

PREPARATION AND REACTIONS WITH AMINES OF
4,4,4-TRICHLORO-2-BUTENOIC ACID

by

JERRY LEROY WHITE

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STATEMENT OF THE PROBLEM

This thesis is concerned primarily with the improvement of existing methods or developing a new method of preparation of 4,4,4-trichloro-2-butenic acid (trichlorocrotonic acid) and the investigation of reactions this acid might undergo.

The purpose of this thesis is to indicate with a strong amount of evidence the probable structure of the new series of compounds discovered. The purpose in this regard is to use principles of analogy, of probable and logical course of reaction, and the process of elimination to deduce the most logical structure.

With this introduction, one can say that chemically the main purposes of this thesis are definitely expressed as follows:

I. Preparation of trichlorocrotonic acid.

- A. To try to improve the procedure and yields of the synthesis as given by von Auwers (2) who obtained this acid in 44% yield by dehydration of 4,4,4-trichloro-3-hydroxybutanoic acid.
- B. If attempts failed to improve von Auwers' procedure, it was desirable to develop a new procedure. Thionyl chloride offered excellent possibilities since good results have been obtained using this agent in dehydration of 4,4,4-trichloro-2-methyl-2-propanol (20). An alternative procedure would be the indirect dehydration of the corresponding acetate by pyrolysis.

II. Investigation of reactions of trichlorocrotonic acid.

- A. Fumaric acid is known to react with anthracene in the Diels-Alder reaction (26), and diethyl fumarate reacts with diethyl malonate in a Michael reaction (12) to give a 94% yield. Consequently, the similar trichlorocrotonic acid might be expected to undergo the same reactions.
- B. To treat trichlorocrotonic acid with a variety of significant amines and determine the nature of the products.

II B developed naturally in trying to obtain a Michael reaction using ethyl trichlorocrotonate with malonic ester catalyzed by piperidine.

HISTORICAL BACKGROUND

Only limited work has been carried out on reactions and preparations of 4,4,4-trichloro-2-butenoic acid. In 1923 K. von Auwers and coworkers prepared this compound, some of its derivatives, and elucidated its configuration (2) (3). Von Auwers prepared this compound from 4,4,4-trichloro-3-hydroxy butanoic acid by dehydration with acetic anhydride and sodium acetate in a 44% yield.

Only three other methods were found in the literature for the preparation of this acid. In one method the amide (25) was prepared in 5% yield from chloral and diacetylamine by a modified Perkin reaction. In the method of Kurien and coworkers (21) it is questionable whether 4,4,4-trichloro-2-butenoic acid was

actually obtained. In the latter, chloral was condensed with malonic acid in the presence of a small amount of pyridine which is the same as the method used by von Auwers (3) to prepare 4,4,4-trichloro-3-hydroxybutanoic acid except that von Auwers used a large excess of pyridine. The product obtained by Kurien and coworkers had the same melting point as the one obtained by von Auwers. The fourth method by Nesmeyanov, et al. (22) consisted of dehydrohalogenation of 3,4,4,4-tetrachlorobutanoic acid.

In 1954 Nesmeyanov and coworkers (22) questioned some interpretation in von Auwers' work; however, the trans configuration as shown by von Auwers was confirmed by Nesmeyanov.

Other than the classical derivatives prepared by von Auwers and Nesmeyanov, the only reaction concerning 4,4,4-trichloro-2-butenic acid, reported in the literature, was by Nesmeyanov, et al. (24) who demonstrated that this acid would undergo a Friedel-Crafts reaction with benzene. A similar Friedel-Crafts reaction with benzene has been reported by Grebenyuk and Tsukervanik (13) using α,α,α -trichlorocrotononitrile.

Although pyrolysis of esters to prepare simple types of olefins has been used extensively (5) (8) (26), a general literature search revealed no application of its use for the preparation of chloro-olefins. Also, no evidence was found where olefins were prepared from β -acetoxy acids; however, the pyrolysis of esters has been employed for olefin preparation from α -acetoxy acids and β -acetoxy nitriles (8). This is understandable since, in general, β -hydroxy acids are dehydrated

with ease by many reagents such as thionyl chloride, phosphorus pentoxide, sulfuric acid, and iodine (19).

The mode of preparation of an α -amino acid varies from the general α -halide acid plus amine type reaction to the more specific Strecker, hydantoin and Erlenmeyer azlactone syntheses (10) (11). There are many more specific reactions but further enumeration would be of little value for this thesis. There is no published report on the reaction of amines with 4,4,4-trichloro-2-butenic acid by which a nitrogen-substituted amino acid might be prepared.

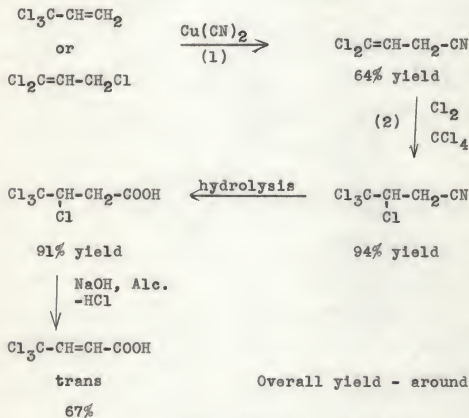
DISCUSSION

Preparations of Starting Materials

Since this thesis is concerned primarily with the reactions of 4,4,4-trichloro-2-butenic acid, hereafter called trichlorocrotonic acid for brevity, it was desirable to find a method of preparation with relatively high yields, short reaction sequence, and simple purification procedures. As reported in the historical background, von Auwers (2) prepared this acid in 44% yield from 4,4,4-trichloro-3-hydroxybutanoic acid, using sodium acetate and acetic anhydride as dehydrating agents. The starting 4,4,4-trichloro-3-hydroxybutanoic acid is easily obtained in nearly quantitative yields (3) by condensing readily available chloralhydrate and malonic acid in the presence of an excess of pyridine. However, the final dehydration step, as given by von Auwers, was somewhat long and tedious. Von Auwers (2) also

reported attempts to dehydrate the hydroxy acid by means of zinc chloride, formic acid, potassium bisulfate, phosphorus tri-chloride, phosphorus pentoxide, and concentrated sulfuric acid but these reagents were found unsatisfactory because of: (1) no reaction, (2) viscous products which resisted purification, and (3) poor yield.

There is only one other plausible method appearing in the literature for the preparation of trichlorocrotonic acid. This method, by Nesmeyanov, et al. (22) (23), originated in the process of structure proofs. This method is best described in an equation sequence as follows:



Obviously, this method has a low yield, long reaction sequence, and the starting 3,3,3-trichloropropene is not readily available.

The present work simplified the work-up procedure of von Auwers but the yields could not be improved. Moreover, other modes of dehydration were deemed unsatisfactory because of the possibility of destroying the trichloromethyl group.

Kundiger and coworkers (20) have reported good results in the dehydration of a similar structural compound, 3,3,3-trichloro-2-methyl-2-propanol, using thionyl chloride. Therefore, dehydration using thionyl chloride appeared to be a possible answer to the problems at hand. Numerous attempts using this method failed to yield greater than 5% of the desired acid. In each case, mostly tar formation occurred. Obviously, the starting hydroxy acid, intermediates, or trichlorocrotonic acid undergo undesirable reactions under the usual conditions employed with thionyl chloride.

