sodium hydroxide solution essentially as described above for IVa. After stirring for 36 hr., the mixture was worked up to give 0.52 g. (33%) of phthalic acid, m.p. 187–188° and at 192–193° (sealed tube) after one recrystallization from water. Lit.[33] m.p. 191° (sealed tube) (identified as described above).

Independent synthesis of XXII was accomplished by refluxing a solution of 41.6 g. (0.225 mole) of *o*-xylyl bromide and 23.7 g. (0.225 mole) of 2,2′-iminodiethanol in 400 ml. of acetonitrile for 1.5 days. The acetonitrile was distilled, and a cold solution of 13.0 g. of sodium hydroxide in 100 ml. of water was added. The resulting basic mixture was extracted three times with ether and the ether extracts dried over anhydrous magnesium sulfate. The solvent was removed, and the residue was distilled to give 34.0 g. (72%) of amino dialcohol XXII, b.p. 153–155° at 0.55 mm. and at 172–174° at 0.95–1.00 mm. on redistillation.

Anal. Calcd. for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.63; H, 9.20; N, 6.57.

The infrared spectrum of this product was identical with that of XXII obtained from the rearrangement of quaternary salt XXI, except for a very small absorption at 700 cm.$^{-1}$ in the spectrum of the latter, which was probably due to the presence of a trace of amino alcohol XXIII.

DURHAM, N. C.

---

(33) See ref. 22, p. 192.

[CONTRIBUTION NO. 1102 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Direction of Opening of Styrene Oxide by Acetic Acid[1]

THEODORE COHEN, MARYLOU DUGHI, VINCENT A. NOTARO, AND GERALDINE PINKUS

Received August 10, 1961

Oxidation of the acetolysis products of styrene oxide after equilibration for various lengths of time gives mixtures of phenacyl acetate (XIII), acetylmandelic acid (XIV), 2-acetoxy-2-phenylethyl acetylmandelate (XVIII), 2-acetoxy-1-phenylethyl acetylmandelate (XIX), and benzoic acid. The variation with time of the ratio of acetylmandelic acid to phenacylacetate indicates that the predominant product of the ring opening reaction is 2-acetoxy-2-phenylethanol (XII) and that this rearranges slowly in the reaction medium to a mixture rich in 2-acetoxy-1-phenylethanol (X). A mechanism for the formation of the complex esters XVIII and XIX is proposed.

Eliel[2] has called attention to the confusion that sometimes arises in the study and interpretation of the openings of unsymmetrical epoxides due to contradictory experimental results. The reasons which he lists for this state of affairs include difficulties in separating and analyzing for the two isomeric products, rearrangements occurring during the synthesis of authentic specimens of possible isomeric products and sensitivity of the product ratio to minor changes in reaction conditions. To this list of difficulties, we should now like to add one more, namely the possibility of a rearrangement of the first formed isomer to the product that would have been formed first had it opened in the other possible direction.

The opening of epoxides[3] under acidic conditions is thought to occur by coordination of a proton or other Lewis acid with the epoxide oxygen followed by a nucleophilic attack on one of the carbon atoms of the epoxide ring. This latter step is thought to have both SN 1 and SN 2 character. Because of the formal positive charge on the ring oxygen atom, the transition state (Fig. 1) for the nucleophilic step in the acid catalyzed reactions is thought to involve more bond breaking than that for the nonacid catalyzed reactions.

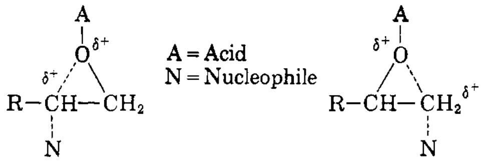


Fig. 1. Possible transition states for acid-catalyzed ring openings of unsymmetrical epoxides

Propylene oxide (I. R = methyl), with a variety of acidic reagents, gives mixtures of products (II and III. R = methyl, in the case of alcohols and phenols) arising from ring openings at the secondary and primary positions.[4–6] The acid ring openings of styrene oxide (I. R = phenyl), which has a phenyl group capable of stabilizing a positive charge, is supposed to involve a much higher degree of SN1 character, thereby favoring attack at the secondary carbon atom. This expectation is born out in the reaction of styrene oxide with methanol[7] and allyl alcohol.[8,9] In both cases, the very predominant

---

(1) (a) Taken, in part, from the Master's thesis of Marylou Dughi, at the University of Pittsburgh, 1960; (b) Present address of M.D.: Ciba Pharmaceutical Products Inc., Summit, N. J.

(2) E. L. Eliel, in *Steric Effects in Organic Chemistry,* M. S. Newman, ed., John Wiley and Sons, New York, 1956, p. 106.

(3) For recent reviews of epoxide reactions, see reference 2 and R. E. Parker and N. S. Isaacs, *Chem. Revs.*, **59**, 737 (1959).

