dried, was taken up in boiling petroleum ether (60–68°). Evaporation of the filtered solution left a colorless product (m.p. 74–76°) which, after one recrystallization, melted at 83–84°. A mixed melting point with authentic lichesterylic acid showed no depression. Ultraviolet analysis showed no evidence for simple hydrolysis to *dl*-lichesterinic acid.

Catalytic Reduction of *d*-Lichesterinic Acid.—The reduction of 540 mg. of *d*-lichesterinic acid was carried out in 200 ml. of glacial acetic acid over 200 mg. of platinum oxide catalyst. After 54.8 ml. of hydrogen (theoretical uptake for one mole, 40.7 ml.) had been consumed, the catalyst was removed by filtration, and the product isolated by dilution of the acetic acid solution with water. Extraction of the mixture with boiling petroleum ether (60–68°) followed by three recrystallizations from glacial acetic acid yielded 250 mg. (46%) of pure tetrahydroacid X, m.p. 135.5–136.5°.

Anal. Calcd. for $C_{19}H_{36}O_4$: C, 69.47; H, 11.05. Found: C, 69.58; H, 11.20.

The anhydride, m.p. 34° (uncor.), was obtained in 57% yield by dehydration of the diacid (82 mg.) with acetyl chloride (0.4 ml.), a reaction carried out in a sealed tube at 100° for one hour. After removal of the acetyl chloride by evaporation, the product was crystallized at Dry Ice–acetone temperature from petroleum ether (60–68°). The infrared spectrum possessed bands at 5.40 and 5.65 μ, indicative of a five-membered cyclic anhydride.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

Dehalogenative Decarboxylation[1]

BY WYMAN R. VAUGHAN AND ROBERT L. CRAVEN[2]

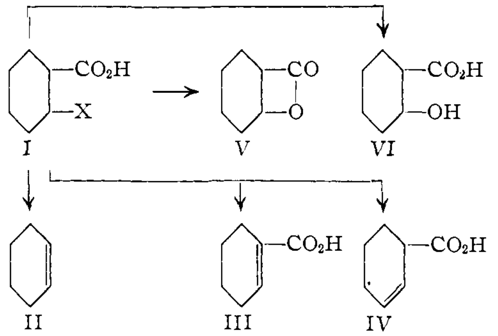
RECEIVED OCTOBER 18, 1954

The dehalogenative decarboxylation reaction has been investigated with respect to the stereochemistry of the starting material. In agreement with previous findings *trans* elimination is encountered. It is shown further that where *trans* disposition of the halogen and carboxyl is prevented (and involvement of neighboring groups is avoided) the reaction will not occur. The present evidence indicates that dehalogenative decarboxylation is not effected by purely electrophilic attack on the halogen.

The suggestion[3] that halide ion and carbon dioxide are eliminated in a *trans* sense recently has been amply confirmed.[4–7] However, none of the work cited does more than imply that the elimination *must* be *trans*, only that *trans* elimination occurs to the virtual exclusion of *cis* elimination[5–7] in non-ionizing solvents (*e.g.*, acetone). In more polar solvents (*e.g.*, ethanol or water) the products of *cis* elimination are formed, owing to a proposed duality of mechanism. This observation is the more disturbing since one of us has observed that exclusively *cis* elimination is in fact possible. However, by invoking neighboring group participation the *trans* character of eliminations may be preserved in the instance cited.

In order to see to what extent *cis* elimination may occur (without neighboring group participation) in a system of known and rigid structure, four 2-halocyclohexanecarboxylic acids were prepared: *cis*- and *trans*-2-chloro- and *cis*- and *trans*-2-bromocyclohexanecarboxylic acids.[8] Since essentially the same reactions were observed for both epimeric pairs and since the chloro acids were distinctly less reactive, the arguments presented herewith will be based principally on the reactions of the bromo acids, with qualitative similarity implied for the related chloro acids. The various possible reaction products are illustrated in Chart I.

CHART I



The present investigation involves three sets of reaction conditions: (1) aqueous bases—essentially nucleophilic attack, (2) sodium bicarbonate suspended in acetone,[7] and (3) electrophilic attack by silver ion in non-aqueous media.