The foregoing account has eliminated the more common methods of dehydration and, in fact, leaves only indirect dehydration as a possible improvement over the methods previously described. The pyrolysis of the acetoxy ester of 4,4,4-trichloro-3-hydroxybutanoic acid appeared to be of interest on four counts:

1. The necessary acetate was readily available in good yields.
2. Pyrolysis of this type of compound has not been reported

previously in the literature.

3. If this procedure were successful, would it be superior to von Auwers' method?

4. Since the proposed mechanism (26) for ester pyrolysis is a cyclic intermediate, viz.,



would the cis and/or trans isomer of trichlorocrotonic acid be obtained?

The results from the pyrolysis of 4,4,4-trichloro-3-acetoxybutanoic acid are summarized in Table 1. The general procedure is explained in the Experimental.

Pyrolysis did not take place at temperatures below 400°, and complete decomposition resulted at temperatures above 500° (see run 4). Run 2 exemplifies the importance of the rate in determining the completeness of pyrolysis. It is readily seen from the chart, the temperature for effective pyrolysis is between 425-490°. Since the lower range of 425-460 gives some starting material which was found to be somewhat difficult to separate from the product, the higher range of 475-490° was chosen because the product was essentially free of starting material. Pyrolysis has been successful using porous tile (28). Porous tile would appear to be an excellent inert media for pyrolysis because of the large surface area but in runs 5 and 6, the starting ester underwent complete decomposition. The

Table 1. Pyrolysis of 4,4,4-trichloro-3-acetoxybutanoic acid.

Run	Rate ^a	Furnace temp. ^b	Pressure ^c	Yield ^d	Recovered starting material ^e
1	0.286	425-460	45	9.1 g. (60%)	1.7 g. 2.5 g. mixture
2	0.7	450-490	38-42	3.1 g. (16%)	5.4 g. 3.6 g. mixture
3	0.3	475-490	23	8.6 g. (57%)	None
4	0.4	500-550	40-50	None	None
5*	0.5	325-425	23	None	None
6*	0.5	450-500	23	None	None

^a Rate is in grams per minute which was obtained by dividing total grams of starting material by the time required for pyrolysis.

^b Furnace temperature is in ° C.

^c Pressure is in mm.

^d Yield based on trichlorocrotonic acid obtained.

^e This column gives the recovered starting material in grams and the "mixture" of starting material and trichlorocrotonic acid also obtained.

* Runs 5 and 6 were attempts using porous tile in the place of glass helices in the pyrolysis tube.

method of pyrolysis as given in the Experimental, corresponding to run 3, is an improvement in yield of 10-14% over the method by von Auwers, and the purification procedure is unnecessary.

The trans configuration of the trichlorocrotonic acid obtained by pyrolysis was proven by mixed melting point with an authentic sample prepared by von Auwers' method. In addition, the infrared spectra of the pyrolytic and von Auwers' trichlorocrotonic acid samples were identical.

Brief mention at this point should be made to show how the trans configuration has been determined. Von Auwers (3) hydrolyzed trichlorocrotonic acid with concentrated sulfuric acid in acetic acid to yield the trans-fumaric acid. Von Auwers also proved that cis-maleic acid does not undergo isomerization to fumaric acid under these conditions. Further proof of the trans form was given by Nesmeyanov, et al. (22) who dehydrohalogenated 3,4,4,4-tetrachlorobutanoic acid to yield the same trichlorocrotonic acid obtained by von Auwers. The dehydrohalogenation of a compound (14) is generally accepted to be trans elimination, hence giving the trans compound.

The formation of the trans isomer in the pyrolysis of ester method in the present work does not necessarily dispose of the generally accepted cyclic structure for cis elimination (26), since the cis compound could very well rearrange at the high temperature of pyrolysis.

To extend the applicability of indirect dehydration of chlorocarbonols, it was decided to attempt a pyrolysis of the acetate of the simpler 3,3,3-trichloro-2-methyl-2-propanol. This compound also was of interest since reported (20) preparations of 3,3,3-trichloro-2-methylpropene were complicated by obtaining the allylic isomer, 1,1,3-trichloro-2-methylpropene. Royals (26) reported that "acetate pyrolysis has been applied to the indirect dehydration of a number of alcohols, and in no case has double bond migration or Wagner-Meerwein rearrangement been observed." Consequently, one would expect 3,3,3-trichloro-2-methylpropene as the pyrolytic product without the undesired

allylic isomer. However, experimentation did not bear this out; in fact, the allylic isomer, 1,1,3-trichloro-2-methylpropene, was obtained as the sole product in 68% yield. Assuming that rearrangement does not occur during elimination of acetic acid, it would appear that 3,3,3-trichloro-2-methylpropene is extremely unstable at high temperatures (425-490°) and readily undergoes rearrangement to the more stable allylic isomer.

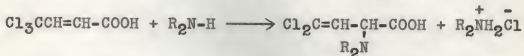
Preliminary Exploratory Experiments

The 71% recovery of anthracene in the attempted Diels-Alder reaction of trichlorocrotonic acid with anthracene clearly showed that the expected adduct was not formed. The base soluble tar obtained suggests a predominate side reaction with subsequent decomposition or polymerization. As previously discussed, the preparation of trichlorocrotonic acid by pyrolysis showed its remarkable stability to heat. Therefore, one would further conclude the side reaction might be due to a solvolytic effect. Because of the unpromising result here (two trial experiments), further attempts to obtain a Diels-Alder adduct were not made.

The attempted Michael reaction of ethyl trichlorocrotonate with malonic ester under catalysis by piperidine failed to give the expected addition product as evidenced by the recovery of the starting materials. However, the piperidine hydrochloride obtained as a result of the trial reaction indicated another reaction of equal importance, and led to reactions of trichlorocrotonic acid with amines.

Reaction of 4,4,4-Trichloro-2-butenic Acid
with Amines

General Comments. In each of the following reactions it appears that the general structure of the product of trichloro-crotonic acid with secondary amines is as indicated below:



The details, evidence, and discussion in support of this general structure are presented later in the section "Probable Course of Reaction, etc."

The reaction with primary amines and ammonia is not completely understood but it was obvious that they followed a different course.

In many of the following reactions, considerable difficulty was encountered in separating the product from the hydrochloride salt of the amine. Seemingly, the obvious method of separation would be the use of base to obtain the free amine and extraction with ether, thus leaving the product and inorganic salts in the base layer. This method, of course, was attempted in the case of piperidine and morpholine reactions; but none or only small amounts of the product could be obtained. Consequently, the slight differences in solubility were relied on for separation. The possible separation procedures were also limited because many of the compounds were unstable to heat and/or solvents. (Discoloration of solvent on crystallization was often noted.) This instability was noted especially in the case of morpholinium 4,4-dichloro-2-morpholinyl-3-butenate.

The reaction of trichlorocrotonic acid with secondary amines takes place readily at room temperature. When heated on the steam cone, this reaction was violent with immediate formation of intractable tars. In general, the best reaction conditions were a one-to-four ratio of trichlorocrotonic acid to amine, minimum amount of solvent, and use of a controlled temperature at 0° to 30°.

The biological importance of amino acids is well known; therefore, this new series of chloro amino acids offer an excellent prospect for use in biochemical applications.