(4) A. R. Sexton and E. C. Britton, *J. Am. Chem. Soc.*, **70**, 3606 (1948).

(5) H. C. Chitwood and B. T. Freure, *J. Am. Chem. Soc.*, **68**, 680 (1946).

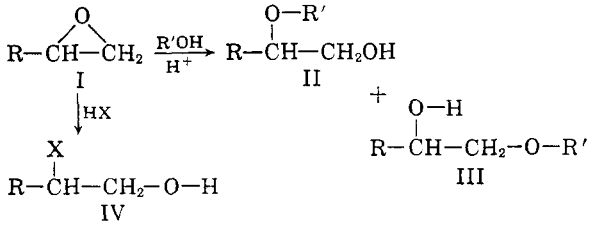
(6) C. A. Stewart and C. A. VanderWerf, *J. Am. Chem. Soc.*, **76**, 1259 (1954).

(7) W. Reeve and I. Christoffel, *J. Am. Chem. Soc.*, **72**, 1480 (1950).

(8) F. N. Hayes and C. Gutberlet, *J. Am. Chem. Soc.*, **72**, 3321 (1950). In this paper, the erroneous conclusions of Swern *et al.*[9] are corrected.

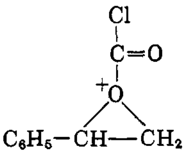
(9) D. Swern, G. N. Billen, and H. B. Knight, *J. Am. Chem. Soc.*, **71**, 1152 (1949).

product is the 2-alkoxy-2-phenylethanol (II. R = phenyl). Even when the ring opening of the protonated styrene oxide is brought about by very nucleophilic species, the S_N1 character seems to be retained. This is illustrated by the reaction of styrene oxide (I. R = phenyl) with pyridinium ions[10] and with hydrogen iodide.[11] In these cases, the primary alcohols (IV. X = pyridinium and I respectively) are formed.

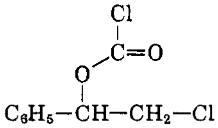


However, there are two anomalous cases in which acidic reagents are reported to react with styrene oxide to yield the product that would arise from cleavage of the *primary* carbon-oxygen bond. Thus carbonyl chloride is reported[12] to yield only 2-chloro-1-phenylethyl chloroformate (VI) while acetic acid gives 2-acetoxy-1-phenylethanol (X).[13] The former reaction presumably involves attack of chloride ion on an oxonium ion such as V while the latter reaction probably proceeds by attack of acetic acid or an acetate ion on the oxonium ion IX. In neither paper is the possibility rigorously excluded that some of the isomer arising from ring opening in the expected direction is also formed.[14] Nevertheless, the isolation of substantial quantities of VI and X does confuse the question of the direction of acid-catalyzed ring opening of styrene oxide and the apparent anomaly requires resolution.

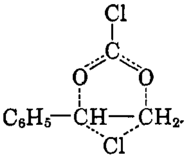
It should be noted that in both of the cases cited reasonable mechanisms exist for the interconversion of the products of the two possible modes of ring opening. Interconversion of VI and VIII could occur through an intermediate such as VII.[16] This rearrangement has close analogies in the rearrangements of acylated halohydrins discovered by Barton and King[17] in the steroids. The interconversion of X and XII could occur by way of the intermediate XI. Such oxygen to oxygen acyl transfers are well known. Indeed, Stevens, Dykstra, and Gillis[18] have shown that the initial products of the reactions of α-epoxy ethers with carboxylic acids rearrange by oxygen to oxygen acyl transfer. In the present case, the rearrangements of VIII and XII to VI and X could have possibly occurred before or during the work-up procedure.



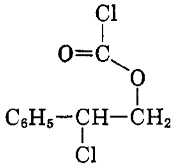
V



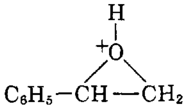
VI



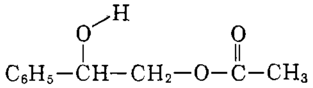
VII



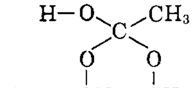
VIII



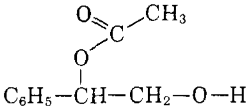
IX



X



XI



XII

We have undertaken a study of the reactions of styrene oxide with acetic acid and with carbonyl chloride in order to determine if the direction of ring opening in these cases is truly anomalous or whether the products isolated do not arise directly from the ring opening reaction but are rearranged isomers of the proximate products. In this paper we report the results of our investigation of the reaction of styrene oxide with acetic acid.

Since the two expected products (X and XII) would have similar properties and might be interconvertible, the ratio of the two products could best be determined by converting them under mild conditions to two daughter compounds which could be easily distinguished and which would be incap-

---

[10] L. C. King, N. W. Berst, and F. N. Hayes, *J. Am. Chem. Soc.*, **71**, 3498 (1949).