The expected course of reaction for the *cis*-halo acids with aqueous bases, if the dehalogenative decarboxylation is required to be *trans*, should lead primarily to cyclohexene-1-carboxylic acid (III) with some *trans*-2-hydroxycyclohexanecarboxylic acid formed by direct displacement of halogen (and possibly some cyclohexene-3-carboxylic acid (IV)). The analytical data presented in Table I support this hypothesis.

The *trans*-halo acids under similar conditions should afford chiefly cyclohexene II and 2-hydroxycyclohexanecarboxylic acid, the *trans* isomer where sodium bicarbonate is the base,[9] and the *cis* isomer where the *p*H is higher.[4]

The analytical data in Table I confirm the hypothesis that dehalogenative decarboxylation and hydroxy acid formation are the predominant reactions, and the identification of *trans*-2-hydroxycyclohexanecarboxylic acid from the *trans*-bromo acid and sodium bicarbonate confirms the alkyl–oxygen

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[1] Abstracted from a portion of the Ph.D. Dissertation of Robert L. Craven, University of Michigan, 1954.

[2] American Brake Shoe Fellow 1951–1952; Albert B. Prescott Fellow, 1953.

[3] P. Pfeiffer, *Z. physik. Chem.*, **48**, 40 (1904).

[4] W. R. Vaughan and K. M. Milton, THIS JOURNAL, **74**, 5623 (1952).

[5] S. J. Cristol and W. P. Norris, *ibid.*, **75**, 632 (1953).

[6] E. Grovenstein and D. E. Lee, *ibid.*, **75**, 2639 (1953).

[7] S. J. Cristol and W. P. Norris, *ibid.*, **75**, 2645 (1953).

[8] W. R. Vaughan, R. L. Craven, R. Q. Little, Jr., and A. C. Schoenthaler, *ibid.*, **77**, 1594 (1955).

[9] A. R. Olson and R. J. Miller, *ibid.*, **60**, 2687 (1938); A. R. Olson and J. L. Hyde, *ibid.*, **63**, 2459 (1941); J. N. E. Day and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 693 (1941).

TABLE I

NUCLEOPHILIC ATTACK ON 2-HALOCYCLOHEXANECARBOXYLIC ACIDS IN WATER AT ROOM TEMPERATURE

Isomer	Base	Time, hr.	Reacn.,[a] %	Composition of product,[b] % Cyclohexene	Unsatd. acid	Hydroxy acid[c]
cis-Br	$NaHCO_3$	56	71.6	7.5	89.4	3.1
cis-Br	KOH	35	100	2.1	96.5	1.4
cis-Cl	KOH	4[h]	97.5	<1.0	85.7	13.3[d]
trans-Br	$NaHCO_3$	21	95.6	49.7	2.1	48.2[e]
trans-Br	KOH	59	100	74.9	<1.0	24.1
trans-Cl	Na_2CO_3[f]	56	36.2[g]	41.7	<2.8	55.5

[a] Based on precipitated silver bromide. [b] Actual percentage divided by per cent. reaction. [c] Value obtained by subtracting sum of preceding two columns from 100 since the hydroxy acids are extremely difficult to isolate. [d] 5.9% pure *trans*-hydroxy acid actually isolated. [e] 18.4% pure *trans*-hydroxy acid actually isolated: m.p. 106–108°; mixed m.p. 106–110°. [f] Runs on both chloro acids with bicarbonate and hydroxide were made at elevated temperatures which obviate simple methods of estimating the total quantity of cyclohexene produced. [g] There was recovered 63.8% of the original chloro acid. [h] At 65–75°.

cleavage of the lactone V, which is the expected intermediate. No attempt was made to isolate the hydroxy acid from reactions at higher *p*H values since previous work[4] has clearly shown the inverting character of this reaction for *trans*-2-halo acids.

The stereospecific *trans*-dehalogenative decarboxylation of β-haloacids in acetone over sodium bicarbonate already has been demonstrated,[7] and a glance at Table II shows that in the present rigid system very little cyclohexene was produced from the *cis*-acid.

