lents of sodium were required. The ammonia was allowed to evaporate spontaneously and the final traces removed *in vacuo*. The residue was dissolved in water, the solution acidified to congo red and extracted with ether. No appreciable quantity of ether-soluble material was recovered from the experiments with the carboallyloxy derivatives. The aqueous phase was concentrated *in vacuo* until precipitation occurred. Then 2 volumes of alcohol was added, the *p*H adjusted to 5.5–6 and the mixture cooled. The product was recrystallized in the usual manner. The yields of DL-leucine, DL-methionine and DL-phenylalanine from the corresponding N-carboallyloxy derivatives were 65–85%.

(b) **With Phosphonium Iodide in Acetic Acid.**—The method of Harington and Mead[4] was followed. The reaction was stopped when the evolution of carbon dioxide had ceased. The solvent was removed *in vacuo* and the residue worked up as described above. Experiments with the N-carboallyloxy derivatives of DL-leucine, DL-methionine and DL-phenylalanine gave 70–75% yields of the pure amino acids.

***n*-Propyl Chloroformate.**—One mole of *n*-propyl alcohol was placed in a cylinder arranged with inlet and outlet tubes so that phosgene from a tank could be bubbled into it. The outlet tube was connected to a trap containing toluene. Both solutions were kept in an ice-bath and the final exit tube passed into a good hood. Approximately 0.9 mole (87 g.) of phosgene was allowed to bubble into the propyl alcohol over a period of ten hours. The mixture was then allowed to stand at room temperature for twenty-four hours. Without further purification, the solution was used in the following preparation.

N-Carbopropyloxy-DL-phenylalanine.—Five grams of DL-phenylalanine was dissolved in 9 ml. of 4 *N* sodium hydroxide, the solution cooled in an ice-bath, and treated with seven 1-ml. portions of *n*-propyl chloroformate (above). Simultaneously, sufficient amounts of 4 *N* alkali were added to keep the mixture alkaline to phenolphthalein. The mixture was vigorously shaken after each addition and cooled in an ice-bath. After all the reagents had been added, the mixture was shaken for an additional ten minutes and then allowed to stand for twenty minutes at room temperature. The cold solution was extracted with two 10-ml. portions of ether and the aqueous phase was aerated to remove ether. The solution was cooled and acidified to congo red with concd. hydrochloric acid. The mixture was extracted with two 25-ml. portions of ether and the ether fraction was concentrated *in vacuo*. The residue was dissolved in 45 ml. of warm benzene, an equal volume of petroleum ether was added and the solution was cooled for several hours. The crystalline product amounted to 7.5 g. (97%), m. p. 74–76°, neutralization equivalent 250 (calculated 251).

Experiments with N-carbopropyloxy-DL-phenylalanine showed that it was recovered unchanged in almost quantitative yield when subjected to the catalytic hydrogenolysis procedure using Adams catalyst, or to treatment with sodium in liquid ammonia. However, when treated with phosphonium iodide in glacial acetic acid very little of the starting material was recovered, and a reasonably good yield (55%) of pure DL-phenylalanine was obtained.

Summary

1. A series of naturally-occurring amino acids has been shown to react with allyl chloroformate to yield the corresponding carboallyloxy derivatives.

2. The ready cleavage of the carboallyloxy group has been demonstrated: (1) by catalytic hydrogenolysis using platinum or palladium catalysts, (2) by the use of metallic sodium in liquid ammonia and (3) by the use of phosphonium iodide in glacial acetic acid. The yield from catalytic hydrogenolysis has been shown to be somewhat reduced by the competing reaction leading to hydrogenation of the allyl group.

3. The probable utility of the procedures in the synthesis of peptides and related compounds has been pointed out.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE DEFENSE RESEARCH LABORATORY, THE UNIVERSITY OF TEXAS]

Allylic Chlorides. IX. Preparation of *cis* and *trans* Crotyl Chloride

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References to crotyl chloride have appeared frequently in the literature but in no case have the two geometrical isomers been separated and identified.[1,2,3,4] Young and Andrews[5] have noted, however, that crotyl chloride which had been obtained by the chlorination of a butene mixture showed a slightly higher refractive index than any previously reported. In addition they found that the rate of reaction with sodium ethoxide was somewhat higher for this crotyl chloride than for crotyl chlorides obtained by other methods. This was interpreted to be evidence for the presence of the *cis* isomer.