[11] C. Golumbic and D. L. Cottle, *J. Am. Chem. Soc.*, **61**, 996 (1939); M. Tiffeneau, *Ann. chim. et phys.*, **10**, 322 (1907).

[12] J. I. Jones, *J. Chem. Soc.*, 2735 (1957).

[13] W. J. Hickinbottom and D. R. Hogg, *J. Chem. Soc.*, 4200 (1954).

[14] Compound VI was identified[12] by hydrolysis to a chloro alcohol assigned the structure 2-chloro-1-phenylethanol. Although the method of arriving at this conclusion is not stated, the assumption is probably valid (although contamination by the isomeric 2-chloro-2-phenylethanol is not precluded) since the refractive index reported by Jones[12] is identical to that reported[15] for an authentic sample of 2-chloro-1-phenylethanol. The structure of the alcohol X was determined[13] by oxidation to phenacyl acetate. However, a yield for the oxidation was not reported and it is not clear from the experimental section whether or not acetylmandelic acid, the oxidation product of XII, would have been isolated if it had been present.

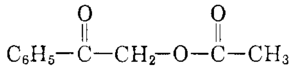
[15] W. E. Hanby and H. N. Rydon, *J. Chem. Soc.*, 114 (1946).

[16] It is also conceivable that an intermediate similar to VII could be formed directly from V by cleavage of the bond between the oxygen and secondary carbon followed by attack of the carbonyl oxygen on the positive benzylic carbon. In this case isotopic labeling experiments would be necessary in order to establish the direction of opening.

[17] D. H. R. Barton and J. F. King, *J. Chem. Soc.*, 4398 (1958).

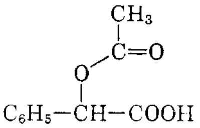
[18] C. L. Stevens and B. T. Gillis, *J. Am. Chem. Soc.*, **79**, 3448 (1957); C. L. Stevens and S. J. Dykstra, *J. Am. Chem. Soc.*, **75**, 5975 (1953).

able of interconversion. In order to avoid the necessity of isolating X and XII subsequent to the acetic acid reaction, we chose chromium trioxide oxidation in aqueous acetic acid as the means of converting X and XII to the easily distinguished and separable compounds, phenacyl acetate (XIII) and acetylmandelic acid (XIV).



$C_6H_5-C(=O)-CH_2-O-C(=O)-CH_3$

XIII



XIV

RESULTS AND DISCUSSION

The absence of the strong styrene oxide absorption at 871 cm.$^{-1}$ in the infrared spectrum of the product of a two-hour reaction of styrene oxide with glacial acetic acid at room temperature indicated that reaction was essentially complete under these conditions. It was therefore decided to carry out the reaction of styrene oxide and acetic acid for lengths of time varying from two hours to several weeks and to determine the ratio of the two oxidation products XIV to XIII in each of these runs. A decreasing ratio with time would then indicate that the initial product was indeed the primary alcohol (XII) and that it was rearranging to the secondary alcohol (X) in the acetic acid solution.[19]

Complete oxidation of the reaction products with chromium trioxide in aqueous acetic acid at room temperature in a period of two and one-half hours required a considerable excess of the oxidizing agent. Under these conditions, the acid fraction was found to contain benzoic acid as well as acetylmandelic acid. Fortunately, these two components could be quantitatively determined by ultraviolet analysis. However, control experiments indicated that both of the primary oxidation products, phenacyl acetate (XIII) and acetylmandelic acid (XIV) were partially (24% and 14%, respectively)[20] converted into benzoic acid when subjected to the oxidizing conditions.[21] The data are summarized in Table I.

TABLE I

Length of Time, Hr.[a]	Yield, % Benzoic acid	XIV	XIII	Other neutral material[b]	Yield XIV/Yield XIII
2	16	40	6.1	17	6.6
12	18	33	10	18	3.3
64	14	38	24	17	1.6
742	11	25	44	22	0.58

[a] Room temperature. [b] Computed on the basis that it is exclusively XVIII and XIX.

Whereas the acid fractions were found by ultraviolet analysis to consist only of acetylmandelic and benzoic acid contaminated with acetic acid, similar analyses of the neutral fractions indicated the presence of both phenacyl acetate and another material. As shown below, this material, which does not absorb in the ultraviolet region used for analysis of the phenacyl acetate, consisted mainly of 2-acetoxy-2-phenylethyl acetylmandelate (XVIII) and 2 - acetoxy - 1 - phenylethyl acetylmandelate (XIX), both probably produced during the oxidation of the glycol monoacetates, X and XII. The yields of the nonketonic neutral material given in the fifth column of Table I are computed on the basis that it consists exclusively of XVIII and XIX.

A number of factors which tend to minimize the *quantitative* significance of the data can be cited. The glycol monoacetates (X and XII) are not quantitatively converted to phenacyl acetate (XIII) and acetylmandelic acid (XIV). Both are converted in part to the complex esters XVIII and XIX and to benzoic acid. The minor fluctuations in the total yields of products and in the yields of acetylmandelic acid are probably due to small variations in the efficiencies of the several extractions required in each run and to slight variations in the rate of addition of oxidizing agent leading to inexact temperature control.