TABLE II

NUCLEOPHILIC ATTACK ON 2-HALOCYCLOHEXANECARBOXYLIC ACIDS IN REFLUXING ACETONE OVER SODIUM BICARBONATE

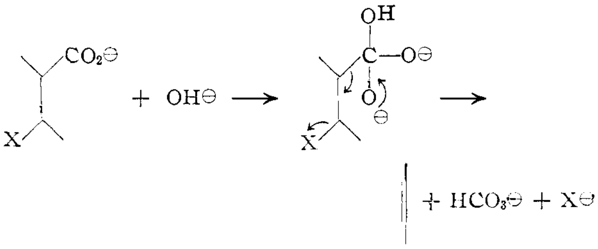
Isomer	Time, hr.	Reaction,[a] %	Composition of product,[b] % Cyclohexene[c]	Unsatd. acid	Hydroxy acid
cis-Br	18	98.8	5.2	94.8	0.0
trans-Br[d]	18	99.3	96.4	1.1	2.5[e]
trans-Cl	48	96.5	96.0	1.3	2.7 max.

[a] Based on precipitated silver bromide. [b] Actual percentage divided by per cent. reaction: see footnote *c*, Table I. [c] Value obtained by subtracting sum of succeeding two columns from 100: see text. [d] Averaged results of two identical runs, except for nitrogen atmosphere in second run. [e] A small quantity of water-soluble oil which detonated violently on contact with concentrated alkali was isolated. In a similar run under nitrogen no such product was obtained. Results were otherwise similar.

Thus, in view of the fact that sodium bicarbonate affords approximately the same relative quantity of cyclohexene in both water and acetone, it is apparent that the dual mechanisms[5-7] are all but inoperative in this system. It hardly seems likely that a dipolar ion[5-7] (*e.g.*, $\overset{+}{R}CH{-}CHRCO_2^-$) would be formed as readily in acetone as in water, thus it must be assumed that the extent to which apparent *cis*-dehalogenative decarboxylation (non-stereospecific) is encountered in acetone solution is the minimum possible. It may be attributed either to the dipolar mechanisms or, less probably, to base-induced epimerization at C^1. Failure to observe appreciably more apparent *cis*-dehalogenative decarboxylation (presumably *p*H-independent) in water may be attributed to a lower activation energy for competing *trans*-α,β-dehydrohalogenation (presumably *p*H-dependent).

It is clear from recent studies of dehalogenative decarboxylation[6,7] that the products formed by this reaction are obtained in *lower* yield as the ionizing power of the solvent increases. This is reasonably attributable to more effective competition by other processes *with the non-stereospecific mechanism* (dipolar ion), since the suggested stereospecific mechanism should operate with nearly equally intrinsic effectiveness in the various media used.

Some support for the hypothesis that *trans*-α,β-dehydrohalogenation is in fact competing with the non-stereospecific dehalogenative decarboxylation is found in the small decrease in yield of cyclohexene from the *cis* isomer when stronger base is present. On the other hand, the use of a stronger base with the *trans* isomer actually increases the yield of cyclohexene in the water reaction. It has been suggested that the better relative yield at higher *p*H values may be attributed to a change in mechanism for the stereospecific processes which would render more facile the formation of an olefin[4,10] (relative to β-lactonization)



Inasmuch as both dehalogenative decarboxylation and β-lactonization have been shown to be first order in the halo acid (anion) and *p*H-independent[6,10-13] in a range below *p*H $\approx$ 8.5, the difference in yield of olefin obtained in aqueous solution and in acetone with sodium bicarbonate poses a problem. Since the relative proportions of products should remain the same while the reactions remain within a given kinetic order,[14] it would appear that the change of solvent from water to acetone actually affects the mechanism of either or both reactions. For example, effective solvation of halogen may be essential to formation of the strained lactone system and helpful, but not essential, to dehalogenative decarboxylation. It was precisely this discrepancy in yields which led us to investigate the effect of silver ion on β-halo acids in acetone solution, and, while an exact analogy is not possible since the system we studied did not involve the anion of the acid, the fact that lactonization is effected by electrophilic attack, even on the undissociated acid, certainly indicates that anything, *e.g.*, solvation, which would tend to facilitate removal of the halogen will promote lactonization.

Where the initiating reagent is an electrophilic

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(10) W. R. Vaughan and R. Q. Little, Jr., THIS JOURNAL, **76**, 2952 (1954).

(11) W. Lossen and E. Kowski, *Ann.*, **342**, 128 (1905).

(12) G. S. Simpson, THIS JOURNAL, **40**, 674 (1918).

(13) H. Johansson and S. M. Magman, *Ber.*, **55B**, 647 (1922).

