amino acid in the sample. If a decrease during the synthesis is due to blocking, the titration results will show the actual content of the amino acids. In the present experiment it has not been possible to explain the reason for the gradual slight decrease of the titration values during the synthesis.

In the synthesis of still larger amounts of resin bound peptides, determination of the proportion of the sample to the entire amount by weighing is not possible in practice. In such cases an internal standard has to be used for determination of the amount of derivatized polystyrene in the actual sample, allowing the results to be calculated per weight unit of the polymer. Whether a radioactive labelling of the methylene group in the benzyl ester linkage insures a sufficient accuracy will have to be evaluated by experiments.

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Resolution and Absolute Configuration of 1-Ethyl-1-methyl-2-propynylamine

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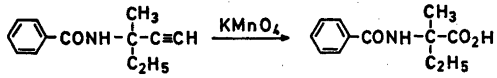
The enantiomers of some *N*-(4-*tert*-amino-1-methyl-2-butynyl)-substituted succinimides and 2-pyrrolidones show strong stereospecificity in blocking the motor effects of the muscarinic agent oxotremorine, *N*-(4-pyrrolidino-2-butynyl)-2-pyrrolidone. The (*R*)-(+)-isomers are about twice as active as their corresponding racemates in this respect while the (*S*)-(−)-isomers are practically inactive.[1,2] In order to investigate the influence of further alkyl substitution on stereospecificity we decided to prepare optical isomers of compounds containing both a methyl and an ethyl group in the 1-position of the butynyl chain. For this purpose we needed the enantiomers of 1-ethyl-1-methyl-2-propynylamine (*1*) as starting material and this communication deals with the resolution of this amine and the determination of its absolute configuration.

The amine was resolved into its (+)- and (−)-enantiomers by fractional crystallization of its (+)- and (−)-hydrogen tartrates, respectively. In order to estimate the optical purity of the enantiomers we used ^{1}H NMR spectroscopic analyses of the diastereomeric amides formed when optically impure amine is acylated with optically pure (−)-*O*-methylmandelyl chloride.[2,3]

The absolute configuration of the amine was established by transforming its benzoyl derivative to the corresponding isovaline derivative.



The benzoyl derivative obtained from the (+)-enantiomer of the amine yielded upon oxidation with potassium permanganate the benzoyl derivative of (+)-isovaline. Thus (+)-*1* and (+)-isovaline must be configurationally identical. The latter compound has been correlated into the natural amino acid series (L- or *S*-configuration) both by chemical[4] and enzymatic methods.[5] Dextrorotatory *1* can therefore be assigned the *S* configuration.

Experimental. Melting points were determined in a metal block using open capillary tubes and calibrated Anschütz thermometers. Microanalyses were carried out at the Microanalytical Laboratory, Royal Agricultural College, Uppsala. IR spectra were run on a Perkin-Elmer 157 G spectrophotometer and ^{1}H NMR spectra

on a Perkin-Elmer R 12 B spectrometer. Optical rotations were measured with a Perkin-Elmer 141 spectropolarimeter.

Resolution of 1-ethyl-1-methyl-2-propynylamine. Racemic amine (60 g, 0.62 mol), prepared as previously described,[6] was added to a solution of (+)-tartaric acid (92.5 g, 0.62 mol) in 300 ml of absolute ethanol. The solution was left overnight at room temperature. The salt obtained (60.5 g) required several recrystallizations from about 10 % solutions in 95 % ethanol before constant physical properties of the salt, of the hydrochloride, and of the (−)-*O*-methylmandelyl derivative of the liberated amine were obtained. Yield 18.0 g (24 %) of resolved (+)-hydrogen tartrate, m.p. 164.5–166 °C, $[\alpha]_D^{22}$ +17.8° (*c* 1.0, water). Anal. $C_{10}H_{17}NO_6 \cdot \frac{1}{2}H_2O$: C, H, N.

The first filtrate from the above resolution was concentrated *in vacuo* and the residue dissolved in saturated K_2CO_3-solution. After extracting the amine with ether and drying the extract (K_2CO_3), the solution was fractionated through a helix-packed column. The amine fraction was added to a solution of (−)-tartaric acid in 95 % ethanol and the salt formed was purified as described above for the enantiomeric salt. The yield, based on recovered amine, of resolved (−)-hydrogen tartrate was 26 %, m.p. 165–166 °C, $[\alpha]_D^{22}$ −18.5 (*c* 1.0, water). Anal. $C_{10}H_{17}NO_6 \cdot \frac{1}{2}H_2O$: C, H, N.