The present paper describes the preparation of both the *cis* and *trans* isomers of crotyl chloride from the corresponding crotyl alcohols by treatment of the alcohol with phosphorus trichloride in the presence of pyridine. The synthesis of *trans*-crotyl alcohol was effected by reduction of the commercially available *trans*-crotonaldehyde by the use of both lithium aluminum hydride and aluminum propoxide.

The *cis*-crotyl alcohol was synthesized by two methods each of which was designed to give an alcohol of known configuration. One procedure consisted of the hydrogenation of 2-butyn-1-ol by use of a palladium catalyst suspended on barium sulfate. This catalyst has been shown to cause the *cis* addition of hydrogen to acetylenic bonds.[6] The 2-butyn-1-ol was obtained by dehydrochlorination of 3-chloro-2-buten-1-ol, a reaction which will be discussed in detail in a forthcoming paper. The

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[1] Baudrenghien, *Bull. soc. chim. Belg.*, **31**, 160 (1922).

[2] Henne, Chanan and Turk, THIS JOURNAL, **63**, 3474 (1941).

[3] Kharasch, Kritchevsky and Mayo, *J. Org. Chem.*, **2**, 489 (1937).

[4] Gredy, *Bull. soc. chim.*, [5] **2**, 1029 (1935).

[5] Young and Andrews, THIS JOURNAL, **66**, 421 (1944).

[6] Kharasch, Walling and Mayo, *ibid.*, **61**, 1559 (1939).

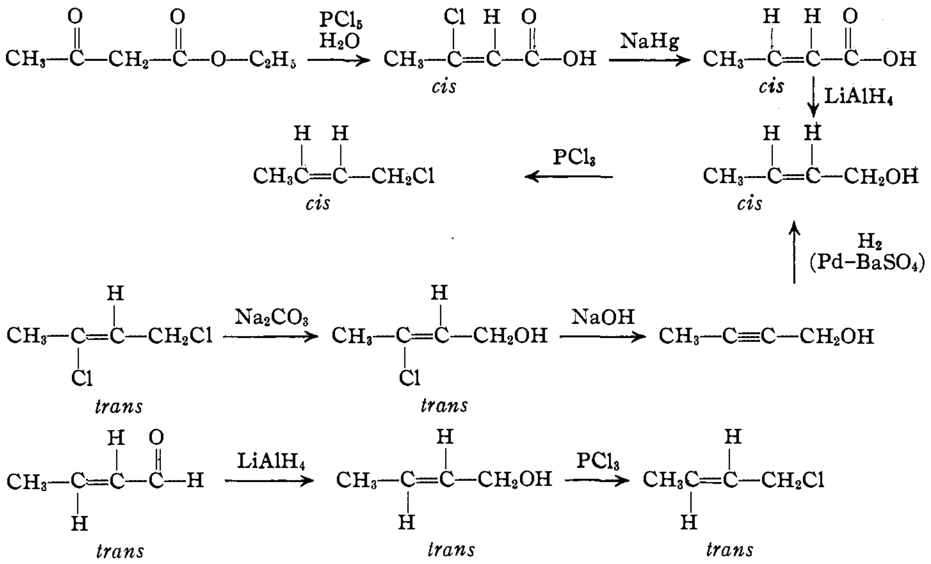

Fig. 1.—Preparation of *cis*- and *trans*-crotyl chlorides.

chloro alcohol was prepared by hydrolysis of 1,3-dichloro-2-butene (DCB) with dilute sodium carbonate solution.

Additional evidence for the configuration of *cis*-crotyl alcohol was obtained by the synthesis of this alcohol from isocrotonic acid. This acid, which has been established as having the *cis* configuration,[7] was reduced to the alcohol by the use of lithium aluminum hydride.