Some of these factors are partially cancelled by examining the ratios of the yields of acetylmandelic acid to those of phenacyl acetate. These are given in the last column of Table I. Results similar to those of the 742-hour run were obtained when the mixture of styrene oxide and acetic acid was heated on a steam bath for two hours and then allowed to remain at room temperature for 450 hours. Oxidation produced acetylmandelic acid and phenacylacetate in a molar ratio of 0.40. The sharp decrease of this ratio with reaction time clearly allows the *qualitative* conclusion that the predominant product of the reaction of styrene oxide with glacial acetic acid is 2-phenyl-2-acetoxyethanol (XII), the product of ring opening at the carbon atom most capable of bearing a positive

---

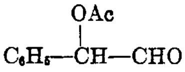
(19) Hickinbottom and Hogg[18] allowed the reaction mixture to stand for two days and then distilled the products.

(20) Of course, these yields must be considerably higher than those actually produced from XIII and XIV during the oxidation of the glycol monoacetates, X and XII. This follows from two factors: (i) During the oxidation of X and XII the concentration of chromic acid must decrease rapidly due to its expenditure in the conversion of X and XII to XIII and XIV, whereas in the control oxidations of XIII and XIV under the same conditions the chromic acid is used up much more slowly, and (ii) during the 2.5-hr. oxidation of X and XII, the concentrations of XIII and XIV must rise from zero to a maximum and then decrease gradually, whereas in the control oxidations, these two substances are present at their highest concentration at the start of the reaction and the material is therefore subject to the action of the oxidizing agent for a longer period.

(21) However, some of the benzoic acid produced in the oxidation of the reaction products of styrene oxide with acetic acid might have been formed by oxidation of small amounts of phenylacetaldehyde, a product of the ring opening reaction observed by Hickenbottom and Hogg.[18]

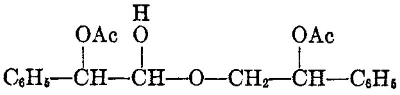
charge. The ring opening reaction is then followed by a comparatively slow equilibration of XII and whatever X might be formed to a mixture containing predominantly X. The results of the reaction of styrene oxide with acetic acid do not thus require a special mechanistic interpretation.

The esters XVIII and XIX were isolated in large scale runs by removing the phenacyl acetate from the neutral fraction with Girard's reagent P and distilling the remainder. The liquid distillate and the crystalline residue had infrared spectra which were very similar except in the fingerprint region. An elemental analysis and molecular weight determination on the crystalline material indicated the formula $C_{20}H_{20}O_6$. Vigorous saponification of both liquid and solid yielded styrene glycol and mixtures of acids. The odor and infrared spectra of the latter indicated that they were composed of an aromatic acid contaminated with acetic acid. The ester XVIII was prepared by treating the product (very predominantly 2-acetoxy-2-phenylethanol, XII) of a two-hour acetolysis of styrene oxide with acetylmandelyl chloride. The crystallized distillate was found to be identical with the solid obtained in the isolation experiments. The ester XIX was prepared by similar acylation of the product of a two-day acetolysis after it had been equilibrated in the acetic acid reaction mixture for several hours on a steam bath. Distillation of the acetylated product yielded a liquid, the infrared spectrum of which in the fingerprint region was distinctly different from that of the solid ester XVIII. The residue from the distillation was predominantly this solid ester XVIII. Comparison of the infrared spectrum of the liquid distillate from the isolation experiments with those of the esters XVIII and XIX indicated that this liquid is a mixture of XVIII and XIX, somewhat richer in the latter component. These syntheses of XVIII and XIX lend support to the hypothesis that the first formed product of the acetolysis of styrene oxide is slowly rearranged by remaining in the acetic acid medium and that this rearrangement involves oxygen to oxygen acyl transfer.



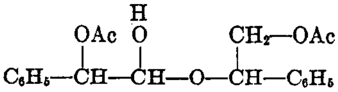
$C_6H_5-\underset{}{\overset{\displaystyle OAc}{\overset{|}{C}}}H-CHO$

XV



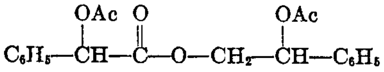
$C_6H_5-\overset{\displaystyle OAc}{\overset{|}{C}}H-\overset{\displaystyle \overset{H}{O}}{\overset{|}{C}}H-O-CH_2-\overset{\displaystyle OAc}{\overset{|}{C}}H-C_6H_5$

XVI



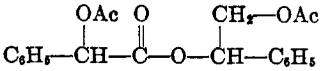
$C_6H_5-\overset{\displaystyle OAc}{\overset{|}{C}}H-\overset{\displaystyle \overset{H}{O}}{\overset{|}{C}}H-O-\overset{\displaystyle CH_2-OAc}{\overset{|}{C}}H-C_6H_5$

