separated was filtered and washed with water and finally with acetone in a Waring blender. The resulting product was an almost white granular solid.

Anal. C, 39.65; H, 5.68; S, 11.16.

A portion was dissolved in dimethylformamide by heating to 50°. Evaporation of the solvent from a glass plate left the product as a clear, tough film.

Internal esterification of II. Two grams of the modified cellulose was dissolved in 25 ml. of dimethylformamide by warming. A small amount of concentrated H_2SO_4 was added from a stirring rod and the solution was heated under vacuum at 90–95° for 4 hr. with slow distillation of the solvent. The solution remained clear upon cooling. Upon evaporation of the solvent a clear, brittle film was obtained. *Anal.* C, 40.71; H, 5.58; S, 11.01.

Esterification of II *with butanol.* Two grams of the modified cellulose was dissolved in 25 ml. of dimethylformamide by warming. To this solution was added 10 ml. of butanol. Some gellation of the solution occurred at this point but it remained stirrable. Once again a trace of H_2SO_4 was added and the mixture was heated under vacuum at 80–85° for 3 hr. with slow distillation. Evaporation of the product left a clear film of better flexibility than the original modified cellulose.

Anal. C, 41.47; H, 5.82; S, 10.91.

Acetylation of II. (a) One gram of the modified cellulose was heated to reflux for 1 hr. with 10 ml. of acetic anhydride containing a trace of sulfuric acid. During this period appreciable swelling of the polymer took place. Upon cooling, water was added to decompose excess acetic anhydride after which the granular solid was separated by filtration and was washed thoroughly with water and finally ethanol. Upon drying there was obtained 1.27 g. of the acetylated product which was found to be completely insoluble in acetone, alcohol, and dimethylformamide.

Anal. C, 45.33; H, 5.52; S, 8.36.

(b) One gram of the modified cellulose was heated at 90–100° for 1 hr. with 10 ml. of pyridine, 10 ml. of acetic anhydride, and 10 ml. of dimethylformamide. After quenching with water, separation of the solid, and finally washing with water and alcohol, there was obtained 1.08 g. of material.

Anal. C, 44.20; H, 5.28; S, 6.55.

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Synthesis of γ-Aminobutyryl-γ-aminobutyric Acid

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γ-Aminobutyric acid has been found in brain extracts by Awapara *et al.*,[2] Roberts and Frankel,[3] and Udenfriend.[4] Recently an analog, γ-guanidinobutyric acid, was isolated from brain by Irreverre *et al.*[5] Due to the demonstration of enzymatic interconversion between these two butyric acids[6,7] and their possible role as humoral agents,[8–10] we were prompted to synthesize the dipeptide of γ-aminobutyric acid for physiological testing and for comparison on paper chromatography.

The synthesized γ-aminobutyryl-γ-aminobutyric acid in a concentration of 5.3 μm/ml. is not effective in blocking the neutromuscular transmission of crustaceans while γ-aminobutyric acid was effective at the threshold concentration of 9.7×10^{-3} μm/ml.[11] The dipeptide as well as the benzyl ester of γ-aminobutyric acid give negative reactions in the specific enzymatic method for the determination of γ-aminobutyric acid developed by Jakoby and Scott.[12]

EXPERIMENTAL

N-Carbobenzoxy-γ-aminobutyric acid. This compound was prepared by a procedure similar to that used for the preparation of *N*-carbobenzoxyglycine,[13] using 0.05 mole of γ-aminobutyric acid and 0.05 mole of carbobenzoxy chloride. The yield was 7.8 g. (66%). Recrystallized from ethylacetate-petroleum ether the compound melted at 66–67°.

Anal. Calcd. for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.89; H, 6.23; N, 5.90.

γ-Aminobutyric acid benzyl ester hydrochloride. This derivative was prepared using the procedure employed by Erlanger and Hall[14] for the synthesis of D,L-phenylalanine benzyl ester hydrochloride. Using 0.033 mole of γ-aminobutyric acid and 70 ml. of benzyl alcohol there was obtained 5.2 g. of material (69%). Recrystallized three times from ethyl acetate it melted at 109–110°.

Anal. Calcd. for $C_{11}H_{16}O_2NCl$: C, 57.66; H, 7.02; N, 6.10. Found: C, 57.38; H, 7.05; N, 5.81.

N-Carbobenzoxy-γ-aminobutyryl-γ-aminobutyric acid benzyl ester. To a mixture of 2.6 g. of *N*-carbobenzoxy-γ-aminobutyric acid and 1.51 ml. of triethylamine in 20 ml. of methylene chloride pre-cooled to −5° was added 1.0 ml. of ethylchloroformate and stored at −5° for 5 min. A second flask containing a solution of 2.6 g. of γ-aminobutyric acid benzyl ester hydrochloride and 4.68 ml. of triethylamine in 20 ml. of methylene chloride pre-cooled to −5° was added to above mixture. An additional 10 ml. of methylene chloride was used for washing out the flask. The reaction mixture was kept at −5° for 20 min. and allowed to come to room temperature with continuous stirring (magnetic) for 4 hr. The solution was extracted with 50 ml. of dilute hydrochloric acid, then with a cold, saturated solution of $NaHCO_3$ and finally with water. The methylene chloride layer was

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dried over Na_2SO_4, filtered and concentrated *in vacuo* to the point of crystallization. The flask was warmed to redissolve the crystals, petroleum ether was added, and the flask placed in the ice box overnight. The precipitate of soft needles was filtered and washed with petroleum ether. The yield was 3.3 g. (73%) and it melted at 86–87°. After recrystallization from 75% ethyl alcohol and drying *in vacuo* the melting point was unchanged.