Figure 1 shows in outline form the steps used in the present investigation for the preparation of the *cis* and *trans* isomers of crotyl chloride and the relationship of these isomers to *trans*-crotonaldehyde and isocrotonic acid. Table I contains physical data for both isomers along with data for some closely related compounds.

Figure 2 contains the infrared spectra of both *cis*- and *trans*-crotyl chloride. The infrared absorption curve for *trans*-crotyl chloride shows a strong absorption band at 10.4 microns. The *cis* isomer shows a much weaker band at 10.6 microns and the trend in the curve at 14.5 to 15 microns seems to indicate a strong absorption band in the region just beyond 15 microns. In these respects the infrared spectra of *cis*- and *trans*-crotyl chloride appear to have characteristics which are similar to those obtained for closely related hydrocarbons.[8]

The chemical properties of *cis*- and *trans*-crotyl chloride will be the subject of a paper now being prepared.

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Experimental

All temperatures are corrected.

Crotyl Chloride from 3-Buten-2-ol.—Crotyl chloride was prepared by the treatment of 152 g. (2.1 moles) of 3-buten-2-ol (methylvinylcarbinol,[9] 96.5–97°) with 400 ml. of 37% hydrochloric acid. The mixture was held at room temperature for thirteen hours and shaken frequently during the first five hours. One-hundred and eighty grams of chlorides was obtained (95% yield).

The mixture of chlorides was dried and distilled through a 3-ft. glass helix-packed column. Thirty-five per cent. of the mixture boiled between 63 and 65°. A center fraction boiled at 63.7° (748 mm.), n^{20}D 1.4151, which indicated that the material was 3-chloro-1-butene.[5] The remainder of the material distilled between 82 and 85° with a center fraction boiling at 84.2° (748 mm.), n^{20}D 1.4350. These data indicate that this material was *trans*-crotyl chloride.

Crotyl Chloride by Rearrangement of 3-Chloro-1-butene.—Three and a half moles (317 g.) of 3-chloro-1-butene was treated with 400 ml. of 37% hydrochloric acid containing 3 g. of ferric chloride. The mixture was allowed to stand for thirty-six hours at room temperature then the organic layer was separated, washed free of hydrogen chloride, dried over potassium carbonate and distilled. Approximately 37% of the 3-chloro-1-butene was rearranged to *trans*-crotyl chloride as indicated by the distillation curve and the boiling point (84.2°) and index of refraction (n^{20}D 1.4350) of the crotyl chloride fraction.

Another quantity of 3-chloro-1-butene was rearranged to crotyl chloride under identical conditions except the mixture was maintained at 64° for thirteen hours. Distillation data and physical constants indicated a rearrangement of 78% of the 3-chloro-1-butene to *trans*-crotyl chloride.

Crotyl Chloride from Butadiene.—Crotyl chloride was prepared by treatment of pure grade butadiene (Phillips Petroleum Company, Bartlesville, Oklahoma) with especially concentrated hydrochloric acid. This acid was made by saturating 37% hydrochloric acid with hydrogen

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(7) Auwers and Wissebach, *Ber.*, **56B**, 715 (1923).

(8) Rasmussen, Brattain and Zucco, *J. Chem. Phys.*, **15**, 136 (1947).

(9) Furnished by the Northern Regional Research Laboratories, Peoria, Illinois.

