SYNTHESIS OF (2,4-DIMETHYL-3-CARBETHOXY-5-PYRROLYL)-SUCCINIC ACID AND ITS DERIVATIVES

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UDC 547.74/75.746.07

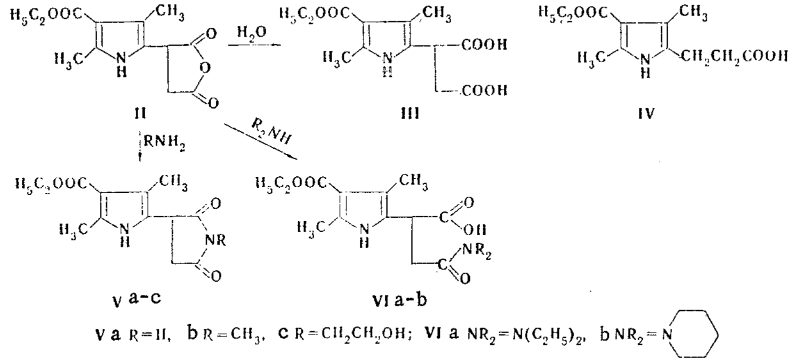
α-Pyrrolylsuccinic and (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic anhydrides were obtained by the reaction of pyrrole and 2,4-dimethyl-3-carbethoxypyrrole with maleic anhydride. (2,4-Dimethyl-3-carbethoxy-5-pyrrolyl)succinic acid and its imides and dialkylamides were synthesized by hydrolysis and aminolysis of the anhydrides.

The reaction of alkylpyrroles with anhydrides of unsaturated dicarboxylic acids in benzene gives the corresponding α-pyrrolylsuccinic anhydrides [1,2]. The reaction of pyrrole with maleic anhydride in water gave α,α'-di(ω-carboxyethyl)pyrrole in low yield.

We have demonstrated that pyrrole reacts with maleic anhydride without a solvent and catalyst to give α-pyrrolylsuccinic anhydride (I), the structure of which was proved by IR spectroscopy.

An attempt to synthesize α-pyrrolylsuccinic and α-pyrrolylpropionic acids from anhydride I was unsuccessful. The reaction of α-pyrrolylsuccinic anhydride with water gave a high-melting nitrogen-containing substance of polymeric character that was very sparingly soluble even in polar organic solvents. Polymeric nitrogen-containing products were also obtained when pyrrole was fused with maleic and citraconic acids.

As expected, 2,4-dimethyl-3-carbethoxypyrrole reacts readily with maleic anhydride to give (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic anhydride (II):



The hydrolysis of II gives (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic (III) (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)propionic (IV) acids. The reaction of II with primary aromatic amines gives alkali-insoluble cyclic imides (V) of (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic acid. Monoamides (VI) of the same acid are obtained with secondary amines.

When 2,4-dimethyl-3-carbethoxypyrrole is fused with maleic acid in alcohol, dioxane, and water at 150-170°C, only isomerization of the maleic acid to fumaric acid is observed, as in the case of pyrrole [3].

Institute of Organic Chemistry, Academy of Sciences of the Armenian SSR, Yerevan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1523-1524, November, 1972. Original article submitted June 7, 1971.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrophotometer. The purities of the synthesized amides and imides were confirmed by chromatography on activity II aluminum oxide with ether–alcohol (95 : 5).

α-Pyrrolylsuccinic Anhydride (I). A mixture of 2 g (0.03 mole) of pyrrole and 2.94 g (0.03 mole) of maleic anhydride was heated on a water bath for 2.5 h. The mixture was freed of the starting reagents by refluxing with dry ether to give 3.34 g (67.1%) of anhydride I with mp 106-108° (see [1,2]). IR spectrum: C=O 1759, 1838 cm^{-1}, N–H 3308-3337 cm^{-1}.