(14) E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 657 (1941).

species, the course of the reaction in acetone should be different from that previously encountered. If, as previous evidence seems to imply, the carboxylate *ion* is required for dehalogenative decarboxylation, no cyclohexene should be produced. The absence of detectable quantities of carbon dioxide from either the *cis* or *trans* acid and silver trifluoroacetate in acetone or acetonitrile confirms this. The course of the reaction thus is limited to dehydrohalogenation and β-lactone and/or hydroxy acid formation, and the difference between the percentage reaction and unsaturated acid is a clear indication of the extent of β-lactonization and/or hydrolysis.

In either acetone or acetonitrile, the principal product from the *cis*-bromo acid should be cyclohexene-1-carboxylic acid (III). Table III shows that these assumptions are correct, and the structure of III was confirmed by the bromination to 1,2-dibromocyclohexanecarboxylic acid. *trans*-2-Bromocyclohexanecarboxylic acid with silver ion should produce the β-lactone V in appreciable quantities, with cyclohexene-3-carboxylic acid as the chief product. The presence of V is confirmed by the presence of bands at 5.51 μ in isoöctane (from the acetone reaction) and 5.56 μ in acetonitrile. This is the expected position for the strained lactone carbonyl stretching frequency, and no comparable absorption is observed for the products from the reaction of the *cis*-acid with silver ion.

TABLE III

ELECTEOPHILIC ATTACK ON 2-BROMOCYCLOHEXANECARBOXYLIC ACIDS BY SILVER ION AT ROOM TEMPERATURE

Isomer	Solvent	Time, hr.	Reaction,[a] %	Unsatd. acid, %	V or VI, %
cis	Acetone	30	99.6	83.8	15.8
cis	Acetonitrile	24	59.0[b]	58.7	0.3
trans	Acetone	24	80.6	17.2	63.4
trans	Acetonitrile	24	51.0[b]	43.1	7.9

[a] Based on precipitated silver bromide. [b] After somewhat more than one month this value was increased to approximately 1.2–1.3 times the recorded figure. Analysis for unsaturated acid was not attempted on the longer runs.

That the unsaturated acid produced by dehydrobromination of the *trans*-acid by silver ion is in fact IV is indicated by spectroscopic analysis. While the infrared spectrum of the unsaturated product from the *cis*-acid possesses the bands at 5.90 and 6.11 μ (acetonitrile) present in the spectrum of III, the spectrum of the unsaturated product from the *trans*-acid possesses the corresponding bands at 5.82 and 6.02 μ (acetonitrile), the shorter wave lengths expected for an unconjugated carboxyl and isolated double bond. The carboxyl bands for the *cis*- and *trans*-bromo acids, for example, appear at 5.80 and 5.81 μ (acetonitrile), respectively.

Further support is adducible from the bromination of the unsaturated product derived from the *trans*-bromo acid. The brominated product, unlike that from III, was not crystallizable. If the bromination of both III and IV is *trans*,[15] it is seen readily that while III affords but one racemic dibromo acid, IV affords two, which might well account for the low-melting mixture obtained.

The greater proportion of dehydrobromination relative to hydrolysis and/or lactonization in acetonitrile (both isomers) may be attributed to the greater dielectric constant of this solvent,[16] which should facilitate ionization and dissociation of the bromine to give a carbonium ion. At the same time the greater extent of reaction in acetone may be due to the greater basic strength of acetone,[17] which would assist in the removal of a proton, a necessary condition for the formation of any of the products.

The *cis*-bromo acid can afford the *trans*-hydroxy acid only if water is available to permit displacement. Thus, in anhydrous acetonitrile no hydroxy acid is to be expected. However, since dehydrobromination with silver trifluoroacetate affords a strong acid which can promote self-condensation of acetone, of which water is a by-product, one might expect a certain amount of hydroxy acid to be formed in acetone solution. That cessation of reaction in acetonitrile may be attributed to increasing acidity of the medium was shown by preparing a mixture containing *trans*-2-bromocyclohexanecarboxylic acid and trifluoroacetic acid in acetonitrile in approximately the proportions present when the reaction of this isomer with silver trifluoroacetate had essentially stopped. Silver trifluoroacetate then was added, and no precipitate of silver bromide appeared on standing for several days. An infrared spectrum of the solutions showed bands due only to the solvent or the reactants. On addition to this solution of an amount of pyridine equivalent to the trifluoroacetic acid present, silver bromide began to precipitate at once, and upon standing for several weeks, with the further addition of pyridine from time to time, about 70% of the theoretical quantity of silver bromide was collected. An increase in the hydrogen ion concentration would adversely affect all factors tending to compensate for the positive charge of the potential carbonium ion (*e.g.*, ionization of the carboxyl and consequent dehalogenative decarboxylation or lactonization); thus, since acetonitrile has a poorer capacity for accepting protons[17] than has acetone, the reaction should be more difficult in the former solvent.

