reaction between L-leucyl-L-leucine and trichloroacetyl chloride in aqueous NaOH.

N-Trichloroacetylglycine.—Glycine, 1.00 g (13.35 mmol), 8 ml (13.98 g, 52.25 mmol) of hexachloroacetone, and 25 ml of DMSO were magnetically stirred at room temperature for 24 hr. The reaction solution was diluted with 85 ml of water and the reaction solution was diluted with 85 ml of water and the resultant mixture was extracted with three 50-ml portions of *n*-BuOH. The butanol extract was chromatographed on a silicic acid column. A mixture of benzene, acetone, and methanol (5:4:1) was the eluting solvent. A DMSO-free oil was obtained which crystallized from methyl isobutyl ketone and petroleum ether (bp 30–60°). The yield of product was 1.88 g (63.7%); mp 130.0–130.5° (lit.[5] 131–132°). This product was identical (thin layer R_f value, melting point, and ir spectra) with that obtained from the reaction of glycine with trichloroacetic anhydride.

Larger scale preparations of N-trichloroacetylglycine showed that the reaction with hexachloroacetone in DMSO is exothermic. In one such preparation (0.134 mol of glycine) the reaction solution was poured into about 100 ml of water and the resultant solution was distilled at atmospheric pressure. At 60° (vapor temperature) a distillate was collected which was identified as chloroform by its gas chromatography retention time and by its infrared spectrum: yield, 13.32 g (0.112 mol).

Registry No.—Hexachloroacetone, 116-16-5; 2 ($R^1 = R^2 = R^3 = H$), 24299-47-6; 2 ($R^1 = R^2 = i$-Bu; $R^3 = H$), 24299-25-0; 2 ($R^1 = R^2 = H$; $R^3 =$ Me), 24299-74-9; 2 ($R^1 = i$-Pr; $R^2 = i$-Bu; $R^3 = H$), 24299-26-1; 2 (R^1 = benzyl; $R^2 = i$-Bu; $R^3 = H$), 24299-27-2.

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Synthesis of Derivatives of 2-Aminoproline and 5-Aminoproline

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Synthesis of α-amino acids containing a nitrogen or oxygen atom on the carbon linked with nitrogen have been described in reports from several laboratories, and some of these compounds are constituents of Ergot alkaloids. Proline derivatives of the type previously indicated have not yet been prepared, and we present here the synthesis of derivatives of 2-amino-DL-proline and 5-amino-DL-proline.

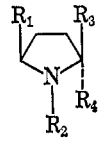
Addition of acetamide[1] to N-acetyl-Δ²-pyrroline-2-carboxylic acid[2] occurred on heating a mixture of the two substances, which produced a compound to which we attributed the structure of N,N′-diacetyl-2-amino-DL-proline (**1**). This structure is in accord with the spectral data and was confirmed through acid hydrolysis,[3] which gave α-keto-δ-acetylaminovaleric acid, recognized as the 2,4-dinitrophenylhydrazone.[2]

(1) Addition of acetamide to α-acylaminoacrylic acids has been reported: D. Shemin and R. Herbst, *J. Amer. Chem. Soc.*, **60**, 1954 (1938).

(2) K. Hasse and P. Homann, *Biochem. Z.*, **335**, 474 (1962).

(3) *trans*-N,N′-Diacetyl-3-amino-DL-proline, prepared by us [*Tetrahedron Lett.*, **35**, 3055 (1969)], was stable under the conditions employed in the hydrolytic degradation of **1**.

Starting material for synthesis of *cis*-N,N′-dicarbobenzyloxy-5-amino-DL-proline (**5**) was N-carbobenzyloxy-DL-pyrrolidine-2,5-dicarboxylic acid anhydride.[4] This compound was transformed to the corresponding monoazide **4** and gave **5** through the Curtius reaction. Catalytic hydrogenation (palladium on charcoal in acetic acid) of *cis*-N,N′-dicarbobenzyloxy-5-amino-DL-proline led to proline, which was recognized as the N-2,4-dinitrophenyl derivative.



(L forms only are shown)

Compd	R_1	R_2	R_3	R_4
1	H	$COCH_3$	COOH	$NHCOCH_3$
2	H	$COCH_3$	$COOCH_3$	$NHCOCH_3$
3	H	$COCH_3$	$CONHNH_2$	$NHCOCH_3$
4	CON_3	$COOCH_2C_6H_5$	COOH	H
5	$NHCOOCH_2C_6H_5$	$COOCH_2C_6H_5$	COOH	H

Experimental Section[5]

N,N′-Diacetyl-2-amino-DL-proline (1).—N-Acetyl-Δ²-pyrroline-2-carboxylic acid (1 g) and 2 g of acetamide were finely powdered and heated in a vacuum sublimator at 110° for 3 hr after removal of air under high vacuum. The excess acetamide was sublimed off and the residue was crystallized from methanol to give 1.15 g (75%) of **1**, mp 175–77°.

Anal. Calcd for $C_9H_{14}N_2O_4$: C, 50.46; H, 6.59; N, 13.08. Found: C, 50.20; H, 6.78; N, 12.95.