XVII



$C_6H_5-\overset{\displaystyle OAc}{\overset{|}{C}}H-\overset{\displaystyle O}{\overset{\|}{C}}-O-CH_2-\overset{\displaystyle OAc}{\overset{|}{C}}H-C_6H_5$

XVIII



$C_6H_5-\overset{\displaystyle OAc}{\overset{|}{C}}H-\overset{\displaystyle O}{\overset{\|}{C}}-O-\overset{\displaystyle CH_2-OAc}{\overset{|}{C}}H-C_6H_5$

XIX

Esters of the type XVIII have been frequently observed[22] as products of the chromic acid oxidation of primary alcohols. The production of both esters, XVIII and XIX, can be explained by assuming that the intermediate aldehyde (XV), arising from the oxidation of the primary alcohol (XII), is further oxidized in part by way of the hemiacetals, (XVI and XVII) derived from XV and the primary and secondary alcohols (XII and X). Adequate precedent exists for this type of scheme.[22] The oxidation of the hemiacetals could proceed by a mechanism analogous to the chromate ester[23] or hydride abstraction[24] mechanisms previously proposed for the oxidation of aldehyde hydrates.

EXPERIMENTAL[25]

Reactants. Eastman styrene oxide was distilled before use, b.p. 40.5–41° (0.5 mm.), n^{20}_D 1.5368.

Acetolysis runs. The procedure was the same for each of the four runs of Table I. The 64-hr. run is described.

To a solution of 2.017 g. (16.7 mmoles) of styrene oxide in 20 ml. of glacial acetic acid which had been allowed to remain at room temperature for 64 hr. was added dropwise a solution of 4.42 g. (44.2 mmoles) of chromium trioxide in a minimum quantity of 75% acetic acid. During the addition, the reaction mixture was swirled and cooled in an ice bath. After 2.5 hr. at room temperature, the reaction mixture was diluted several fold with water and extracted with ether in a continuous extraction apparatus for 5 hr. A 10% aqueous solution of sodium carbonate was mixed in portions with the ether extract until carbon dioxide evolution ceased. The organic phase was washed with a dilute solution of sodium carbonate and with water. The combined aqueous phase was washed with ether and the extract added to the organic phase. The latter was dried with calcium sulfate and evaporated to yield a neutral fraction weighing 1.207 g. All of the prominent bands of phenacyl acetate were present in the infrared spectrum of this material. However, the absorption at 1742 cm.$^{-1}$ (ester C=O) was stronger than that at 1701 cm.$^{-1}$ (ketone C=O) whereas these peaks are of equal intensity in the spectrum of phenacyl acetate. This is undoubtedly due to the presence of the esters XVIII and XIX which absorb strongly in this region. Ultraviolet analysis indicated that this fraction contained 4.01 ± 0.04 mmoles (0.715 g.) of phenacyl acetate and, by difference, 0.492 g. of other neutral material.

The aqueous sodium carbonate solution was acidified with concd. sulfuric acid (cooling) and continuously extracted with ether for 6 hr. The extract was dried with calcium sulfate and evaporated to produce a semisolid which, as determined by its odor, still retained some acetic acid. The latter could be removed by storing the acid fraction in a vacuum desiccator over potassium hydroxide for 2 weeks. In this way, an acid fraction weighing 1.509 g. was obtained. All of the prominent bands of benzoic acid and of acetylmandelic

---

[22] W. A. Mosher and D. M. Preiss, *J. Am. Chem. Soc.*, **75**, 5605 (1953), and references cited therein.

[23] K. B. Wiberg and T. Mill, *J. Am. Chem. Soc.*, **80**, 3022 (1958); G. T. E. Graham and F. H. Westheimer, *J. Am. Chem. Soc.*, **80**, 3030 (1958); A. C. Chatterji and S. K. Mukhergee, *J. Am. Chem. Soc.*, **80**, 3600 (1958).

[24] J. Roček, *Tetrahedron Letters*, **5**, 1 (1959).

[25] Melting points were determined on a Kofler block with a stage calibrated thermometer. Infrared spectra were determined with a Perkin-Elmer Model 21 spectrophotometer with sodium chloride optics and ultraviolet spectra with a Cary Model 14 spectrophotometer. The microanalysis was performed by Alfred Bernhardt, Max-Planck-Institut für Kohlenforschung, Mulheim, Ruhr, Germany.

acid[26] were present in the infrared spectrum of this material. Ultraviolet analysis indicated that the fraction contained 2.28 ± 0.02 mmoles (0.279 g.) of benzoic acid and 6.34 ± 0.07 mmoles (1.230 g.) of acetylmandelic acid. In the other runs, the acetic acid was not removed as thoroughly, but it was found not to interfere with the ultraviolet analysis.