(2,4-Dimethyl-3-carbethoxy-5-pyrrolyl)succinic Anhydride (II). A mixture of 1.67 g (0.01 mole) of 2,4-dimethyl-3-carbethoxypyrrole [4,5] and 0.98 g (0.01 mole) of maleic anhydride was heated on a water bath for 2-3 h. The reaction product was dissolved in dry ether, and the solution was poured into petroleum ether to give 1.74 g (66%) of light-brown crystals of anhydride II with mp 117-120° and R_f 0.75. IR spectrum: N–H 3300 cm^{-1}, C=O 1785, 1860 cm^{-1}. Found, %: C 58.7; H 5.8; N 4.9. $C_{13}H_{15}NO_5$. Calculated,%: C 58.8; H 5.7; N 5.3.

Hydrolysis of Anhydride II. Water was added to 1.3 g (0.005 mole) of anhydride II, and the mixture was heated on a water bath for 3 h. The aqueous solution was decanted from the resulting dark precipitate and cooled to give 0.35 g (25%) of white-rose crystals of (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic acid (III) with mp 183-185° and R_f 0.74. IR spectrum: N–H 3571-3325 cm^{-1}, C=O 1646-1688 cm^{-1}. Found, %: C 55.1; H 6.5; N 5.1. $C_{13}H_{17}NO_6$. Calculated, %: C 55.1; H 6.1; N 4.9. The dark precipitate was separated, dissolved in warm alkali solution, and precipitated by the addition of acetic acid to give 0.55 g (45%) of α-(2,4-dimethyl-3-carbethoxy-5-pyrrolyl)propionic acid (IV) with mp 116-118° (mp 120° [6]) and R_f 0.79. IR spectrum: N–H 3268-3326 cm^{-1}, C=O 1663-1688 cm^{-1}. Found, %: C 60.3; H 7.1; N 6.1. $C_{12}H_{17}NO_4$. Calculated, %: C 60.2; H 7.2; N 5.9.

Imides of (2,4-Dimethyl-3-carbethoxy-5-pyrrolyl)succinic Acid (V). A 10-ml sample of 28% ammonium hydroxide was added to 1.32 g (0.005 mole) of anhydride II, and the mixture was allowed to stand for 2 days to complete the exothermic reaction. The solution was decanted, and acetic acid was added dropwise until the pH was 7. The mixture was filtered to give 0.7 g (53%) of (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinimide with mp 165-170° and R_f 0.79. Found, %: C 59.1; H 6.3; N 10.5. $C_{13}H_{16}N_2O_4$. Calculated, %: C 59.0; H 6.1; N 10.6.

The methylimide (50% yield, mp 165-167°, R_f 0.74. Found, %: C 60.8; H 6.6; N 10.0. $C_{14}H_{18}N_2O_4$. Calculated, %: C 60.4; H 6.5; N 10.1), and β-hydroxyethylimide of the same acid (29% yield, mp 147°, R_f 0.73. Found, %: C 58.9; H 6.5; N 9.0. $C_{15}H_{20}N_2O_5$. Calculated, %: C 58.4; H 6.5; N 9.1.)

Monoamides of (2,4-Dimethyl-3-carbethoxy-5-pyrrolyl)succinic Acid (VI). A mixture of 1.04 g (0.004 mole) of anhydride II and 0.58 g (0.008 mole) of diethylamine was heated on a water bath for 3 h. Acidification of the mixture with dilute acetic acid precipitated 0.75 g (55%) of (2,4-dimethyl-3-carbethoxy-5-pyrrolyl)succinic acid diethylamide with mp 150-152° and R_f 0.81. Found, %: C 60.0; H 7.7; N 8.6. $C_{17}H_{26}N_2O_5$. Calculated, %: C 60.3; H 7.7; N 8.3.

The same method was used to obtain the piperidide (33% yield, mp 120-125°, R_f 0.87. Found, %: C 61.7; H 7.8; N 8.5. $C_{18}H_{26}N_2O_5$. Calculated, %: C 61.7; H 7.5; N 8.0),and benzylamide [the yield of salt with benzylamine was 91%. The product had mp 132-136° (from ether). Found, %: C 68.0; H 6.5; N 8.5. $C_{20}H_{24}N_2O_5 \cdot C_7H_9N$. Calculated, %: C 67.5; H 6.9; N 8.8.]

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