Reaction with Piperidine. The reaction of trichlorocrotonic acid with piperidine gave a 28% yield of 4,4-dichloro-2-piperidyl-3-butenoic acid. The low yield was due to difficulties in separation. This is supported by obtaining a higher yield (66%) of piperidine hydrochloride. Similar runs made by increasing the temperature and/or the reaction time resulted in decomposition and tar formation. The reaction was also carried out in acetone but the product (believed to be the piperidinium salt) could not be obtained without piperidine hydrochloride as an impurity. The 4,4-dichloro-2-piperidyl-3-butenoic acid apparently exists as the zwitterion since its infrared spectrum is compatible with this hybrid carboxylate anion structure; accordingly there is no carbonyl band in the infrared; and also the solubility in water is great.

Reaction with Piperazine. The only pure product obtained in the reaction of trichlorocrotonic acid with piperazine was the methyl ester of 4,4-dichloro-2-piperazinyl-3-butenoic acid

in a 12% yield. Amino acids are known (10) to undergo esterification under rather mild conditions. Therefore, it is not surprising that ester formation occurred in refluxing methanol with the piperazine dihydrochloride. The ester was insoluble in cold water as expected.

The difficulties encountered in purification of the remaining product(s) had been anticipated since five possible products could form, each having similar solubilities. The reaction conditions were adjusted to favor the formation of 4,4-dichloro-2-piperazinyl-3-butenic acid (i.e., high dilution and excess piperazine). However, the product(s), as shown in the experimental, could not be separated.

Reaction with Morpholine. The reaction of morpholine with trichloroacetic acid resulted in a quantitative yield of morpholine hydrochloride and a 74% yield of morpholinium 4,4-dichloro-2-morpholinyl-3-butenate. This compound was found to be very sensitive to heat, and the work-up procedure required keeping the temperature below 50°. Purification was simplified because the product was slightly soluble in ether, giving a higher yield than in the previously described reactions. The slight solubility in ether probably resulted from the higher molecular weight and the two ether functions present.

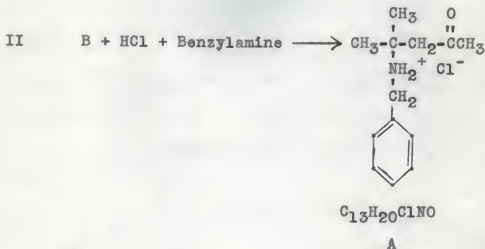
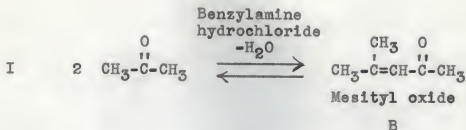
Reaction with p-Anisidine. Attempts to isolate the product of the reaction of trichloroacetic acid and p-anisidine were unsuccessful, although the theoretical amount of p-anisidine hydrochloride was isolated. An oil was obtained which resulted

in a polymeric black tar on crystallization from ether-acetone solvent. The conditions in this reaction were essentially the same as in the previous reactions with secondary amines.

Reaction with Benzylamine. Analysis for product A, m.p. 155.5-156° indicates the expected product analogous to the secondary amine reaction product was not obtained. The simplest empirical formula obtained from the analysis of product A is $C_{13}H_{20}ClNO$ to $C_{13}H_{22}ClNO$. Benzylammonium 4,4-dichloro-2-benzylamino-3-butenate (empirical formula $C_9H_{10}ClNO$) is the expected analogous product and was therefore, not obtained.

On the other hand, the analyses for C, H, Cl, and N, as well as O by difference, agree with the empirical and molecular formula of the hydrochloride salt of 4-methyl-4-benzylamino-2-pentanone, and the infrared spectrum obtained is also compatible with this compound. The usual criteria showed that product A is pure.

Since acetone was used in large excess as a solvent, a reasonable explanation of the results is as follows:



4-Methyl-4-benzylamino-2-pentanone hydrochloride

The following facts support structure A and the reaction sequence as given above.

1. Acetone is known (9) to react with ammonia to produce 4-methyl-4-amino-2-pentanone.
2. Acetone is known to condense with itself in the presence of hydrochloric acid (4) and also aniline hydrochloride (18) to form mesityl oxide.
3. Primary amines and ammonia are known (26) to react with mesityl oxide, usually by 1,4-addition.
4. Product A gives a positive halogen test with aqueous silver nitrate in the cold.

5. The infrared spectrum of product A shows bands corresponding to a hydrochloride at 3.9 and 4.26 μ (7); an isopropyl group at 7.3, 7.42, 8.62, and 8.7 μ (7); carbonyl at 5.85 μ ; and bands characteristic of benzylamine. The carbonyl band is very sharp and intense.

Though product A, 4-methyl-4-benzylamino-2-pentanone hydrochloride, does not form a 2,4-dinitrophenylhydrazone, this N-substituted β -aminoketone was found to yield the correct N-nitroso derivative for the same compound as reported in the literature by Jones and Kenner (17). The reaction of benzylamine with mesityl oxide and hydrogen chloride had given Jones and Kenner (17) the 4-methyl-4-benzylamino-2-pentanone hydrochloride as identified by them only by nitrogen analysis and the stated N-nitroso derivative. Significantly, they reported no carbonyl derivative (17).

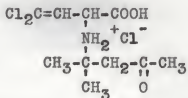
The above sequence I and II would acquire the hydrogen chloride from trichloroacetic acid, probably via benzylamine. On the basis of the limiting factor being hydrogen chloride, assuming 1 mole hydrogen chloride eliminated per mole of trichloroacetic acid, a yield of 45% of suggested product A and 32% of benzylamine hydrochloride was obtained. The reaction product of trichloroacetic acid evidently underwent polymerization.

Further investigation of this and similar reactions should prove interesting, but are beyond the scope of this thesis.

Reaction with Ammonia. Reaction of ammonia with trichloroacetic acid was not entirely analogous to the reaction of

secondary amines. Experimental results indicate interaction in some way with acetone.

Analysis of product C, m.p. 109-110°, indicates the lowest possible molecular weight of about 300 with a 3 to 1 ratio of chlorine to nitrogen. A suggested product in accord with the analysis would be



with a molecular weight of 304.6 (Analysis calculated for $\text{C}_{10}\text{H}_{16}\text{Cl}_3\text{NO}_3$: C, 39.43; H, 5.29; Cl, 34.92; N, 4.60; O, 15.76. Found: C, 39.77; H, 5.38; Cl, 34.95; N, 4.76, 4.84; O, 15.10). Product C gave a positive test for halogen with aqueous silver nitrate but failed to form a 2,4-dinitrophenylhydrazone.

Reasoning, as previously described in the benzylamine reaction, could account for the formation of mesityl oxide which could, in turn, react with the expected product, 4,4-dichloro-2-amino-3-butenic acid, to give the product proposed above. This author does not infer this is the actual reaction path but the illustration is given as plausible for the formation of the proposed product.

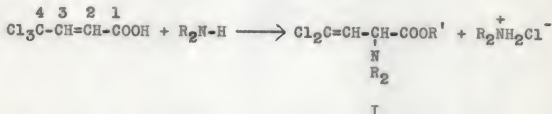
The infrared spectrum of this compound was, in general, compatible with the proposed structure. However, in this particular case the maze of infrared bands present defied a clear interpretation of the fine structure of the compound.

No other compounds that might be rationalized theoretically as coming from reaction of ammonia with trichlorocrotonic acid come anywhere near fitting the four analytical values obtained.

