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# Synthesis and Properties of 2-Alkyl-1-(2-aminoethyl)pyrroles

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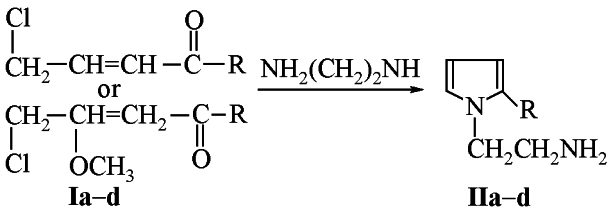
**Abstract**–3-Chloropropenyl alkyl ketones or 2-methoxy-3-chloropropyl alkyl ketones in reaction with ethylenediamine furnish previously unknown 2-alkyl-1-(2-aminoethyl) pyrroles. Their reaction with 2,2'-dichlorodiethyl ether gave rise to 2-alkyl-1-(2-morpholinoethyl)pyrroles, and with anhydrides of dicarboxylic acids the corresponding amidoacids and imides of dicarboxylic acids were obtained.

It was shown formerly that reaction of 1,2-dichloropropyl cyclohexyl ketones with ethylenediamine in alkaline medium resulted in 1.2-dipyrrolylethanes [1], whereas reactions of 3-chloropropenyl alkyl ketones or 2,3-dichloropropyl alkyl ketones with 2-substituted ethylamines provided 1-[2-bromo-(alkoxy, dialkylamino)ethyl]-2-alkylpyrroles [2].

The present study demonstrated that 3-chloropropenyl alkyl ketones and 2-methoxy-3-chloropropyl alkyl ketones (**I**) in reaction with three-fold excess of ethylenediamine furnish 2-alkyl-1-(2-aminoethyl) pyrroles (**II**).

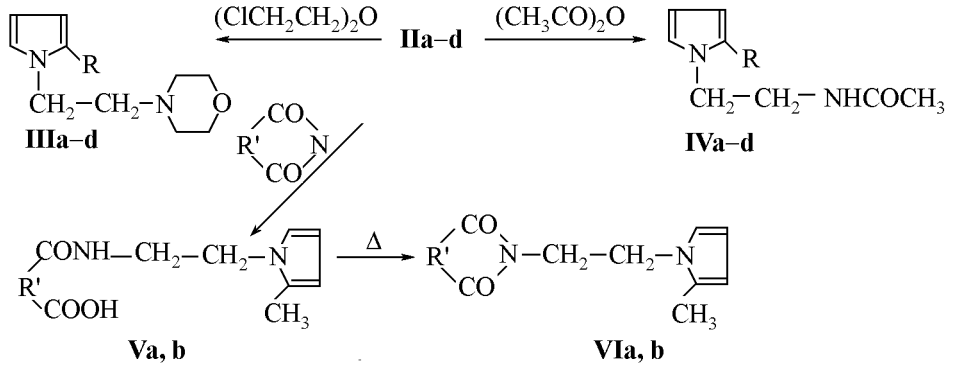



**Ia–d** **IIa–d**

**I, II** R = $CH_3$ (**a**), $C_2H_5$ (**b**), *iso*-$C_3H_7$ (**c**), $C_4H_9$ (**d**).

The reaction is carried out in water-ether mixture, and the yields of compounds **II** amount to 67–78%. The reaction of 2-alkyl-1-(2-aminoethyl)pyrroles with 2,2'-dichlorodiethyl ether (Chlorex) in the presence of the double excess of triethylamine performed in boiling dioxane gives rise to 2-alkyl-1-(2-morpholinoethyl)pyrroles (**III**). The acetic anhydride readily acylates the amino group to afford 2-alkyl-1-(2-acetamidoethyl)pyrroles (**IV**). The direction of reaction between pyrrole **IIa** and maleic or phthalic anhydrides was established to depend on temperature. The reaction at 25–30°C affords mono-*N*-(2-methylpyrrol-1-yl)ethylamides of the dicarboxylic acids (**V**), and at 150–155°C *N*-(2-methylpyrrol-1-yl)imides of the dicarboxylic acids (**VI**) are obtained. It was also demonstrated that monoamides **V** in boiling DMF underwent dehydration and intramolecular cyclization providing in 3 h the corresponding imides **VI** (Table 1).

The formation of imides **VI** from amidoacids **V** indicates that the latter are intermediates in the reaction providing imides **VI**. However as was already




**IIIa–d** **IVa–d** **Va, b** **VIa, b**

**III,IV**, R = $CH_3$ (**a**), $C_2H_5$ (**b**), *iso*-$C_3H_7$ (**c**), $C_4H_9$ (**d**); **V, VI**, R'= –CH=CH– (**a**); °-phenylene (**b**).