It now remains to account for the failure to observe the operation of the dipolar ion mechanism with our *cis*-halo acids in aqueous solution, *i.e.*, under conditions where it is found to be operative for cinnamic acid dibromide.[5-7] We have ascribed our failure to observe it to a comparatively lower activation energy in our system for the *trans*-α,β-dehydrohalogenation. Thus, if the activation energy for the dipolar ion mechanism could be lowered, this mechanism should become significant. The presence of a phenyl group on the β-carbon, as in cinnamic acid dibromide, is precisely what is required, for this group can effectively lower the energy barrier to ionization of the halide by its resonance-induced stabilization of the carbonium ion needed for the reaction. Inasmuch as there are numerous examples of apparently stereospecific de-

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[15] I. Roberts and G. E. Kimball, THIS JOURNAL, **59**, 947 (1937); S. Winstein and H. J. Lucas, *ibid.*, **61**, 2845 (1939).

[16] "International Critical Tables," Vol. VI, p. 84.

[17] W. Gordy and S. C. Stanford, *J. Chem. Phys.*, **9**, 204 (1941).

halogenative decarboxylations[18–22] of β-halo acids which do not possess an aryl group on the β-carbon, while at the same time those β-halo acids which do possess such an aryl group afford mixtures of *cis*- and *trans*-olefins[5–7,23–26] with aqueous bases, it is safe to ascribe instances of product formation *via* a non-stereospecific route to factors tending to promote carbonium ion formation at the β-carbon. Pure *cis* dehalogenative decarboxylation will be encountered only when participation by a neighboring polar group lowers the energy barrier so that it is comparable with that of possible competitive reactions.[4,27] Thus, barring the two preceding conditions, it may be stated unequivocally that dehalogenative decarboxylation of β-halo acids is a stereospecific reaction of the anion in which the elimination is *trans*. The reaction is favored over competing reactions by use of a solvent of low dielectric constant (*e.g.*, acetone) and the presence of a comparatively weak base (*e.g.*, bicarbonate). The present work supports previous findings[4,6,7] and further shows that hydroxy acid formation is eliminated by solvents of low solvating power for halide ion, whereas it is facilitated by way of β-lactonization, by electrophilic attack on the halogen.

Experimental[28]

β-Halo Acids.—Complete details for preparation of these compounds are reported in a previous paper.[8]

Analytical Procedures. 1. Extent of Reaction.—The total amount of halo acid reacting was determined, after extracting the olefinic fractions, by precipitating the halide ion with silver nitrate solution and weighing (except when the attacking reagent was silver trifluoroacetate, in which case the silver halide precipitated during the reaction and was filtered off as the first step in the work-up).

2. Unsaturated Products.—The main organic products of elimination were cyclohexene and cyclohexenecarboxylic acid. The amounts of these substances were determined by titration with bromine in a water–carbon tetrachloride system using a modification of a procedure described by Lewis and Bradstreet.[29]

The titration was tested on 5-meq. samples of redistilled cyclohexene, which were titrated, after being separated from a water–cyclohexene mixture, by the procedure used in the actual runs (see method A below).[30] The amount of cyclohexene calculated from the titration was consistently 3–5% below theoretical. Hence, a 4% blank has been included in the results recorded in Table I. Titrations of weighed samples of cyclohexenecarboxylic acid (better than 99% pure by neutral equivalent) gave values less than 2% below theoretical. Thus, a 2% blank is included in the results reported for this compound. After titration, the dibromo acid was isolated, purified and identified, by comparison with an authentic sample, in several of the runs. This acid could be recovered in yields of only about 30%, even from the titrations of pure cyclohexenecarboxylic acid.