As is evident from the above, the main purpose here was to compare ammonia with the secondary amines. This has been done. It appears that further elaboration of the structure of the product is not within the scope of this thesis, but rather is for an extension in a future investigation.

Probable Course of Reaction and Suggested Structure of
the Products from the Reaction of 4,4,4-Trichloro-
2-butenic Acid with Amines

Structure I is suggested for the reaction product of trichlorocrotonic acid with secondary amines.

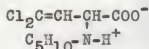


where R' is equal to hydrogen, methyl, and morpholinium; and R₂N-H corresponds to piperidine, piperazine, and morpholine, respectively.

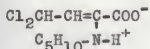
The following is offered as reasonable justification for the suggested structure I. The product obtained from the reaction of trichlorocrotonic acid and piperidine will be used for all illustrative examples.

The four formal structures below could account for the molecular formula of the product, C₉H₁₃Cl₂NO₂, obtained in the

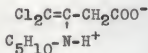
reaction of piperidine with trichlorocrotonic acid.



I

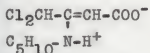


II



(cis-trans)

III



(cis-trans)

IV

Amine substitution at the trichloromethyl position (carbon 4) is eliminated on the grounds that the trichloromethyl group has proven inert (23) towards the action of nucleophilic reagents.

Compound II is untenable since α - β unsaturated α -amino acids are apparently unknown (11) without an acyl group on the nitrogen atom.

Compounds III and IV are unlikely because the expected attack of a nucleophilic reagent on trichlorocrotonic acid would be at the number 2 carbon for the following reasons:

1. The bulk and electron density of the trichloromethyl group would be expected to greatly hinder attack at the number 3 carbon.

2. Theoretically, carbon 2 would possess a partial positive charge in relation to carbon 3 because the relative electron withdrawing effect of a trichloromethyl group is considered greater than a carboxylate anion. This reasoning may be rationalized as follows:

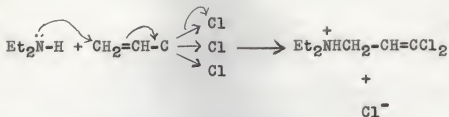
(a) The electron withdrawing effect of a trichloromethyl group is about equal to a carboxyl group.

(b) The negative inductive effect of the carboxylate anion is considerably less than the carboxyl group (16).

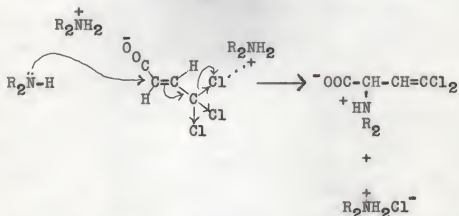
(c) Consequently, one would conclude the relative -I effect of a trichloromethyl group is greater than the carboxylate anion. The reacting species is no doubt the amine salt of trichloro-crotonic acid. Hence the carboxylate anion is at play, not the carboxyl group.

3. An allylic rearrangement would greatly enhance the positive character of carbon 2, and this shift would facilitate the removal of the chloride ion. The formation of amine hydrochloride demonstrates that bond breaking must occur during the reaction. The bond breaking is best explained by an allylic rearrangement as will be shown later in the discussion.

In support of the proposed allylic attack are the results obtained by Nesmeyanov and coworkers (23). They reported that in all cases studied, the action of nucleophilic compounds on 3,3,3-trichloropropene took place with allylic rearrangement, giving products identical with those obtained by reaction of the same reagents with 1,1,3-trichloro-1-propene. They also proposed a "transfer of reaction center" with the reaction taking place as follows:



A similar reaction path appears reasonable for reactions of trichlorocrotonic acid with secondary amines as follows:



The protonated amine shown is in close proximity to the reacting molecule as indicated. Probably by electrostatic attraction the protonated amine attracts and aids the expulsion of the chlorine atom as chloride ion in the modified allylic rearrangement as shown in the equation. Experimental findings suggest intermolecular interaction since high concentration of reactants in minimum solvent were found to give the best results.

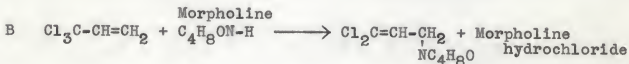
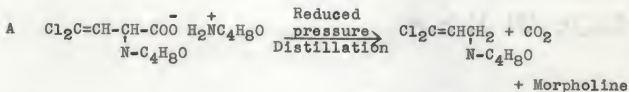
A closer correlation would be the reaction of trichlorocrotonic acid with benzene in the Friedel-Crafts reaction (24). In this example the allylic product was obtained as the sole product. Although other mechanisms are possible, i.e., aluminum chloride complex with the double bond, the reaction path which best explains the result is as follows:

be the most plausible.

Hydrolysis and reduction, as two separate steps, would indicate the position of the double bond and nitrogen substitution in that order. However, these methods would be limited because they would require (1) two separate steps, (2) preparation of two compounds by unambiguous routes, and (3) a great deal of time. Moreover, it was doubtful if the amino acids would be stable to the conditions normally required for hydrolysis of the dichlorovinyl or dichloromethyl groups.

The resolution of a d-l pair would be conclusive proof of structure I since only the suggested structure I of the four formal structures would have an optically active carbon. The difficulties often encountered in resolution of optically-active compounds is well known. Therefore, lack of resolution would prove nothing.

The decarboxylation of morpholinium 4,4-dichloro-2-morpholinyl-3-butenate appeared to offer the best possible means of structure proof as indicated below.



The product from the morpholine reaction was chosen because it was on hand in greater quantities than the piperidine product.

Also, the piperidine product from a similar reaction as B, was known (27) to be unstable.

The preparation of the previously unknown 1,1-dichloro-3-morpholinyl-1-propene was accomplished in essentially quantitative yield (as shown in reaction B just above). Although this product was unstable in air, it apparently was stable under reduced pressure in the absence of oxygen.

Attempts to isolate the expected decarboxylated product from reaction A failed, but morpholine, as the hydrochloride, was isolated, and the qualitative determination of carbon dioxide indicated decarboxylation had taken place.

The decomposition of β -amino acids normally proceeds by elimination of ammonia (11) rather than decarboxylation. Therefore, the liberation of carbon dioxide indicates the substituted α -amino acid is present, as shown in equation A.

EXPERIMENTAL

General Points of Procedure

All melting points and boiling points are uncorrected. The melting point apparatus used consisted of a melting point block with a 50-power microscope for viewing the sample.

Preliminary Exploratory Experiments

Attempted Diels-Alder Reaction of 4,4,4-Trichloro-2-butenoic Acid with Anthracene. A mixture of 2 g. (0.0105 mole) of 4,4,4-trichloro-2-butenoic acid and 1 g. (0.0056 mole) of

anthracene was refluxed in 30 ml. of dried xylene for 17 hours. The xylene was removed under vacuum, and the remaining residue was stirred in 40 ml. of 5% sodium bicarbonate for two hours. The basic solution was filtered, and the solid remaining was dried and crystallized from benzene to yield 0.708 g. of anthracene, m.p. 208-211° (reported m.p. 217° (213°) [6]). The basic filtrate was acidified with dilute hydrochloric acid, but no precipitate was obtained. The acidified solution was evaporated to dryness by an air stream. The residue was intractable brown tar, and no starting 4,4,4-trichloro-2-butenic acid could be recovered.