2,4-Dinitrophenylhydrazone of α-Keto-δ-acetylaminovaleric Acid.—A 90-mg portion of **1** was dissolved with stirring and was gently heated in 25 ml of a solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl (4 mg/ml). When the reaction mixture was maintained at room temperature overnight, the hydrazone crystallized. The melting point of a sample recrystallized from acetic acid was 231° dec.

Anal. Calcd for $C_{13}H_{15}N_5O_7$: C, 44.19; H, 4.28; N, 19.83. Found: C, 43.98; H, 4.45; N, 19.61.

N,N′-Diacetyl-2-amino-DL-proline Methyl Ester (2).—Methyl ester **2** was obtained by addition of ethereal diazomethane to the parent acid in methanol at 0°. Evaporation of the solvent and crystallization from ethyl acetate gave **2**: 90% yield; mp 140–141°; nmr ($CDCl_3$) δ 1.99 and 2.04 (two s, 3, $CH_3CON<$), 2–3 range (m, 4, C-3 and C-4 H of the ring), 3.79 (s, 3, CH_3OCO), 3.6–4.2 range (m, 2, C-5 H of the ring), 7.14 (broad signal, 1, NHCO). The assignments were made on the basis of the chemical shift and ratio of intensities values.

Anal. Calcd for $C_{10}H_{16}N_2O_4$: C, 52.62; H, 7.07; N, 12.27. Found: C, 52.71; H, 7.01; N, 12.32.

N,N′-Diacetyl-2-amino-DL-prolinehydrazide (3).—Methyl ester **2** (1 g) was dissolved in 8 ml of monohydrated hydrazine which was removed 5 min later under vacuum at 30°. The residue was crystallized from ethanol–ethyl ether to give the hydrazide in 80% yield, mp 171–172°.

Anal. Calcd for $C_9H_{16}N_4O_3$: C, 47.36; H, 7.07; N, 24.55. Found: C, 47.23; H, 7.09; N, 24.68.

***cis*-N,N′-Dicarbobenzyloxy-5-amino-DL-proline (5).**—N-Carbobenzyloxy-DL-pyrrolidine-2,5-dicarboxylic acid anhydride (1.24 g) was dissolved in 75 ml of warm acetone. The solution was cooled in ice and 750 mg of sodium azide in 5 ml of water was added with stirring and cooling, immediately followed by a further amount of water to dissolve the sodium azide which separated as a solid. After the mixture stirred for 1 hr at 0°, 20 ml of water was added and the acetone was evaporated off at 30°. The cooled aqueous solution was acidified to pH 4 with 2 *N* hydrochloric acid and extracted with ethyl ether, which was

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(5) Melting points were taken on a Culatti apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 221 infrared spectrophotometer. Nmr spectra were recorded on a Varian A-60 spectrometer, at room temperature, and are given in δ units relative to TMS as internal standard.

washed with water, dried (Na_2SO_4), and evaporated at reduced pressure to give 1.40 g of the azide **4**, thick oil, ir (liquid film) 2130 cm^{-1} (azide).

The azide was warmed for 2 hr at 70° in 10 ml of anhydrous benzyl alcohol. The mixture was diluted with ethyl ether and extracted with 2 *N* sodium carbonate. The cooled alkaline solution was acidified with 2 *N* hydrochloric acid to pH 4 and reextracted with ether which was washed with water and dried (Na_2SO_4); solvent was evaporated off at reduced pressure. The oily residue was crystallized from ethanol–water to give 500 mg (28%) of *cis*-N,N′-dicarbobenzyloxy-5-amino-DL-proline, mp 141–142°.

Anal. Calcd for $C_{21}H_{22}N_2O_6$: C, 63.31; H, 5.57; N, 7.03. Found: C, 63.39; H, 5.65; N, 7.06.

Registry No.—**1**, 24377-91-1; **2**, 24377-92-2; **3**, 24377-93-3; **5**, 24377-94-4; α-keto-δ-acetylaminovaleric acid (2,4-dinitrophenylhydrazone), 24378-14-1.

A Facile Preparation of 3-Thujene from Thujone

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The bicyclic monoterpene 3-thujene (**1**) is much less readily available from natural sources than is thujone (**2**). The methods previously used[1,2] for obtaining **1** from **2** involve reduction to the thujyl alcohols, separation of isomers, and eliminations. We have found that it is possible to obtain **1** from **2** in a rather simple procedure which is applicable to large-scale work by use of the Bamford–Stevens rearrangement.[3]

Thujone (**2**) was readily converted to the *p*-toluenesulfonylhydrazone which was initially decomposed with a solution of sodium in ethylene glycol. The hydrocarbon product was analyzed by preparative vpc and shown to contain 3-thujene (**1**, 42%), 2-thujene (**3**, 16%), γ-terpinene (**4**, 13%), a fourth unidentified compound, and a trace of *p*-cymene. Using acetamide as a solvent,[4] the hydrocarbon product (97% yield) consisted of **1** (80%) and **4** (20%), **4** being slightly contaminated with an unidentified isomer. 3-Thujene was characterized by its spectral properties and by conversion to terpinene dihydrochloride.[5] This procedure therefore represents a simple process for obtaining 3-thujene from readily available thujone.