In some of the reactions a little 2-hydroxycyclohexanecarboxylic acid, the product of the competing displacement reaction in aqueous medium, was isolated. This compound is so soluble in water that it could be recovered only by extraction with large volumes of ether after carbon tetrachloride extraction of the olefinic fractions (and after saturating the aqueous layer with ammonium sulfate).

Conditions and Procedures for Carrying Out the Reactions and Isolating the Products. A.—These reactions were run in a sealed separatory funnel at room temperature, and all were reactions with an inorganic base in aqueous medium. The halo acid (usually 0.005 mole) was placed in a separatory funnel to the stem of which was sealed a hollow ₸10/30 joint. Part of the solvent, 10–30 ml., also was added and the funnel was sealed with a 1-oz. serum bottle syringe stopper. An aqueous solution, 10–15 ml., containing a twofold excess of base was added by means of a hypodermic syringe.[31] After adding the base, the funnel was shaken, and as soon as all the acid had dissolved, 5–10 ml. of carbon tetrachloride was introduced (by syringe as were all subsequent additions for the extractions). The reaction was allowed to stand at room temperature with occasional shaking. At intervals the carbon tetrachloride layer was drawn off[32] directly into a pre-formed bromine solution without exposure to the atmosphere. The first extraction usually was not made until at least two hours after mixing the reactants.

When the formation of neutral olefin was judged to be complete, or so slow as to make further extraction impractical, the funnel was opened and the solution acidified with dilute sulfuric acid. The acidified solution, or, in some cases, suspension of solid or oil, was extracted with at least three portions of carbon tetrachloride. The combined extracts were washed once with water and the wash returned to the aqueous layer. Next, the volume of the carbon tetrachloride was reduced to 10–20 ml. by evaporation under an air stream and the titration for acidic olefin was run. Then the aqueous residue was treated with silver nitrate solution, and the precipitate of silver halide was collected and weighed.

B.—These reactions were run according to the general procedure of Cristol and Norris.[7] The halo acid (0.005–0.010 mole) was dissolved in 40–50 ml. of acetone, a twofold excess of solid sodium bicarbonate was added and the mixture was refluxed for 18–48 hours, usually under nitrogen. The solutions were stirred mechanically throughout the reflux period. In the longer runs it usually was necessary to add more acetone during the reaction. Stirring was especially important during the first three hours of heating to avoid a tendency to bump severely. After cooling to room temperature, the acetone was removed and the residues were added to excess dilute sulfuric acid, and the acidic solutions extracted with carbon tetrachloride. The extracts were titrated for acidic olefin, and the halide in the aqueous layer was treated with silver nitrate. No attempt was made to isolate or analyze for cyclohexene since the conditions used in removal of the acetone also would have completely removed any cyclohexene.

C.—These reactions were run on the bromo acids only, using silver trifluoroacetate as the attacking reagent. They were carried out at room temperature in glass stoppered flasks with both acetone and acetonitrile as solvents. Equivalent quantities (0.005 mole) of the reactants were dissolved in the solvent and mixed. Solid began to precipitate almost immediately. The solid was nearly white at first, especially in acetonitrile, but very rapidly became yellow, and, if exposed to light, brown. There was no evidence of carbon dioxide evolution even when the reaction stood for over a week connected to a bubbler immersed in saturated barium hydroxide solution.

In both solvents, the bulk of the precipitate formed within the first hour. The reaction then appeared to slow down markedly. In acetone, the reaction with the *trans* isomer was complete in 24 hours[33]; 80% of the *cis*-acid had reacted after 30 hours.[33] In acetonitrile, however, only

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[18] W. G. Young, R. T. Dillon and H. J. Lucas, THIS JOURNAL, **51**, 2528 (1929).

[19] W. M. Lauer and F. H. Stodola, *ibid.*, **56**, 1216 (1934).

[20] H. J. Lucas and A. N. Prater, *ibid.*, **59**, 1682 (1937).

[21] M. L. Sherrill and E. S. Matlack, *ibid.*, **59**, 2134 (1937).

[22] E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 2078 (1951).

[23] S. Reich, *Arch. Sci. Phys. Nat.*, **45**, 191 (1918); *cf. C. A.*, **12**, 1876 (1918).

[24] S. Reich and N. Y. Chang, *Helv. Chim. Acta*, **3**, 235 (1920).

[25] A. Dann, A. Howard and W. Davies, *J. Chem. Soc.*, 605 (1928).