Ultraviolet analyses. Solutions in 95% alcohol were used for the spectral measurements. The Beer-Lambert equation, $\log \frac{I_0}{I} = a_s bc$ was found to hold over the concentration ranges used for phenacyl acetate, acetylmandelic acid and benzoic acid. In the case of phenacyl acetate, the wave length maximum at 279.5 mμ ($a_s = 1.18 \times 10^3$) was used for the measurements. The extinction coefficients of the other major components of the neutral fraction, the esters XVIII and XIX, at this wave length were negligible. In the case of benzoic acid, the maximum at 279 mμ ($a_s = 751$) was used for the measurements. The extinction coefficient of acetylmandelic acid at that wave length was found to be negligible in comparison. In the case of acetylmandelic acid, the maximum at 257 mμ ($a_s = 244$) was used. The spectrum of benzoic acid, the other component of the acid fraction, exhibited a minimum at that wave length but the extinction coefficient was nevertheless appreciable ($a_s = 611$) and the equation $\log \frac{I_0}{I} = a_{s_1}bc_1 + a_{s_2}bc_2$ was used, where the subscripts 1 and 2 refer to the quantities for acetylmandelic acid and benzoic acid, respectively. In the analyses for benzoic acid and phenacyl acetate, the extinction coefficients, a_s, were determined at four dilutions, while in the case of acetylmandelic acid, three dilutions were used.

Control oxidations of acetylmandelic acid and phenacyl acetate. When acetylmandelic acid (1.083 g., 5.57 mmoles) in 20 ml. of glacial acetic acid was subjected to the oxidation procedure (4.49 g. of chromium trioxide) used in the previous runs, there was obtained an acid fraction containing 0.788 mmole (14% yield) of benzoic acid and 3.68 mmoles of acetylmandelic acid by ultraviolet analysis. Phenacyl acetate (0.502 g., 2.81 mmoles) when subjected to the same conditions (4.49 g. of chromium trioxide) yielded an acid fraction containing 0.669 mmoles (24% yield) of benzoic acid and a neutral fraction consisting of 2.03 mmoles of recovered phenacyl acetate.

Isolation and structural investigation of nonketonic neutral material. A solution of 45 g. (0.38 mole) of styrene oxide in 315 ml. of acetic acid was allowed to remain at room temperature for two hr. The oxidation was then carried out as above using 99 g. (0.99 mole) of chromium trioxide. The resulting mixture was extracted four times with ether. Aqueous potassium hydroxide was stirred into the ether layer until the acids present were almost neutralized. The neutralization was then completed with sodium carbonate solution. During the separation of the alkaline layer from the ether layer and in the subsequent ether extractions of the aqueous layer, *n*-octyl alcohol and ethanol were added to break emulsions. The ether extract was dried with sodium sulfate and evaporated to produce 20.12 g. of a liquid residue containing a substantial amount of *n*-octyl alcohol. To a solution of this oil in 95% ethanol containing 10% acetic acid was added 10 g. of Girard's P reagent (Arapahoe Chemicals, Inc.) and the mixture was refluxed for 2 hr. The cooled reaction mixture was shaken with a mixture of water, ether, and saturated sodium chloride solution.[27] The ether layer was separated and washed successively with water, sodium bicarbonate solution, saturated sodium chloride solution, and finally with water. Evaporation of the solvent from the dried (sodium sulfate) extract yielded an oil which weighed 18.32 g. and which still retained the odor of *n*-octyl alcohol.

Distillation of all but 0.24 g. of this material at 1 mm. pressure produced a forerun containing octyl alcohol and phenacyl alcohol (b.p. 45–53°) and the following fractions: (1) 0.85 g., b.p. 103–110°; (2) 0.57 g., b.p. 112–164°; (3) 2.31 g., b.p. 165–170°, and a residue (5.0 g.) which was too viscous to be distilled. Fraction 1 was shown by infrared analysis to be a monoacetate of styrene glycol. Fractions 2 and 3 had similar infrared spectra with carbonyl absorption at 1718 cm.$^{-1}$ The residue, when mixed with ether and cooled, deposited colorless crystals of XVIII (0.165 g.), m.p. 82–88°. A somewhat purer sample (m.p. 86–93°) was obtained from the 0.24 g. of undistilled material. Several recrystallizations from petroleum ether (b.p. 64–66°) containing a trace of benzene brought the m.p. to 94.5–95°.

Anal. Calcd. for $C_{20}H_{20}O_6$: C, 67.40; H, 5.67; mol. wt., 356.4. Found: C, 67.54; H, 5.44; Rast mol. wt., 358.