Attempted Michael Reaction of Ethyl 4,4,4-Trichloro-2-butenate with Malonic Ester under Catalysis by Piperidine.

A mixture of 10.88 g. (0.05 mole) of ethyl 4,4,4-trichloro-2-butenate (2), 8 g. (0.05 mole) of diethyl malonate, and 1 g. (0.0118 mole) of freshly-distilled piperidine in 25 ml. of absolute ethanol was stirred under reflux for 48 hours. On removal of the ethanol under vacuum, a precipitate formed which was filtered and washed with acetone to yield 0.6 g. of piperidine hydrochloride, m.p. 243-245° (reported m.p. 246° [6]), no depression of melting point on admixture with an authentic sample. Distillation of the filtrate yielded essentially quantitative recovery of the diethyl malonate and the ethyl 4,4,4-trichloro-2-butenate.

Preparations of Starting Materials

Dehydration of 4,4,4-Trichloro-3-hydroxybutanoic Acid.

Modification of von Auwers' method (2) is given here because of more speed and convenience. There was added 100 g. (0.48 mole) of 4,4,4-trichloro-3-hydroxybutanoic acid to 200 g. (1.96 mole) of acetic anhydride and 20 g. (0.24 mole) of fused sodium acetate. This mixture was heated on the steam bath for four hours with occasional swirling. The excess acetic anhydride was removed by distilling under water vacuum. The remaining brown, heavy liquid was added slowly, with stirring, to 500 ml. of ice water. After stirring for three hours, a light brown precipitate formed which was filtered and dried. The filtrate was acidified with 0.25 mole of concentrated hydrochloric acid which resulted in precipitation of a reddish-brown oil. The oil was separated from the water layer, and the remaining water in the oil removed by azeotroping with ligroin (b.p. 70-80°). The original precipitate and the ligroin solution above were combined, treated with Norite, and recrystallized twice from ligroin (b.p. 70-80°) to yield 36.0 g. (40%) of 4,4,4-trichloro-2-butenoic acid, m.p. 113-114° (reported m.p. 113-114° [27]).

Dehydration of 4,4,4-Trichloro-3-hydroxybutanoic Acid

Using Thionyl Chloride. A mixture of 10 g. (0.052 mole) of 4,4,4-trichloro-3-hydroxybutanoic acid and 60 g. (0.5 mole) of thionyl chloride were refluxed for three hours. The excess thionyl chloride was removed and the remaining brown, heavy oil yielded less than one gram of product boiling at approximately

107° under 1 mm. pressure. This product, when crystallized from ligroin (b.p. 70-80°), yielded 0.5 g. (5%) of 4,4,4-trichloro-2-butenic acid, m.p. 113-115°. Similar runs using quinoline as a catalyst gave only intractable tarry materials, and no product or starting material could be isolated.

Preparation of 4,4,4-Trichloro-3-acetoxybutanoic Acid.

Two hundred grams (approximately 2.4 moles) of acetyl chloride were mixed with 100 g. (0.48 mole) of 4,4,4-trichloro-3-hydroxybutanoic acid, and refluxed for three hours. The excess acetyl chloride was recovered by distillation, and the remaining oil evacuated overnight. The oil was added slowly to 500 ml. of ice water, and the solution stirred until the product solidified. The light yellow solid was filtered, dried, Norited, and crystallized from ligroin (b.p. 70-80°) to yield 115.2 g. (96%) of fine, white needles of 4,4,4-trichloro-3-acetoxybutanoic acid, m.p. 96.5-97.5° (reported m.p. 97-99° [27]).

This reaction was essentially the same as that given by von Auwers (2) but with modification in the work-up procedure.

Pyrolysis of 4,4,4-Trichloro-3-acetoxybutanoic Acid. The apparatus used consisted of a horizontal Pyrex tube 25 mm. in diameter and 500 mm. long, placed in an electrically-heated furnace with controls and a thermocouple for temperature readings. The pyrolysis tube was equipped with standard taper joints and packed with 3/16 inch Pyrex helices. At each end of the pyrolysis tube there were attached two 250 ml. flasks which had small side joints. The first flask for input of material was equipped with a fine ebullator tube for passing a continuous

stream of nitrogen through the system. The receiving flask was attached through a condensing train (traps cooled by ice-salt) to a vacuum pump. The material to be pyrolyzed was placed in the first flask, and heated by infrared lamps to give a controlled distillation rate. For best results, 0.3 g. per minute of 4,4,4-trichloro-3-acetoxybutanoic acid was distilled through the pyrolysis tube at 20 mm. pressure while maintaining the furnace temperature at 470 to 480° C. The nitrogen stream was adjusted to sustain a smooth, steady bubbling of the acetate. The product of pyrolysis was found to be trans-4,4,4-trichloro-2-butenic acid by mixed melting point with an authentic sample as prepared by the von Auwers procedure (2). It solidified readily in the receiving flask without cooling, and had only minor discoloration from the 475° temperature. Under the conditions specified, the product was essentially free of starting material. The 4,4,4-trichloro-2-butenic acid from the receiver flask was recrystallized twice from petroleum ether (70-80°) which yielded white rectangular crystals. From pyrolysis of 50 g. of 4,4,4-trichloro-3-acetoxybutanoic acid in a typical run, and use of the above procedure, there was isolated 20.3 g. (54%) of pure 4,4,4-trichloro-2-butenic acid, m.p. 112-113° (the literature [2] reports m.p. 113-114°).

Pyrolysis of 3,3,3-Trichloro-2-methyl-2-propyl Acetate.

The apparatus was the same as in the procedure for the pyrolysis of 4,4,4-trichloro-3-acetoxybutanoic acid, except the pyrolysis tube was supported in a vertical position and the first flask was replaced by an addition funnel. The pyrolysis was carried

out at atmospheric pressure after the furnace had been preheated to 475° and the system flushed with nitrogen for 30 minutes. The nitrogen flow was adjusted to one ml. per second and the rate of addition of 65.3 g. (0.298 mole) of 3,3,3-trichloro-2-methyl-2-propyl acetate (1) from the addition funnel was 0.5 ml. per minute. The receiver flask was cooled with ice, and the nitrogen stream of effluent gas was allowed to pass through a basic solution after passing through the salt-ice trap. The colorless contents of the receiver flask and the salt-ice trap were combined and then washed twice with 30 ml. portions of distilled water. Back titration of the combined basic solution and aqueous washings with standard hydrochloric acid indicated that 75% of the theoretical amount of acetic acid had been liberated. The washed pyrolysate was dissolved in 150 ml. of ether, and then washed with two 30 ml. portions of 5% aqueous sodium bicarbonate to remove traces of acetic acid. The ether solution was dried over magnesium sulfate, filtered, and the ether removed on a steam bath. The dried solution was fractionated through a 6-inch, helix-packed column to yield 31.5 g. (68%) of 1,1,3-trichloro-2-methylpropene, b.p. 154-158° at atmospheric pressure, n_D^{20} 1.4971 (reported b.p. 154-157° [$\bar{7}40$ mm.] n_D^{20} 1.4993 [$\bar{2}0$]).

Reactions of 4,4,4-Trichloro-2-butenic Acid
with Amines

Reaction of 4,4,4-Trichloro-2-butenic Acid with Piperidine.