Experimental Section[6]

***p*-Toluenesulfonylhydrazide.**[7]—Hydrazine hydrate (40 g, 85%) was slowly added to a benzene solution of 60 g of *p*-toluenesulfonyl chloride (recrystallized from an ether–ligroin mixture) at 5° through the condenser into a 500-ml flask. After 2 hr the solid was filtered and recrystallized from hot water. The yield was 42.6 g (72%), mp 110–112° (lit.[7] 112°).

Thujone *p*-Toluenesulfonylhydrazone.—*p*-Toluenesulfonylhydrazide (42.6 g) and 40 g of **2**, $[\alpha]^{25}D$ +20.13°, were dissolved in 200 ml of ethanol and refluxed in a 500-ml flask for 3.5 hr until the reaction was complete as indicated by thin layer chromatography. Following reflux, the ethanol was removed under reduced pressure until a precipitate formed, and then the mixture was heated on a steam bath to effect solution. The solution was cooled to effect crystallization; the crystals were filtered, recrystallized from ethanol, and dried. The yield was 25.6 g (35%), mp 126–129°, $[\alpha]^{25}D$ +105.7°; ir ($CHCl_3$) 3310 (NH), 2980, 1610, 1170 cm^{-1}.

Anal. Calcd for $C_{17}H_{24}N_2SO_2$: C, 63.75; H, 7.50; N, 8.75. Found: C, 63.99; H, 7.74; N, 8.63.

3-Thujene (1). I. Ethylene Glycol as Solvent.—The hydrazone (5 g) and 50 ml of 1.5 *N* sodium in ethylene glycol were placed in a 100-ml flask. Most of the solid dissolved immediately and the remainder dissolved on the application of heat. Nitrogen evolution continued steadily for 15 min and the resulting organic layer was then distilled off at 141–175° yielding 1.5 ml of product. The vpc analysis indicated four products: 3-thujene (**1**, 42%), 2-thujene (**3**, 16%), contaminated slightly with another compound γ-terpinene (**4**, 13%), and 20% of an unidentified mixture.

II. Acetamide as Solvent.—The acetamide (200 g) was melted in a 500-ml three-necked flask and purged with oxygen-free nitrogen. The acetamide was cooled to 100° and 6.0 g of sodium was added in small quantities under a nitrogen atmosphere (extreme care must be taken to avoid combustion). The hydrazone (38.6 g) was added and the temperature held at 140–150°. Nitrogen evolution ceased after 25 min and the reaction mixture was cooled slightly. Water (200 ml) was added and the organic layer was extracted into petroleum ether. The ethereal solution was dried ($MgSO_4$), filtered, concentrated, and distilled giving 15.9 g (97%) of mixed hydrocarbon product. The mixture was readily separated *via* preparative vpc and **1** was characterized as follows: $n^{29}D$ 1.4471, $[\alpha]^{32}D$ −32.05°, bp 150–151°; ir (neat) 2985, 2881, 3057 cm^{-1}; nmr (neat) δ 0.02 (t, 1, J = 3 Hz), 0.90 (m, 2), 0.98 (d, 6, J = 3 Hz), 1.35 (m, 1), 1.76 (q, 3, J = 2 Hz), 2.30 (m, 2), 4.90 (m, 1); mass spectrum (70 eV) *m/e* 136, 93 (lit.[8]).

Terpinene Dihydrochloride.[5]—To 5 ml of glacial acetic acid was added 0.20 g of **1** and the solution was saturated with gaseous HCl. The mixture developed a red color after 9 hr of standing and was then poured over ice. The resulting solid was filtered and recrystallized from methanol: mp 47–49°; nmr ($CDCl_3$) δ 1.68 (s, 3), 1.90 (d, 6, J = 6 Hz), 1.98 (s, 9).

The absolute configurations of 3-thujene (**1**), thujone (**2**), and 2-thujene (**3**) are those verified by Norin.[9,10]

Registry No.—**1**, 3917-48-4; **2**, 546-80-5; **2** *p*-toluenesulfonylhydrazone, 18791-12-3.

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(6) Melting points were measured on a Kofler hot stage and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrophotometer, nuclear magnetic resonance spectra on Varian A-60 and HA-100 spectrometers with tetramethylsilane as an internal reference, and mass spectra on an AEI MS 9 mass spectrometer. Refractive indices were determined on a Bausch and Lomb ABBE-3L refractometer and optical rotations on the Perkin-Elmer P22 spectropolarimeter. Analytical and preparative vpc analyses were made on a Varian Aerograph Model 700 using a 30% Carbowax column on 45–60 Chromosorb W support at 180°. Thujone was kindly supplied by Fritzsche Bros. Inc., New York, N. Y. Elemental analysis was performed by the Midwest Microlab, Inc., Indianapolis, Ind.
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Alkaline Cleavage of Phosphetane Oxides

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Recently, we reported the alkaline cleavage of several heterocyclic phosphine oxides.[1] In all but one

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