The infrared spectrum of this solid in Nujol mull exhibited an acetate carbonyl band at 1721 cm.$^{-1}$ and a weaker ester carbonyl absorption at 1733 cm.$^{-1}$ In chloroform solution, the weaker band appeared as a slight inflection on the stronger peak. The infrared spectrum of the combined distillation fractions 2 and 3 exhibited a carbonyl absorption at 1718 cm.$^{-1}$ in chloroform solution. Except in the 770–690 cm.$^{-1}$ region, the spectrum of the distillation fractions, as a film, was very similar to that of the solid ester in Nujol mull. In this region, the liquid absorbed strongly at 755 and 676 cm.$^{-1}$ while the solid had four strong peaks at 756, 730, 702, and 690 cm.$^{-1}$ Comparison of the spectra of the liquid distillates with those of authentic samples of the two isomeric esters (see below) indicates that the liquid is predominantly 2-acetoxy-1-phenylethyl acetylmandelate, (XIX) but that it contains some of the isomeric ester (XVIII).

Hydrolysis of the solid (49 mg.) in boiling 6*N* sodium hydroxide solution for 2.5 hr. produced 30 mg. of an alcohol, m.p. 35–60, and 28 mg. of a liquid carboxylic acid fraction containing some acetic acid. Hydrolysis of a portion (1.06 g.) of the combined distillation fractions 2 and 3 in the same way produced 415 mg. of alcohol, m.p. 51–60° and 584 mg. of acid, again containing some acetic acid. Recrystallization of each of these alcohols from benzene-petroleum ether (b.p. 64–66°) yielded styrene glycol, m.p. 64.5–65.5, undepressed on admixture with an authentic sample (see below). The infrared spectrum of the alcohol was also identical to that of an authentic sample. The infrared spectrum of a film of the acid fractions exhibited definite aromatic absorption.

2-Acetoxy-2-phenylethyl acetylmandelate (XVIII). A solution containing 9.89 g. (82.2 mmoles) of styrene oxide in 60 ml. of glacial acetic acid was allowed to remain at room temperature for 2 hr. A portion (23 ml.) was made basic with an aqueous solution of sodium carbonate and then extracted several times with ether. Evaporation of the dried (sodium carbonate) ether extract yielded 4.48 g. of oil which presumably contained mostly unrearranged glycol monoacetate (XII). To a solution of this oil in 25 ml. of dry pyridine was added 5.67 g. (26.6 mmoles, about 4% excess) of acetylmandelyl chloride.[26] During the addition, the exothermic reaction was moderated by cooling in an ice bath. After the product had remained in a refrigerator overnight, enough water was added to dissolve the precipitated pyridine hydrochloride. The solution was then acidified with concd. hydrochloric acid and extracted with ether. The extract was washed with aqueous sodium hydroxide followed by water, dried over sodium sulfate, and the solvent was removed. The red oily residue (6.52 g.) was distilled at 1 mm. pressure. The following fractions were collected: (1) 0.67 g., b.p. 110–130°; (2) 0.61 g., b.p. 140–190°; (3) 2.41 g., b.p. 195–201°; (4) 0.668 g., b.p. 203–197°. Fraction 1 was identified as unreacted glycol monoacetate by infrared analysis. The infrared spectrum of fraction 3 as a film closely resembled that of the solid ester isolated from the styrene oxide acetic acid run. This fraction solidified on being mixed with ether. Recrystallization of the solid three times from a mixture of benzene and petroleum ether (b.p. 64–66°) gave colorless crystals, m.p. 93.5–94.5°. A further recrystallization from a

---

[26] F. K. Thayer, *Org. Synthesis*, **Coll. Vol. I,** 12 (1941).

[27] This procedure is that described in L. F. Fieser, *Experiments in Organic Chemistry*, 3rd ed., D. C. Heath and Co., Boston, 1955, p. 88.

mixture of alcohol and water brought the melting point to 94.5–95°.

2-Acetoxy-1-phenylethyl acetylmandelate (XIX). The remainder of the styrene oxide–acetic acid reaction mixture (see directly above) was allowed to remain at room temperature for several days and was then heated on a steam bath for 3 hr. to effect as complete rearrangement as possible to 2-acetoxy-1-phenylethanol (X). The acetic acid was distilled at atmospheric pressure, the last traces being removed under reduced pressure in a rotory evaporator, to yield 11.11 g. of glycol monoacetate. A portion was distilled at 1 mm. pressure and the following fractions were collected: (1) 1.084 g., b.p. 97–107°; (2) 3.54 g., b.p. 108–110°; (3) 0.34 g., b.p. 110–208°. Acylation of a portion (2.17 g.) of fraction 2 was carried out with 3.19 g. (14.8 mmoles) of acetylmandelyl chloride in the same manner as described in the above preparation, except that the acylation mixture was heated on a steam bath for 1 hr. The dark red oil (4.03 g.) which resulted was distilled at 1 mm. pressure. The rate of distillation was extremely slow and the thermometer was not in equilibrium with the vapor. Thus, no temperatures can be recorded. The infrared spectrum of one of the collected fractions (0.96 g.) exhibited carbonyl absorption at 1736 cm.$^{-1}$ (chloroform) and aromatic C—H bonding absorption at 757 and 689 cm.$^{-1}$ (film). This spectrum is easily distinguishable from that of the isomeric solid ester (XVIII) (see above). The residue from the distillation weighed 2.11 g. and its infrared spectrum as a film and in carbon disulfide solution indicated that it contained predominantly the isomeric ester (XVIII).