[26] W. Davies, B. M. Holmes and J. F. Kefford, *ibid.*, 357 (1939).

[27] W. R. Vaughan and R. Q. Little, Jr., THIS JOURNAL, **76**, 4130 (1954).

[28] Melting points are uncorrected unless otherwise specified.

[29] J. B. Lewis and R. B. Bradstreet, *Ind. Eng. Chem., Anal. Ed.*, **12**, 387 (1940).

[30] Attempts to extract weighed samples of cyclohexene from water mixtures by the ordinary open separatory funnel procedure resulted in a loss by volatilization of about 25%.

[31] When the base was sodium bicarbonate, it was necessary first to evacuate the funnel partially, through a hypodermic needle attached to an aspirator.

[32] In most cases where the system had been evacuated, it was necessary to bleed air into the funnel before any carbon tetrachloride could be run out.

[33] Based on the amount of silver halide precipitated.

50-60% of the material had reacted after 24 hours.[33] Solid was still forming at a very slow rate but, after three weeks, which included several days of continuous shaking in contact with glass beads, only about 10% additional reaction had occurred.

In working up these reactions, the silver salt was first filtered off, washed with the appropriate organic solvent and the washes combined with the original filtrate. The solid then was washed with water, dried and weighed. Subsequent washing with dilute nitric acid and with aqueous sodium bicarbonate did not change the weight. When acetone was the solvent, it was removed, and the residue, after drying thoroughly in an evacuated desiccator, was dissolved in carbon tetrachloride and titrated for unsaturated acid. The reactions run in acetonitrile[34] were titrated directly.

To show the effect of strong acid on the reactions with silver trifluoroacetate in acetonitrile the following mixture was prepared. *trans*-2-Bromocyclohexanecarboxylic acid, 0.259 g. (0.00125 mole), was dissolved in 5 ml. of acetonitrile along with 0.453 g. of trifluoroacetic acid (0.00397 mole). To this was added 0.276 g. of silver trifluoroacetate (0.00125 mole) in 10-15 ml. of acetonitrile. This was approximately the condition of the actual run after solid stopped precipitating. On mixing, no solid formed and after standing for three days, there was only a very slight cloudiness in the solution. To this solution then was added 0.470 g. of pyridine (0.00594 mole); the solution was acid to moist litmus. Solid began to form at once, but slowly, and, after one week, 0.145 g. of silver bromide (0.000773 mole, 61.8% of theory) had precipitated.

Results.—Data are summarized in Tables I, II and III.

ANN ARBOR, MICHIGAN

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[34] Eastman Kodak Co. spectro grade. A blank titration in the presence of this acetonitrile was less than 1% in error.

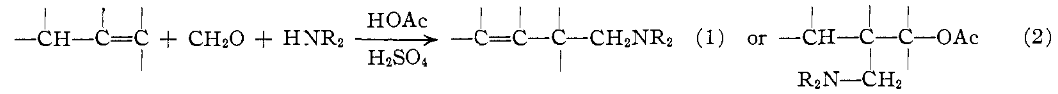
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

The Reaction of Formaldehyde and Secondary Amines with Some Olefins

BY G. F. HENNION, CHARLES C. PRICE[1a] AND VERNON C. WOLFF, JR.[1b]

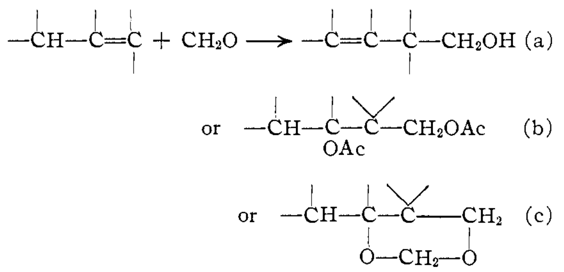
RECEIVED DECEMBER 3, 1954

α-Methylstyrene and β-pinene have been found to condense with formaldehyde and secondary amines in acetic acid-sulfuric acid according to reaction 1. Anethole under similar conditions reacted principally by equation 2 while styrene, cyclohexene and 1,1-diphenylethylene failed to react.