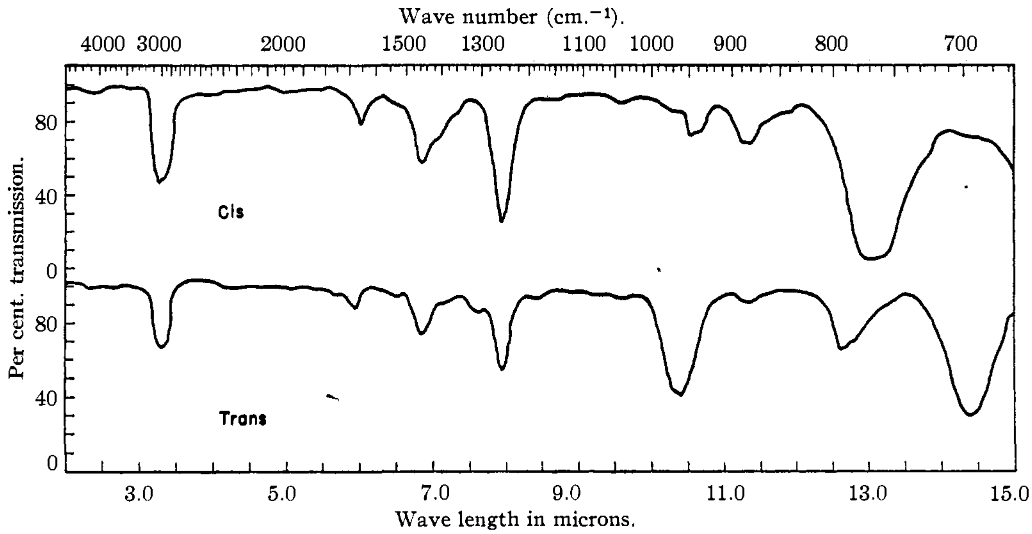

Fig. 2.—Infrared absorption spectra of *cis-* and *trans*-crotyl chloride.

chloride at 0°. Two hundred grams of this concentrated acid in a brown beer bottle was cooled in a Dry Ice–isopropyl alcohol mixture and 1 mole (54. g) of the butadiene was then added by introducing the gas below the surface of the cold acid. The bottle was sealed and it and its contents were permitted to warm to room temperature while being shaken on a mechanical shaker. Total time of shaking was twenty-four hours.

The organic layer was treated as in previously noted preparations of crotyl chloride. The yield of chlorides was 75% of which 35% was 3-chloro-1-butene while the remainder was *trans*-crotyl chloride.

Preparation of *trans*-Crotyl Chloride

trans-Crotyl Alcohol.—*trans*-Crotyl alcohol was prepared from *trans*-crotonaldehyde[10] (101.5°) by reduction using lithium aluminum hydride. The procedure used was essentially the same as the one previously described by Nystrom and Brown.[11] A yield of 65% was achieved. The data for the *trans*-crotyl alcohol thus produced are given in Table I.

trans-Crotyl alcohol was also prepared from *trans*-crotonaldehyde by reduction using aluminum isopropoxide. The product had the same physical properties as that produced by lithium aluminum hydride reduction but the yield was lower.

trans-Crotyl Chloride.—A mixture of 114 g. (2.00 moles) of *trans*-crotyl alcohol and 44.5 g. of pyridine was added slowly to 110 g. (0.80 mole) of phosphorus trichloride. The reaction flask was surrounded by ice-water during the addition. When all the alcohol had been added, the reaction flask was surrounded by a heated oil-bath and the organic chloride was removed from reaction by-products by distillation. The distillate was washed with water and dilute sodium carbonate solution to remove traces of hydrogen chloride. The organic chloride was dried over anhydrous potassium carbonate and fractionally distilled through a three-foot, glass helix-packed column. Ten per cent. of the material obtained was 3-chloro-1-butene. *trans*-Crotyl chloride boiling 84.5 to 84.9° amounted to 115 g. (64% yield). Physical data for this *trans*-crotyl chloride are given in Table I.

Preparation of *cis*-Crotyl Chloride.

3-Chloro-2-buten-1-ol.—Crude 1,3-dichloro-2-butene[12] (DCB) was distilled through a 4-ft., glass helix-packed column to obtain a relatively pure material. A fraction which boiled between 68 and 70° (100 mm.) was obtained; n^{25}D 1.4698 (lit.[13] n^{25}D 1.4695 for the low-boiling isomer).

The conversion of 1,3-dichloro-2-butene to 3-chloro-2-buten-1-ol was effected by treatment of the former with 10% sodium carbonate solution at reflux temperature for three hours. By this process there was obtained from 1075 g. (8.60 moles) of 1,3-dichloro-2-butene a total of 660 g. of 3-chloro-2-buten-1-ol (72% yield), b. p. 91–93° (50 mm.), n^{25}D 1.4630 (lit.[13] n^{25}D 1.4630 for the low boiling isomer).