Styrene glycol. To a slurry of 0.368 g. (9.5 mmoles) of lithium aluminum hydride in 75 ml. of anhydrous ether, an ethereal solution of 1.70 g. (9.5 mmoles) of phenacyl acetate was added dropwise at such a rate as to maintain gentle refluxing. The reaction mixture was then heated for another hour at reflux. Water was slowly added to the cooled reaction mixture in order to decompose the excess hydride. Dilute sulfuric acid was added to dissolve the aluminum hydroxide. The ether layer was separated and the aqueous layer extracted six times with methylene chloride. The combined organic extract was dried over sodium sulfate and evaporated to yield 0.604 g. (4.4 mmoles, 46%) of crystalline material, m.p. 60–65°. Several recrystallizations from benzene–petroleum ether (b.p. 64–66°) raised the m.p. to 64.5–65.5° (lit.[28] m.p. 65–67°).

Acknowledgment. We wish to thank the National Science Foundation and the National Institutes of Health for their help in the purchase of the infrared and ultraviolet spectrophotometers, respectively.

PITTSBURGH 13, PA.

---

(28) S. Winstein and L. L. Ingraham, *J. Am. Chem. Soc.*, **77**, 1738 (1955).

[CONTRIBUTION FROM TOKYO INSTITUTE OF TECHNOLOGY]

The Rate of the Reaction of Isocyanates with Alcohols. II

MASAO SATO

Received January 1, 1961

In order to determine whether or not the equation proposed previously, $dx/dt = k_1(a - x)(b - x)^2 + k_2x(a - x)(b - x) + k_3(\text{cat.})(a - x)(b - x)$, is exactly applicable, the reactions of three isocyanates, *e.g.*, ethyl, propenyl, and phenyl isocyanates, with alcohols were studied in further detail. In noncatalyzed reactions, the k_1 value decreased a little and the k_2 value decreased considerably with increasing initial concentration. In the reaction carried out with a certain concentration of phenyl isocyanate and triethylamine, the k_3 value also decreased with increasing concentration of alcohols. The hydrogen bonding in the solutions was also investigated by infrared spectroscopy. From both results, kinetic and spectroscopic, it was concluded that in the reaction of isocyanates with alcohols the intermediate complex mechanism was operative, that hydrogen bonding among the reactants, the products, and the solvent was involved, and that the equation described above was not exactly applicable.

In previous communications,[1-3] the studies on 1-alkenyl isocyanates have been reported. The isocyanate is one of the staple compounds in organic chemistry, especially in the field of polymer chemistry, and it is also interesting to study the mechanism and kinetics of the reaction of the NCO group with another functional group. The kinetics and mechanism of the reaction with the OH group have been studied by many authors,[4-11] and it is commonly accepted that the reaction follows second-order kinetics,

$$dx/dt = k(a - x)^2 \qquad kt = x/a(a - x) \tag{1a}$$

$$dx/dt = k(a - x)(b - x) \qquad kt = \frac{2.303}{a - b}\log\frac{b(a - x)}{a(b - x)} \tag{1b}$$

However, this author proposed third-order kinetics and the following equation,[3]

$$dx/dt = k_1(a - x)(b - x)^2 + k_2x(a - x)(b - x) + k_3(\text{cat.})(a - x)(b - x) \tag{2}$$

By this mechanism the reaction of isocyanates with alcohols was explained satisfactorily, but it was not determined whether the k_1 and k_2 values in

---

(1) M. Sato, *J. Org. Chem.*, **26**, 770 (1961).

(2) K. Orita, M. Sato, and Y. Iwakura, *J. Chem. Soc. Japan, Ind. Chem. Sect.* (*Kogyo Kagaku Zasshi*), **64**, 1404 (1961).

(3) M. Sato, *J. Am. Chem. Soc.*, **82**, 3893 (1960).

(4) J. W. Baker and J. B. Holdsworth, *J. Chem. Soc.*, 713 (1947).

(5) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 9 (1949).

(6) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 19 (1949).

(7) J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 27 (1949).

(8) E. Dyer, H. A. Taylor, S. J. Mason, and J. Samson, *J. Am. Chem. Soc.*, **71**, 4106 (1949).

(9) S. Ephrain, A. E. Woodward, and R. B. Mesrobian, *J. Am. Chem. Soc.*, **80**, 1326 (1958).

(10) J. Burkus and C. F. Eckert, *J. Am. Chem. Soc.*, **80**, 5948 (1958).

(11) A. Farkas and K. G. Flynn, *J. Am. Chem. Soc.*, **82**, 642 (1960).