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**Table 1.** Yields, melting or boiling points, densities, refractive indices, and elemental analyses of pyrroles **II**–**VI**

| Compd. no. | Yield, % | bp, °C (*p*, mm Hg) (mp, °C) | $d_4^{20}$ | $n_D^{20}$ | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | | C | H | N |
| **IIa** | 78 | 76–77 (4) | 0.9843 | 1.5210 | 67.21 | 9.47 | 22.13 | $C_7H_{12}N_2$ | 67.74 | 9.68 | 22.58 |
| **IIb** | 74 | 79–80 (3) | 0.9802 | 1.5183 | 69.03 | 10.49 | 20.64 | $C_8H_{14}N_2$ | 69.56 | 10.14 | 20.29 |
| **IIc** | 70 | 84–86 (3) | 0.9771 | 1.5156 | 70.82 | 10.31 | 18.19 | $C_9H_{16}N_2$ | 71.05 | 10.53 | 18.42 |
| **IId** | 67 | 101–102 (3) | 0.9653 | 1.5100 | 71.79 | 10.52 | 16.59 | $C_{10}H_{18}N_2$ | 72.29 | 10.84 | 16.87 |
| **IIIa** | 80 | 117–118 (2) | 1.0279 | 1.5160 | 68.41 | 9.56 | 14.89 | $C_{11}H_{18}N_2O$ | 68.04 | 9.34 | 14.43 |
| **IIIb** | 77 | 121–123 (2) | 1.0104 | 1.5123 | 68.79 | 9.87 | 13.76 | $C_{12}H_{20}N_2O$ | 69.20 | 9.60 | 13.50 |
| **IIIc** | 73 | 128–129 (1) | 0.9984 | 1.5104 | 69.83 | 9.62 | 12.87 | $C_{13}H_{22}N_2O$ | 70.30 | 9.91 | 12.60 |
| **IIId** | 69 | 139–142 (2) | 0.9863 | 1.5078 | 71.96 | 10.64 | 12.11 | $C_{14}H_{24}N_2O$ | 71.20 | 10.20 | 11.86 |
| **IVa** | 74 | 157–158 (3) | 1.0558 | 1.5210 | 65.58 | 8.27 | 17.09 | $C_9H_{14}N_2O$ | 65.06 | 8.43 | 16.87 |
| **IVb** | 66 | 166–168 (2) | 1.0009 | 1.5188 | 67.11 | 8.59 | 15.19 | $C_{10}H_{16}N_2O$ | 66.66 | 8.88 | 15.55 |
| **IVc** | 60 | 176–177 (2) | 0.9846 | 1.5140 | 67.73 | 9.42 | 14.15 | $C_{11}H_{18}N_2O$ | 68.04 | 9.28 | 14.43 |
| **IVd** | 62 | 181–183 (1) | 0.9732 | 1.5109 | 68.71 | 9.50 | 13.77 | $C_{12}H_{20}N_2O$ | 69.23 | 9.61 | 13.46 |
| **Va** | 84 | (75–76) | – | – | 59.83 | 6.64 | 12.26 | $C_{11}H_{14}N_2O_3$ | 59.46 | 6.31 | 12.61 |
| **Vb** | 82 | (170–172) | – | – | 66.84 | 6.03 | 10.57 | $C_{15}H_{16}N_2O_3$ | 66.18 | 5.88 | 10.29 |
| **VIa** | 81 | (140–141) | – | – | 64.19 | 5.69 | 13.99 | $C_{11}H_{12}N_2O_2$ | 64.70 | 5.88 | 13.72 |
| **VIb** | 75 | (98–100) | – | – | 70.36 | 5.70 | 11.21 | $C_{15}H_{14}N_2O_2$ | 70.87 | 5.51 | 11.02 |

**Table 2.** $^1$H NMR spectra, δ, ppm, of pyrrole derivatives **IIa**–**IVa, Vb, VIa, b**

| Compd. no. | Solvent | $H^3$, m | $H^4$, m | $H^5$, m | $CH_2$–$CH_2$, t.t | $CH_3$, s | Other signals |
|---|---|---|---|---|---|---|---|
| **IIa** | $CCl_4$ | 5.63 | 5.77 | 6.28 | 2.65, 3.47 | 1.97 | 0.80 s $NH_2$ |
| **IIIa** | $CCl_4$ | 5.65 | 5.80 | 6.35 | 2.40, 3.70 | 2.08 | 2.22 t (4H, $CH_2N$), 3.50 t (4H, $CH_2O$) |
| **IVa** | $CCl_4$ | 5.60 | 5.73 | 6.25 | 3.27, 3.73 | 1.82 | 2.10 s (3H, $CH_3CO$), 7.50 s (1H, NHCO) |
| **Vb** | DMSO-$d_6$ | 5.90 | 6.05 | 6.75 | 3.65, 4.20 | 2.35 | 7.40–8.05 m (4H, H arom), 10.40 s (1H, NHCO), 12.85 s (1H, COOH) |
| **VIa** | DMSO-$d_6$ | 5.50 | 5.65 | 6.32 | 3.60, 3.90 | 2.20 | 6.56 m (2H, CH=CH) |
| **VIb** | DMSO-$d_6$ | 5.55 | 5.80 | 6.40 | 3.85, 4.02 | 2.10 | 7.75 m (4H, H arom) |