TABLE I

cis- AND *trans*-CROTYL CHLORIDE AND RELATED COMPOUNDS

	trans-Crotyl chloride	*cis*-Crotyl chloride	*trans*-Crotyl alcohol	*cis*-Crotyl alcohol	2-Butyn-1-ol
B. p., °C. (mm.)	84.8 (752)	84.1 (758)	121.2 (754)	120.5 (752)	140.0 (758) 87.3 (100)
Index of refraction n^{20}D	1.4350	1.4390		1.4342	
n^{25}D	1.4327		1.4262		1.4520
Density d^{20}_4	0.9295	0.9426		0.8662	
d^{25}_4			0.8454		0.9326
Molecular (calcd.)	25.07	25.07	21.73	21.73	20.20
refr. (obs.)	25.42	25.29	21.86	21.69	20.28
3,5-Dinitrobenzoate, m. p., °C.			70.0[a]	51.0[a]	71.0

[a] Young and Andrews, THIS JOURNAL, 66, 421 (1944), give 70.5° for the *trans* isomer and 54–56° for the *cis* isomer.

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[10] Furnished by Tennessee Eastman Corporation, Kingsport, Tennessee.

[11] Nystrom and Brown, THIS JOURNAL, **69**, 1197 (1947).

[12] Furnished by E. I. du Pont de Nemours and Company, Wilmington, Delaware.

[13] Hatch and Ballin, THIS JOURNAL, **71**, 1039 (1949).

2-Butyn-1-ol.—The 3-chloro-2-buten-1-ol (660 g., 6.2 moles) was refluxed with vigorous stirring for two hours with a solution of 272 g. of sodium hydroxide in 530 ml. of water. The product was worked up in the usual manner, dried with potassium carbonate and distilled through a 4-ft., glass helix-packed, fractionating column at reduced pressure. A total of 167 g. (40% yield) of 2-butyn-1-ol which boiled at 87 to 88° (100 mm.) was obtained. Physical data for this alcohol are given in Table I.

***cis*-Crotyl Alcohol from 2-Butyn-1-ol.**—Methyl alcohol (290 ml.), 8 g. of catalyst (palladium on barium sulfate, prepared using the method of Schmidt[14]) and 25 g. (0.357 mole) of 2-butyn-1-ol were stirred and treated with 0.357 mole of hydrogen for three hours in a liter suction flask. This procedure was repeated until a total of 121 g. (1.73 mole) of 2-butyn-1-ol had been hydrogenated. The solutions were combined and the methanol was removed by distillation through a 4-ft., glass helix-packed, fractionating column. The *cis*-crotyl alcohol was then distilled through the same column at reduced pressure. A total of 94 g. (76% yield) of *cis*-crotyl alcohol which boiled at 63 to 64° (60 mm.) was obtained. Physical data for this *cis*-crotyl alcohol are given in Table I.

β-Chloroisocrotonic Acid.—Ethyl acetoacetate (124 g., 0.95 mole) was slowly added over a period of three hours to phosphorus pentachloride (453 g., 2.12 moles) in 125 g. of benzene in a one-liter, three-neck flask. The mixture was stirred during the addition of the ethyl acetoacetate and the reaction flask was surrounded by ice-water. After the addition of the ethyl acetoacetate, the ice water was removed and the reaction mixture was efficiently stirred for one hour at room temperature. The reaction flask was then placed on a steam-cone and heated to approximately 60° until the yellow colored reaction mixture became homogeneous. The mixture was cooled and water (600 ml.) was slowly added through the dropping funnel.

After the reaction mixture was worked up, the crystalline β-chloroisocrotonic acid was obtained by distillation using a distillation flask. The yield of β-chloroisocrotonic acid amounted to 15 g. (13%); m. p. 61°, lit.[15] 61°.

Isocrotonic Acid.—Two per cent. sodium amalgam (347 g.) was added to a solution of sodium β-chloroisocrotonate (prepared by adding 25 g. (0.21 mole) of β-chloroisocrotonic acid to a solution of 8.3 g. of sodium hydroxide in 100 ml. of water). This mixture was shaken vigorously for an hour with intermittent cooling in an ice–water-bath in order to prevent the temperature from rising above 40°. The resulting solution was separated from the mercury, and the mercury was washed with a small amount of water. The washings were added to the original aqueous solution. This procedure was repeated until a total of 100 g. of β-chloroisocrotonic acid had been treated with sodium amalgam.