To a stirred solution of 12.8 g. (0.15 mole) of freshly-distilled piperidine was added dropwise 9.2 g. (0.0485 mole) of

4,4,4-trichloro-2-butenic acid in 20 ml. of ether while maintaining the temperature at 25° by means of an ice-water bath. The reaction mixture became solid after a few minutes and 100 ml. of ether was added to aid stirring. The total reaction time was four hours. The reaction mixture was then filtered, and the collected solid washed thoroughly with acetone. The ether and acetone wash did not contain any starting 4,4,4-trichloro-2-butenic acid, indicating complete reaction. The white, crystalline, acetone-insoluble solid was fractionally crystallized numerous times from absolute ethanol yielding 4.1 g. (66%) of piperidine hydrochloride, m.p. 242-245° uncorrected (reported m.p. 246° [67]); mixture melting point with authentic sample was not depressed. (The latter fractions contained small amounts of a substance decomposing at 140° but not depressing the m.p. of the piperidine hydrochloride.) The ethanol solution remaining was evaporated by an air stream, and a white, curdy solid was obtained. This solid was washed with 30 ml. of chloroform (the original mixture of products was soluble in chloroform), and crystallized from 20 ml. of absolute ethanol. This yielded 3.2 g. (28%) of analytical pure 4,4-dichloro-2-piperidyl-3-butenic acid which melted at 139-140° with vigorous bubbling and decomposition to black tar. Its infrared spectrum in potassium bromide showed strong bands at 2.9, 3.2, 4.0-4.5, 6.2 (broad band), 6.69, 6.98, 7.3, 8.22, 9.3 (moderate), 10.38, 10.55, 11.1, 11.28, and 12.4 μ , plus a number of bands characteristic of the spectrum of piperidine.

Anal. Calcd. for $C_9H_{13}Cl_2NO_2$: C, 45.69; H, 5.50;
Cl, 29.78; N, 5.88.

Found: C, 46.00; H, 5.27; Cl, 30.40; N, 5.92.

Reaction of 4,4,4-Trichloro-2-butenic Acid with Piperazine.

Five grams (0.0264 mole) of 4,4,4-trichloro-2-butenic acid in 25 ml. of methanol was added dropwise with stirring to a refluxing solution of 6.8 g. (0.0792 mole) of piperazine in 150 ml. of methanol. After six hours the solution was cooled and evaporated to dryness. The yellow solid obtained was subjected to ether and also benzene continuous extractions, but no separation could be accomplished. From 50 ml. of hot methanol, an insoluble white solid was obtained which was crystallized from water to yield 0.8 g. (12%) of analytically pure methyl 4,4-dichloro-2-piperazinyl-3-butenate, m.p. 180° decomposes. The material remaining in the methanol filtrate resisted purification, and attempts from acetone-water, acetone-methanol, *n*-butanol, ethyl acetate, and various solvent pairs failed.

The infrared spectrum of methyl 4,4-dichloro-2-piperazinyl-3-butenate in potassium bromide showed the following bands: N-H stretch at 3.18μ , carbonyl at 6.09μ , c-c double bond at 6.3μ (broad), R_2-N - bands at 8.82 and 9.19μ , ester C-O-stretch at 9.62μ , and C-Cl stretch at 11.1 , 11.27 , and 13.7μ , plus numerous bands expected of piperazine.

Anal. Calcd. for $C_9H_{14}Cl_2N_2O_2$: Cl, 28.01; N, 11.07.

Found: Cl, 27.90, 28.50; N, 11.40, 11.30.

Reaction of 4,4,4-Trichloro-2-butenic Acid with Morpholine.

Five grams (0.0264 mole) of 4,4,4-trichloro-2-butenic acid was

added in small portions, with stirring, to 9.1 g. (0.104 mole) of morpholine at room temperature. A temperature rise of around 6° was noted. A few minutes after addition was completed the solution became solid, and 25 ml. of absolute ethanol was added to aid stirring. After a total reaction time of four hours the excess ethanol and morpholine were removed under reduced pressure and warming to not more than 45° . The yellow solid obtained was ground with mortar and pestle to aid extraction, and washed with ether. A continuous ether extraction by means of a Soxhlet extractor yielded 6.3 g. (74%) of fine, white needles (m.p. $112-115^{\circ}$), morpholinium 4,4-dichloro-2-morpholinyl-3-butenate. The solid remaining after extraction was 3.2 g. (100%) of morpholine hydrochloride (m.p. $172-174^{\circ}$) (reported 176° [6]) which gave no depression of melting point when mixed with an authentic sample.

The product (m.p. $112-115^{\circ}$) could be recrystallized in small amounts (0.5 g.) from 200 ml. of ether. An analytical sample thus obtained gave a melting point of $119-120^{\circ}$ with decomposition on further heating over a temperature range of $125-135^{\circ}$.

The infrared spectrum was compatible with morpholinium 4,4-dichloro-2-morpholinyl-3-butenate. A potassium bromide pellet of this compound showed strong bands at 3.4, 4.05, 6.0, 6.3, 6.9, 7.25, 10.5, 10.9, 11.65, and 13.79 μ , plus a number of bands characteristic of morpholine.

Anal. Calcd. for $C_{12}H_{20}Cl_2N_2O_2$: Cl, 21.70; N, 8.56.

Found: Cl, 21.80, 21.65; N, 8.56, 8.17.

Reaction of 4,4,4-Trichloro-2-butenic Acid with p-Anisidine. A solution of 2 g. (0.0155 mole) of 4,4,4-trichloro-2-butenic acid in 15 ml. of absolute ethanol was added dropwise with stirring to 3.7 g. (0.03 mole) of p-anisidine in 10 ml. of absolute ethanol at room temperature. After five hours the ethanol was removed under vacuum from the dark brown reaction mixture. The viscous residue was partially dissolved by 150 ml. acetone. The solution was filtered and 1.5 g. (89%) of p-anisidine hydrochloride, m.p. 208-210°, no depression of melting point on mixing with an authentic sample, was obtained. Removal of the excess acetone was accomplished under reduced pressure and a dark viscous oil remained. Attempted crystallizations did not succeed. With an ether-acetone solvent, some light brown precipitate was obtained but filtration yielded a black tar.

Reaction of 4,4,4-Trichloro-2-butenic Acid with Benzylamine. Five grams (0.0264 mole) of 4,4,4-trichloro-2-butenic acid in 25 ml. of methanol was added dropwise, with stirring, to 6.5 g. (0.06 mole) of benzylamine. The reaction mixture was stirred overnight with no external heat during the entire reaction. The reaction mixture was taken up in 500 ml. of acetone, and the solution was allowed to stand in the refrigerator for two weeks. The solution was then filtered and 2.9 g. (45% yield based on 0.0264 mole with a molecular weight of 242) of product, m.p. 154-156°, was obtained. This product, from data obtained, appeared to be the hydrochloride of 4-methyl-4-benzylamino-2-pentanone. The acetone filtrate was evaporated to dryness under

reduced pressure, and the residue was dissolved in about 500 ml. of chloroform. After standing for two days (10°) the solution was filtered, and 1.2 g. (32%) of benzylamine hydrochloride, m.p. and mixed m.p. $256-259^{\circ}$, was obtained. An analytical sample of the product, m.p. $154-156^{\circ}$, was obtained by dissolving in chloroform, filtering, removal of chloroform under reduced pressure, and crystallizing the residue from acetone. This process was repeated to yield an analytical sample, m.p. $155.5-156^{\circ}$. The product, m.p. $155.5-156^{\circ}$, gave a positive halogen test with aqueous silver nitrate in the cold and a negative test with 2,4-dinitrophenylhydrazine. The infrared spectrum in potassium bromide showed the following strong bands: 3.9, 4.26, 5.85, 7.03, 7.33, 7.42, 7.88, 8.2, 8.62, and 8.7μ , plus a number of bands characteristic of benzylamine. The characteristic carbonyl band at 5.85μ was very sharp and intense.

