reaction is recalled.[17] With the *t*-butyl and isobutyl esters pyrolysis (independent of amine influence) is the main reaction. In no case was the recovered ester contaminated with methyl ester.

Salt Effect.—Duplicate experiments at 140° for 5 hours, except for the addition to one of 0.002 g. and to the other of 0.2 g. (1.50×10^{-3} mole) of the hydrochloride of N-methylpiperidine to the usual charge of methyl ester (2.0×10^{-3} mole), amine (4.0×10^{-3} mole), and methanol (4 cc.) indicated that there was little if any effect on the yield of durenecarboxylic acid produced by the added salt and no noticeable trend.

TABLE I

REACTIONS OF ALKYL DURENECARBOXYLATES WITH N-METHYLPIPERIDINE IN METHANOL (2.0×10^{-3} MOLE, 4.0×10^{-3} MOLE AMINE, 4 CC. OF METHANOL)

$(CH_3)_4C_6HCOOR$ R =	Ester reacted in 25 hours, % At 140°	160°	180°
Methyl	81(0)[a]		
Ethyl	6	8(0)	14(0)
Propyl	1	3(0)	6(0)
Isopropyl	0	0	0(0)
Isobutyl	Trace	3(3)	6(6)
t-Butyl	59(59)	89(86)	

[a] The figures in parentheses represent % ester reacted when amine was omitted.

When experiments were conducted with added sodium methoxide, it was observed that the added methoxide ion produced durenecarboxylic acid in the absence of amine, undoubtedly with the formation of dimethyl ether, as

$$C_{10}H_{13}COOCH_3 + NaOCH_3 \longrightarrow C_{10}H_{13}COONa + CH_3OCH_3 \quad (4)$$

We made no attempt to confirm this in view of the fact that such a reaction has been well established.[18] When both amine and methoxide were added, the amount of acid produced was just about that to be expected from the independent reactions. No catalytic effect was noticed.

Equilibrium Studies.—The low conversions of methyl durenecarboxylate to acid by heating with *t*-amine in solvents such as benzene, dioxane, acetone and nitrobenzene might be a result of the effect of solvent on the position of equilibrium or on the rate of approach to equilibrium (5).

$$C_5H_{10}NCH_3 + C_{10}H_{13}COOCH_3 \rightleftarrows (C_{10}H_{13}COO^-)(C_5H_{10}N(CH_3)_2)^+ \quad (5)$$

Accordingly separate experiments involving the heating of equimolar amounts of reactants on the one hand and product on the other in methanol, dioxane and nitrobenzene at 140° for 280 hours were performed. In methanol, a true equilibrium was at hand in which the salt greatly predominated, the amounts of isolated materials in both cases being 4% of ester and 88% of salt (estimated by acidification and weighing of durenecarboxylic acid). In dioxane: when starting with amine and ester, 90% of ester was recovered and no acid at all; starting with quaternary salt 89% of ester and 6% of salt were isolated. Thus the point of equilibrium in dioxane is far on the ester side. In nitrobenzene: when starting with amine and ester, 70% of ester and no acid were obtained; starting with quaternary salt, 70% of ester and 11% of acid were obtained. Thus the point of equilibrium is far on the ester side in nitrobenzene. The material balance in this solvent was poor because of the formation of a fair amount of discolored decomposition products undoubtedly arising from interaction with the solvent.

COLUMBUS 10, OHIO

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[17] E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 250 (1935), found for the reactions of alkyl iodides and trimethylamine in alcohol the following relative rates: methyl, 100; ethyl, 8.8; propyl, 1.7; isopropyl, 0.2.

[18] J. F. Bunnett, M. M. Robinson and F. C. Pennington, THIS JOURNAL, **72**, 2378 (1950), and references therein.

NOTES

The Boiling Point of Alkane Diols as an Additive Property

BY H. J. BERNSTEIN

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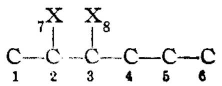
It has been shown[1-4] that the non-bonded interactions will account for the additive properties of the isomeric alkanes. It is of interest therefore to investigate whether non-bonded interactions will also account for the additive properties in the straight chain and branched alkane diols in which there is considerable hydrogen bonding.

A convenient way of taking non-bonded interactions into account so as to distinguish between the isomeric diols is to consider interactions which are two and three bonds apart only. Further, let us assume that the hydroxyl groups may be considered as single particles which we shall call X. We define the contribution to the additive property from interaction between a carbon atom and X which are two and three bonds apart as p_{cx_2} and p_{cx_3}, respectively; the contribution from interaction between two carbon atoms which are two and three bonds apart as p_{cc_2} and p_{cc_3}, respectively; and that due to X with X three bonds apart as p_{xx_3}.

The additive molecular property under consideration may be written as

$$P = A + a_{cx_2}p_{cx_2} + a_{cx_3}p_{cx_3} + a_{cc_2}p_{cc_2} + a_{cc_3}p_{cc_3} + a_{xx_3}p_{xx_3} \quad (1)$$

where *A* is a constant for all molecules and the coefficients *a* are determined for each molecule by inspection of its graphic formula. For example in 2,3-hexanediol shown in the figure there are four



$$\underset{1}{C}-\underset{2}{\overset{{}_7X}{\overset{|}{C}}}-\underset{3}{\overset{X_8}{\overset{|}{C}}}-\underset{4}{C}-\underset{5}{C}-\underset{6}{C}$$

[1] W. J. Taylor, J. M. Pignocco and F. D. Rossini, *J. Research Bur. Standards*, **34**, 413 (1945).

[2] H. Wiener, *J. Chem. Phys.*, **15**, 766 (1947); THIS JOURNAL, **69**, 17, 2636 (1947).

[3] J. R. Platt, *J. Chem. Phys.*, **15**, 419 (1947).

[4] H. J. Bernstein, *ibid.*, **19**, 140 (1951); **20**, 263 (1952).