$$-\text{CH}-\text{C}=\text{C} + \text{CH}_2\text{O} + \text{HNR}_2 \xrightarrow[\text{H}_2\text{SO}_4]{\text{HOAc}} -\text{C}=\text{C}-\text{C}-\text{CH}_2\text{NR}_2 \quad (1) \quad \text{or} \quad -\text{CH}-\underset{\text{R}_2\text{N}-\text{CH}_2}{\text{C}}-\text{C}-\text{OAc} \quad (2)$$

The Prins[2] reaction of formaldehyde with olefins has been shown to result in three major types of products, depending on the olefin and/or the reaction conditions employed.



$$-\text{CH}-\text{C}=\text{C} + \text{CH}_2\text{O} \longrightarrow -\text{C}=\text{C}-\text{C}-\text{CH}_2\text{OH} \quad (a)$$

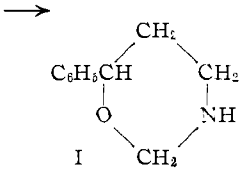
$$\text{or} \quad -\text{CH}-\underset{\text{OAc}}{\text{C}}-\text{C}-\text{CH}_2\text{OAc} \quad (b)$$

$$\text{or} \quad -\text{CH}-\text{C}-\text{C}-\text{CH}_2 \quad (c)$$

The course of these reactions may well all involve a common intermediate.[2b,3] The proposal that the formation of β,γ-unsaturated alcohols (a) proceeded through a pseudocyclic intermediate[3] has been supported by the work of Bain[4] and of Arnold.[5]

Meisel, Hartough and Dickert[6] recently have reported an extension of the Prins type reaction to the preparation of amino compounds.

$C_6H_5CH=CH_2 + CH_2O + NH_4Cl \longrightarrow$



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In addition to 6-phenyltetrahydro-1,3-oxazine (I), its N-bis-methylene derivative or its N-methyl derivative could be obtained by modifying the conditions for the reaction. The authors indicated that the reaction failed for secondary amines.

The work reported herein was undertaken in the hope that olefins more reactive than styrene toward formaldehyde might be induced to condense with secondary amines.

Experimental[7]

Reagents and products were fractionally distilled through a 35 × 1.2-cm. Vigreux column wrapped with aluminum foil (A) or a 40 × 1-cm. electrically heated spiral-packed column (B). Infrared spectra were recorded on a Baird (AB-1-178) or a Perkin-Elmer (model 21) spectrophotometer by Richard Boyle, Anthony Verbiscar or George Svatos and the curves are reproduced in the Ph.D. Dissertation of Vernon C. Wolff, Jr., Science Library, University of Notre Dame.

Dow Chemical Co. α-methylstyrene, Eastman Kodak Co. anethole and Hercules Powder Co. β-pinene were redistilled before use. The β-pinene, after three distillations through column B (15.8-plates) boiled at 56.5-57° (17 mm.), $n^{25}D$ 1.4752.

Methiodides were prepared by stirring a well-cooled solution of the amine in ethyl acetate while three equivalents of methyl iodide were added dropwise. The copious white precipitate was washed with ethyl acetate and recrystallized, usually from ethyl acetate-absolute ethanol.

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[1] (a) Department of Chemistry, University of Pennsylvania, Phila. 4, Pa.; (b) Eli Lilly and Co. Fellow, 1952-1954. Abstracted from the Ph.D. Dissertation of V.C.W.

[2] See, *e.g.*, (a) H. J. Prins, *Proc. Acad. Sci. Amsterdam.*, **22**, 51 (1919); (b) C. C. Price, F. L. Benton and C. J. Schmidle, THIS JOURNAL, **71**, 2860 (1949).

[3] C. C. Price, "Mechanisms of Reactions at the Carbon-Carbon Double Bond," Interscience Publishers, Inc., New York, N. Y., 1946, p. 45.

[4] J. P. Bain, THIS JOURNAL, **68**, 639 (1946).

[5] R. T. Arnold and J. F. Dowdall, *ibid.*, **70**, 2590 (1948).

[6] S. L. Meisel, H. D. Hartough and J. J. Dickert, U. S. Patent 2,647,117, 2,647,118, and 2,652,429 (*C. A.*, **48**, 4826 (1954)).

[7] Nitrogen analyses by G. M. Maciak, W. L. Brown, H. L. Hunter and W. J. Schenck, Eli Lilly and Co., Indianapolis, Ind.; carbon and hydrogen analyses by Micro-Tech Laboratories, Skokie, Ill.