Anal. Calcd. for $C_{13}H_{20}ClNO$: C, 64.6; H, 8.34; Cl, 14.67; N, 5.80; O, 6.62.

Found: C, 64.2; H, 8.85; Cl, 14.7; N, 5.70; O, 6.55.

The N-nitroso derivative of 4-methyl-4-benzylamino-2-pentanone was prepared by adding 2 ml. of concentrated hydrochloric acid to a chilled solution of 0.5 g. of product A in 10 ml. of water. To this cooled solution a concentrated solution of sodium nitrite in water was added slowly until a positive test for nitrous acid was obtained with starch-iodide paper. After 15-20 minutes a precipitate was formed which was filtered and recrystallized from ligroin (b.p. $70-80^{\circ}$) to yield 0.2 g. of fluffy white needles of the N-nitroso derivative, m.p. $81.5-$

82° (reported [17] m.p. 85-86°). Further recrystallizations did not raise the melting point.

Reaction of 4,4,4-Trichloro-2-butenic Acid with Ammonia.

To a well-stirred solution of 5 g. (0.0264 mole) of 4,4,4-trichloro-2-butenic acid in 100 ml. of methanol was added a steady stream of ammonia gas with no external heating. The addition of ammonia was discontinued after two hours and the reaction mixture was stirred overnight. The orange reaction mixture was evaporated under vacuum (25 mm.) to dryness. To the residue was added 75 ml. of acetone. The solution was filtered and about 0.2 g. of ammonium chloride was obtained. (This 0.2 g. of solid melted above 300°; it gave a positive halogen test with an aqueous silver nitrate solution.) The filtrate was reduced to a volume of about 50 ml. Filtration of this solution yielded 0.2 g. of substance, m.p. 83-89°. On slow removal of the acetone under reduced pressure, fraction 2 was obtained, m.p. 103-105° (softened at 100°). Further removal of the acetone, as above, followed by filtration and thorough washing with acetone yielded 0.3 g. of product (fraction 3), m.p. 108-109.5°. The solids from fraction 1 (m.p. 83-89°) and fraction 2 (m.p. 103-105°) were combined with the acetone filtrate, and washes. The resulting acetone solution was slowly evaporated to dryness. The remaining dark brown residue was recrystallized four times (a slight discoloration of the solvent was noted even on the fourth recrystallization) from hot acetone to yield 1.2 g. of fine white needles (fraction 4), m.p. 109-110° (solid specks appeared in the melt at around 118°, and these solid specks melted around

180° under the microscope). Its infrared spectrum in potassium bromide showed strong bands at 3.25, 3.5-3.9 (broad), 4.0, 4.75 (medium), 6.0 (sharp), 6.23, 6.36, 6.55, 6.75, 7.05, 7.45 (broad), 8.03, 8.7, 8.85, 9.36, 10.5, 11.43 (weak), 12.8, 13.05 (broad), and 14.36 μ .

Anal. Calcd. for 4,4-dichloro-2-amino-3-butenic acid,

$C_4H_5Cl_2NO_2$: Cl, 41.71; N, 8.24.

Found for fraction 3: Cl, 35.60; N, 4.89.

Found for fraction 4: C, 39.77; H, 5.38; Cl, 34.95;
N, 4.84, 4.76.

Thus, the difference between the values found and calculated for 4,4-dichloro-2-amino-3-butenic acid shows clearly that quite a different product was obtained than in the cases with the cyclic secondary amines.

In similar reactions, in the absence of acetone, the same product (m.p. 109-110°) could not be isolated. Reactions were attempted by adding 4,4,4-trichloro-2-butenic in methanol to an alcoholic solution of ammonium hydroxide without success.

The addition of ammonia to an ethereal solution of 4,4,4-trichloro-2-butenic acid resulted in an immediate precipitate (m.p. 85-90°), presumably the ammonium salt of 4,4,4-trichloro-2-butenic acid, which was extremely soluble in acetone. An acetone solution of this precipitate, on slow evaporation of solvent and subsequent recrystallization from acetone, yielded the same product, m.p. 109-110°, as previously obtained.

Other Reactions

Decarboxylation of Morpholinium 4,4-Dichloro-2-morpholinyl-3-butenate. The decomposition of 0.6 g. (0.00183 mole) of morpholinium 4,4-dichloro-2-morpholinyl-3-butenate was accomplished in an air-tight 10 ml. test tube with a small length of tubing leading from the test tube to a calcium-hydroxide solution. The test tube was heated by an oil bath to a temperature range of 130-140°. Within seconds, vigorous bubbling occurred in the test tube, and a white precipitate formed in the calcium hydroxide solution. The precipitate was filtered and dried to yield 0.044 g. (24%) of calcium carbonate. The remainder of the starting material remained as black intractable tar in the test tube.

The decarboxylated product could not be isolated in similar runs using 10 g. (0.036 mole) of morpholinium 4,4-dichloro-2-morpholinyl-3-butenate under reduced pressure (0.2-30 mm.) but small amounts of morpholine were isolated in these runs.

Reaction of 3,3,3-Trichloropropene with Morpholine. Nine grams (0.062 mole) of freshly distilled 3,3,3-trichloropropene (n_D^{20} 1.4710) was added dropwise with stirring to 21.75 g. (0.25 mole) of morpholine at room temperature. A white precipitate occurred within the first 30 minutes and the temperature rose spontaneously from 25° to 40-45°. After 2.5 hours 250 ml. of ether was added to aid stirring, and the solution was stirred for an additional two hours. The solution was filtered, and the white crystalline solid obtained was washed twice with

75 ml. portions of ether. A total of 7.5 g. (98%) of morpholine hydrochloride, m.p. 173-175° (reported m.p. 176°), no depression of melting point on admixture with authentic sample, was obtained from the reaction mixture. The ether was removed from the filtrate, and the organic residue was distilled to yield 11.3 g. (93.4%) of colorless and odorless 1,1-dichloro-3-morpholinyl-1-propene, b.p. 115-116° (15 mm.), n_D^{20} 1.5350. This colorless liquid was found to undergo extensive decomposition within 20 minutes after removal from reduced pressure. Traces of air were found to cause this decomposition with formation of 0.2 g. of white solid which turned brown on standing. This brown solid, m.p. 168-171°, gave no depression of melting point with an authentic sample of morpholine hydrochloride. It is interesting to note that the forerun, which contained traces of morpholine, did undergo the same type of decomposition after several weeks.

SUMMARY

The preparation of trans 4,4,4-trichloro-2-butenic acid was undertaken to improve on existing methods, or provide a new method with improved procedure and yields.