Anal. Calcd. for $C_{23}H_{28}O_5N_2$: C, 66.97; H, 6.84; N, 6.79. Found: C, 66.91; H, 7.06; N, 6.79.

γ-Aminobutyryl-γ-aminobutyric acid. To a solution of 2.1 g. (0.0051 mole) of *N*-carbobenzoxy-γ-aminobutyryl-γ-aminobutyric acid benzyl ester in 35 ml. of methyl alcohol were added 2 drops of glacial acetic acid and 0.7 g. of Palladium black catalyst (Fisher Scientific Co.). Hydrogen gas was bubbled through and after 2 hr., 20 ml. of H_2O were added and the hydrogenation continued for an additional 3 hr. The catalyst was removed by filtration and washed with a small volume of water. The filtrate was concentrated *in vacuo* to a crystalline residue. The solid was recrystallized from absolute ethyl alcohol. The yield was 0.75 g. (79%). Dried *in vacuo* at 80–81° it melted at 178–179°. Another crop (0.2 g.) was recovered from the filtrate. Recrystallized from water–ethyl alcohol it melted at 177–178°. The total yield was practically quantitative.

Anal. Calcd. for $C_8H_{16}O_3N_2$: C, 51.04; H, 8.57; N, 14.88. Found: C, 50.89; H, 8.56; N, 14.76.

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A Convenient Synthesis of Cyclohexyl Methyl Ketone and Cyclohexylmethylcarbinol

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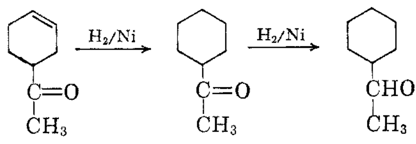
The preparation of a sizable quantity of vinylcyclohexane from cyclohexylmethylcarbinyl acetate[1] required that cyclohexylmethylcarbinol (III) be readily available. This alcohol has been previously prepared by several routes including the reaction of the cyclohexyl Grignard reagent with acetaldehyde,[2,3] the sodium and alcohol reduction of cyclohexen-1-yl methyl ketone[4] and the catalytic hydrogenation of acetophenone.[3,5] The latter method seemed to be the only reported route to III which might be particularly well suited to rather large scale laboratory operation. An investigation of the hydrogenation of acetophenone substantiated the observations of others[3,5] that the hydrogenation of acetophenone is very sensitive to poisons, and the reaction conditions must be controlled extremely carefully. A search for an alternate reliable method of preparing quantities of cyclohexylmethylcarbinol resulted in the development of a procedure based on the Diels-Alder adduct (I) of methyl vinyl ketone and butadiene-1,3.[6] The hydrogenation of I over W-4 Raney nickel was accomplished in two distinct steps, the first being the highly exothermic hydrogenation (25° at 200 p.s.i.g. H_2) of I to cyclohexyl methyl ketone (II) which is further reduced to III under somewhat more strenuous conditions (120° at 1500 p.s.i.g. H_2). The hydrogenation of I to III without isolation of II furnished III in 96% yield. II may also be reduced to III with lithium aluminum hydride, the acetate being isolated to 90% yield.



I II III

EXPERIMENTAL

Cyclohexen-3-yl methyl ketone (I). Equimolar amounts (5.3 moles) of butadiene-1,3 and methyl vinyl ketone[7] were heated at 140° in a sealed reactor during 9 hr. as described by Petrov.[6] The reaction temperature must be approached with caution as in several runs an uncontrollable exothermic reaction was observed. Distillation furnished a 90% yield of ketone; b.p. 78–80° (20 mm.), n_D^{25} 1.4662 [reported b.p. 79.5–80° (20 mm.),[6] n_D^{20} 1.4698[6]].

Cyclohexyl methyl ketone (II). A mixture of I (620 g.; 5 moles) and about 5 g. of W-4 Raney nickel catalyst[8] was treated with hydrogen at 150–200 p.s.i.g. The temperature of the reaction mixture was initially 25° and increased to 60° during 30 min. at which point no further hydrogen was consumed. Distillation furnished 569 g. (89% yield) of II, b.p. 73–74° (17 mm.), n_D^{25} 1.4494 [reported b.p. 72° (18 mm.)[3], $n_D^{25.9}$ 1.44955[3]]. The semicarbazone, after recrystallization from methanol, melted at 177° which is in agreement with the literature value.[4]

Cyclohexylmethylcarbinol (III). A mixture of I (540 g.; 4.35 moles) and about 5 g. of W-4 Raney nickel catalyst in a rocking autoclave pressurized with hydrogen to 900 p.s.i.g. was hydrogenated to II as described above. The temperature of the reaction mixture rose from 20° to 63° in 10 min. and then slowly dropped. Hydrogen was then added until the pressure within the system was 1500 p.s.i.g., and the system heated by an external heater to 120°. By maintaining the hydrogen pressure at about 1500 p.s.i.g. by repressurizations, the hydrogenation of the carbonyl was completed in 1 hr. Distillation furnished 527 g. (96% yield) of alcohol b.p. 85–87° (17 mm.); n_D^{25} 1.4639 [reported b.p. 189.4–189.8°

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