(S)-(+)-*1-Ethyl-1-methyl-2-propynylamine.* Since the amine liberated from the resolved (+)-hydrogen tartrate was found to contain traces of impurities (as shown by ^{1}H NMR and GC, 20 % Carbowax 20 m), the (+)-hydrogen tartrate was dissolved in saturated K_2CO_3-solution and the amine extracted with ether. The hydrochloride of the amine was precipitated from the ethereal extract, dried, and dissolved in saturated K_2CO_3-solution. The pure amine was then obtained through the procedure described above, b.p. 104–105 °C, n_D^{22} 1.435, $[\alpha]_D^{22}$ +6.6° (*c* 1.0, ethanol), yield 58 % (from the hydrochloride). ^{1}H NMR ($CDCl_3$, 37 °C): δ 1.03 (3 H, t, *J* 7.0 Hz, CH_2CH_3), 1.37 (3 H, s, $C-CH_3$), 1.3–1.8 (2 H, m, CH_2) 2.28 (1 H, s, $\equiv CH$). *Hydrochloride:* m.p. > 250 °C (from ethanol-ether), $[\alpha]_D^{22}$ +6.9° (*c* 0.8, ethanol). *Benzamide:* m.p. 104–105 °C (from ligroin), $[\alpha]_D^{22}$ +3.4° (*c* 1.0, ethanol). Anal. $C_{13}H_{15}NO$: C, H, N.

(R)-(−)-*1-Ethyl-1-methyl-2-propynylamine* was obtained similarly from the (−)-hydrogen tartrate *via* the hydrochloride salt, b.p. 104–106 °C, n_D^{22} 1.435, $[\alpha]_D^{22}$ −6.2° (*c* 1.0, ethanol), yield 57 %. *Hydrochloride:* m.p. > 250 °C, $[\alpha]_D^{22}$ −6.4°. (*c* 1.4, ethanol), Anal. $C_6H_{11}N.HCl$: C, H, N, *Benzamide:* m.p. 104–105 °C, $[\alpha]_D^{22}$ −3.4° (*c* 1.0, ethanol). Anal. $C_{13}H_{15}NO$: C, H, N.

N-[(S)-*1-Ethyl-1-methyl-2-propynyl*]-(R)-O-*methylmandelamide.* (*R*)-(−)-*O*-methylmandelic acid,[7] $[\alpha]_D^{22}$ −148.7° (*c* 0.6, ethanol), was converted to its acid chloride with which (*S*)-(+)-1-ethyl-1-methyl-2-propynylamine was acylated according to a method described in the literature,[8] m.p. 53.5–54.5 °C (from light petroleum), $[\alpha]_D^{22}$ −58.5° (*c* 0.7, ethanol). ^{1}H NMR (C_6H_6, 37 °C): δ 0.95 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 1.58 (3 H, s, $C-CH_3$), 2.06 (1 H, s, $\equiv CH$), 1.55–2.45 (2 H, m, CH_2), 2.96 (3 H, s, OCH_3), 4.43 (1 H, s, CH). Anal. $C_{15}H_{19}NO_2$: C, H, N.

N-[(R)-*1-Ethyl-1-methyl-2-propynyl*]-(R)-O-*methylmandelamide* was prepared similarly from (*R*)-(−)-1-ethyl-1-methyl-2-propynylamine, m.p. 31–33 °C (from light petroleum), $[\alpha]_D^{22}$ −68.4° (*c* 1.2, ethanol). ^{1}H NMR (C_6H_6, 37 °C): δ 0.87 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 1.71 (3 H, s, $C-CH_3$), 2.05 (1 H, s, $\equiv CH$), 1.40–2.30 (2 H, m., CH_2), 2.95 (3 H, s, OCH_3) 4.42 (1 H, s, CH). Anal. $C_{15}H_{19}NO_2$: C, H, N.

(S)-(+)-N-*Benzoylisovaline. A. Acylation of* (S)-(+)-*isovaline.* (*S*)-(+)-Isovaline, $[\alpha]_D^{22}$ +10.9° (*c* 1.1, water), obtained by resolution and hydrolysis of (+)-*N*-formylisovaline,[9] was benzoylated under customary Schotten-Baumann conditions. Yield 30 %, m.p. 175–177 °C (from 40 % methanol), $[\alpha]_D^{22}$ +11.2° (*c* 0.7, methanol), lit.[10] m.p. 176–178 °C, $[\alpha]_D^{15}$ +10.3° (*c* 1.4, methanol).

B. Oxidation of (S)-(+)-N-*(1-ethyl-1-methyl-2-propynyl)-benzamide.* A saturated solution of $KMnO_4$ was added dropwise to a stirred suspension of the finely pulverized benzamide (0.85 g, 0.04 mol) in water (25 ml) at 0–5 °C. When no more $KMnO_4$ was consumed the solution was filtered and acidified with 5 M H_2SO_4. Sodium pyrosulfite was added to remove excess of permanganate. The product crystallized from the clear solution. Yield 59 %, m.p. 176–177 °C, $[\alpha]_D^{22}$ +10.8° (*c* 1.2, methanol). Anal. $C_{12}H_{15}NO_3$: C, H, N.

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