A study of the literature indicated the most practical means of preparation of 4,4,4-trichloro-2-butenic acid was the dehydration of the readily available 4,4,4-trichloro-3-hydroxybutanoic acid by the von Auwers method (2). Attempts were made to improve the yield (44%) of von Auwers (2) in the dehydration of 4,4,4-trichloro-3-hydroxybutanoic acid with acetic anhydride

and sodium acetate without success. However, modifications were devised that did shorten and simplify the procedure, and a comparable yield was obtained.

Thionyl chloride has been shown (20) to be an excellent dehydrating agent for 3,3,3-trichloro-2-methyl-2-propanol. However, efforts using thionyl chloride in dehydration of 4,4,4-trichloro-3-hydroxybutanoic acid failed to produce yields greater than 5% of the corresponding unsaturated acid.

Indirect dehydration by pyrolysis of an ester of a trichlorocarbinol was shown to be suitable for chloro-olefin preparation for the first time. Pyrolysis of the readily available acetate of 4,4,4-trichloro-3-hydroxy butanoic acid under carefully controlled conditions resulted in 57% yield of trans 4,4,4-trichloro-2-butenic with essentially no purification problems, unlike the von Auwers method. The pyrolysis of 3,3,3-trichloro-2-methyl-2-propyl acetate proceeded smoothly to provide the allylic olefin, 1,1,3-trichloro-2-methyl-1-propene, in a 68% yield.

The reactions of 4,4,4-trichloro-2-butenic acid with an excess of cyclic secondary amines at room temperature resulted in a new series of compounds. This reaction was carried out with morpholine, piperidine, and piperazine and gave the new compounds in yields of 74, 28, and 12%, respectively. The experimental results and previous investigations indicate the general structure as $\text{Cl}_2\text{C}=\text{CH}-\underset{\text{R}_2\text{N}}{\text{CH}}-\text{COOH}$ with the course of reaction

probably proceeding via an allylic rearrangement with a "transfer of reaction center" accompanied by elimination of hydrogen chloride. The corresponding amine hydrochloride salt was isolated and identified in most cases.

The reaction of 4,4,4-trichloro-2-butenic acid with benzylamine and ammonia was not entirely in agreement with reactions of the cyclic secondary amines observed. Experimental results, in both cases, indicate interaction with the solvent acetone. The product in the reaction of benzylamine was apparently 4-methyl-4-benzylamino-2-pentanone hydrochloride. Experimental evidence from the reaction of ammonia with 4,4,4-trichloro-2-butenic acid indicated the formation of the hydrochloride salt of 4,4-dichloro-2-amino-N-4'(4'-methyl-2'-pentanone)-3-butenic acid. The results obtained from ultimate analyses for the elements in these compounds were excellent.

This investigation has shown that 4,4,4-trichloro-2-butenic acid undergoes reaction with amines with surprising ease. The possibility of this acid reacting with other nucleophilic reagents appears very promising, and such reactions could well lead the way to numerous and interesting compounds.

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PREPARATION AND REACTIONS WITH AMINES OF
4,4,4-TRICHLORO-2-BUTENOIC ACID

by

JERRY LEROY WHITE

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The purpose of this investigation was to devise a good method of preparing 4,4,4-trichloro-2-butenic acid, and study the reactions of this acid with various amines and ammonia.

The yield of trans 4,4,4-trichloro-2-butenic acid could not be increased over that reported by von Auwers (Ber. 46, 487-494 [1913]) for the dehydration of 4,4,4-trichloro-3-hydroxybutanoic acid. However, modifications of his procedure were developed to facilitate ease of operation. Using thionyl chloride as the dehydrating agent gave a 5% yield of the desired acid, plus tar.

The preparation of trans 4,4,4-trichloro-2-butenic acid was best accomplished by pyrolysis of 4,4,4-trichloro-3-acetoxybutanoic acid (available in 96% yield). The yields of 4,4,4-trichloro-2-butenic acid, m.p. 112-113°, by pyrolysis at 475-490° were from 54-57% and there was no problem in purification as previously encountered in von Auwers' procedure (ibid.). The trans configuration was established by comparison of the infrared spectra and mixed melting point with the authentic trans compound prepared by the procedure of von Auwers (ibid.). The synthesis of 1,1,3-trichloro-2-methylpropene, b.p. 154-158° at atmospheric pressure, n_D^{20} 1.4971, was accomplished in 68% yield by the pyrolysis of 3,3,3-trichloro-2-methyl-2-propyl acetate. This result further showed the suitability of an acetate ester of a trichlorocarbonol to undergo pyrolysis to the trichloro olefin. There have been no previous reports of chloro olefin preparation by ester pyrolysis. However, in the cases observed, rearrangement to the more thermodynamically stable

isomer evidently occurred.

The desired product was not obtained in the attempted Diels-Alder reaction of 4,4,4-trichloro-2-butenic acid with anthracene; only intractable tars and 71% recovery of anthracene were isolated. The attempted Michael reaction of ethyl 4,4,4-trichloro-2-butenate and diethyl malonate, catalyzed by piperidine, failed to give the expected addition product. However, piperidine hydrochloride was obtained and revealed the possibility of the reaction of 4,4,4-trichloro-2-butenic acid with amines.

Cyclic secondary amines were found to react readily at room temperature with 4,4,4-trichloro-2-butenic acid to form compounds not previously described in the literature. Reactions of any amines or of ammonia with 4,4,4-trichloro-2-butenic acid are also not described in the literature. Morpholine, piperidine, and piperazine reacted with 4,4,4-trichloro-2-butenic acid, and the following new compounds were obtained: (74%) morpholinium 4,4-dichloro-2-morpholinyl-3-butenate, m.p. 119-120°; (28%) 4,4-dichloro-2-piperidyl-3-butenic acid, m.p. 139-140° d; (12%) methyl 4,4-dichloro-2-piperazinyl-3-butenate, m.p. 180° d. In general, the best reaction conditions were a large excess of amine, minimum solvent, and room temperature. The postulated structures of these compounds, as given above, were based on analysis, qualitative chemical classification tests, infrared spectra, physical properties, and correlation with previous investigations of analogous reactions.

In the attempted process of a conclusive structure proof, a new compound, 1,1-dichloro-3-morpholinyl-1-propene, b.p. 115-118° (15 mm.), n_D^{20} 1.5350, was obtained by the well known reaction (Nesmeyanov and coworkers, Quart. Rev. X. 330-370 [1956]) of 3,3,3-trichloropropene with nucleophilic reagents. This compound was found to be extremely unstable in the presence of air.

Support has been given for the proposed reaction path proceeding by an allylic rearrangement with elimination of hydrogen chloride. The hydrogen chloride was isolated as the cyclic amine hydrochloride.

The reactions of 4,4,4-trichloro-2-butenic acid with benzylamine and ammonia were not altogether in keeping with results observed for secondary amines. All indications suggest reaction in some way with the acetone used as solvent. Thus, the end-product obtained was in keeping with mesityl oxide as a possible reaction intermediate; mesityl oxide being a normal condensation product of acetone. The suggested structure for the reaction product from benzylamine is 4-methyl-4-benzylamino-2-pentanone hydrochloride. A somewhat similar product, 4,4-dichloro-2-amino-N-4'(4'-methyl-2'-pentanone)-3-butenic acid hydrochloride, could account for the results obtained from the reaction with ammonia. The structures proposed above were supported by analysis, qualitative tests, infrared spectrum, physical properties, and the literature on the chemistry of acetone.