The solutions which had been treated with sodium amalgam were combined and placed in a two-liter, round-bottom flask which was surrounded by an ice-water bath. Cold 50% sulfuric acid (60 g.) was slowly added to the solution. The resulting solution was then extracted with 4 portions of alcohol-free ether, the ether extractions were combined and dried with anhydrous calcium chloride. The ether solution was filtered to remove the calcium chloride, and the ether was removed by distillation through a Vigreux column. The residue, after removal of the ether, was distilled through a 30-cm., glass helix-packed, fractionating column at reduced pressure. A total of 34 g. (48% yield) of isocrotonic acid which boiled at 54 to 55° (5 mm.) was obtained; n^{20}_{D} 1.4450, lit.[16] n^{20}_{D} 1.4456; m. p. 13.5–13.8°, lit.[16] 14.0–14.2°; b. p. (atmospheric) 168–169°, lit.[16] 169°.

***cis*-Crotyl Alcohol from Isocrotonic Acid.**—By treatment of isocrotonic acid with lithium aluminum hydride in anhydrous diethyl ether, *cis*-crotyl alcohol was obtained. Properties of *cis*-crotyl alcohol prepared by this method: n^{20}_{D} 1.4338, d^{20}_{4} 0.8663; *MR* (obsd.) 21.67; *MR* (calcd.) 21.73; melting point of 3,5-dinitrobenzoate 51°.

Melting point of a mixture of the 3,5-dinitrobenzoate of *cis*-crotyl alcohol prepared by hydrogenation of 2-butyn-1-ol and of that prepared from isocrotonic acid, 51°.

***cis*-Crotyl Chloride.**—*cis*-Crotyl chloride was prepared from 43.0 g. (0.60 mole) of *cis*-crotyl alcohol in a manner similar to that used in the preparation of *trans*-crotyl chloride by using phosphorus trichloride in the presence of pyridine. In order to avoid elevated temperatures when the *cis*-crotyl chloride was in the presence of hydrogen chloride, the removal of the organic chloride from the reaction by-products was carried out by reduced pressure. In this operation a Dry Ice–isopropyl alcohol trap was connected directly to the reaction flask and the system was maintained at 100 mm. The reaction flask was surrounded by a water-bath at 50° and the organic chloride distilled into the trap. After the organic chloride was washed with 3% sodium carbonate solution to remove traces of hydrogen chloride, it was placed over anhydrous potassium carbonate to dry overnight. The organic chloride was decanted from the potassium carbonate and distilled through a 30-cm., glass helix-packed, fractionating column. After a forerun of 6 ml., there was obtained 28 g. of *cis*-crotyl chloride which boiled at 84.1° (758 mm.); yield 50%.

Anal. Calcd.: Cl, 39.14. Found: Cl, 39.10, 39.11.

Infrared Absorption Spectra.—The infrared absorption spectra[17] were determined for *cis*- and *trans*-crotyl chloride using a model No. I.R. 2 Beckman Infrared Spectrophotometer. The apparatus was fitted with standard gas equipment, and the absorption spectra of each of the isomers were determined in the gas phase—*cis*-crotyl chloride at 60-mm. pressure and *trans*-crotyl chloride at 50-mm. pressure. The data are plotted in Fig. 2.

Summary

Both *cis*- and *trans*-crotyl chloride have been prepared by unambiguous syntheses and the following physical properties were determined: boiling point, density, index of refraction, infrared spectra.

Apparently the crotyl chlorides previously reported have had the *trans* configuration or contained substantially only the *trans* isomer.

AUSTIN, TEXAS RECEIVED MAY 31, 1949

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[14] Schmidt, *Ber.*, **52**, 409 (1919).

[15] Michael and Schulthess, *J. prakt. Chem.*, [2] **46**, 236 (1892).

[16] Auwers, *Ann.*, **432**, 46 (1923).

[17] These determinations were made by J. F. Music of the Spectrographic Service Laboratories, The University of Texas.