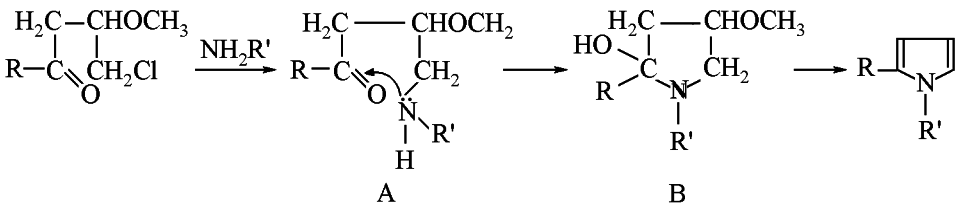
mentioned at high temperature we failed to isolate amidoacids **V** for under these conditions only imides **VI** were obtained.

The structure of synthesized pyrroles **II–VI** was confirmed by $^1$H NMR and IR spectra, by elemental analyses and in some cases by independent synthesis.

In the IR spectra of pyrroles **IIa–VIa** alongside the characteristic absorption bands of pyrrole ring at 3080–3120 ($\nu_{C-H}$), 1450–1568 ($\nu_{C=C}$), 725–780 cm$^{-1}$ ($\nu_{C-H}$) [3] also characteristic absorption bands of functional groups at 3376 ($\nu_{NH}$), 3264 ($\nu_{NH}$), 1620–1702 ($\nu_{C=O}$), and 1560 cm$^{-1}$ ($\delta_{NH}$) were observed.

In the $^1$H NMR spectra (Table 2) of compounds **IIa–VIa** appear characteristic multiplet signals of protons located in positions *3*, *4*, *5* of the pyrrole ring (~5.55, 6.00, 6.40 ppm respectively) [4], the triplets from methylene groups in the fragment $N^1$–$CH_2$–$CH_2$, proton signals of alkyl substituents and functional groups.

We did not specially study the mechanism of pyrrole formation, but various directions of nucleophile attack of amine on molecule **I** were possible. It is most likely that first chlorine atom is substituted by amino group affording aminoketone A. Then ketone A cyclizes into tetrahydropyrrole B as a result of the intramolecular attack of the unshared pair of nitrogen atom on the carbon in the carbonyl group. Then compound B readily transforms into pyrrole with elimination of water and alcohol.



A B

2-Alkyl-1-(2-aminoethyl)pyrroles were also obtained by treating 2-alkyl-1-(2-bromoethyl)pyrroles with excess ammonia.

## EXPERIMENTAL

IR spectra were recorded on spectrophotometer UR-20 from thin films of liquid substances and from mulls in mineral oil of solids. $^1$H NMR spectra were registered from 5–10% solutions of compounds obtained in $CCl_4$ or DMSO-$d_6$ on spectrometer Tesla BS-487B (80 MHz) using HMDS as internal reference. The purity of compounds obtained was checked by GLC on chromatograph Chrom-3-JKZ (stationary phase PMS-100 on Chromosorb W) and by TLC on Silufol UV-254 plates. The initial ketones **I** were prepared by procedure [5].

**2-Alkyl-1-(2-aminoethyl)pyrroles (IIa–d)** (Table 1). (a) To a mixture of 25.7 g (0.3 mol) of 70% water solution of ethylenediamine and 100 ml of ether at 15–20°C was added dropwise while stirring a solution of 0.1 mol of 3-chloro-1-propenyl alkyl ketone or 2-methoxy-3-chloropropyl alkyl ketone in 50 ml of ether. Then the reaction mixture was boiled for 6 h. On cooling the ether layer was separated, washed with water, the water layer was extracted with ether. The combined ether solutions were dried on $MgSO_4$, the solvent was distilled off, and the residue was subjected to vacuum distillation.

(b) To a mixture of 30 ml (0.4 mol) of 25% water solution of ammonia and 50 ml of ether at 25–30°C was added dropwise while stirring a solution of 0.1 mol of 2-alkyl-1-(2-bromoethyl)pyrrole in 50 ml of ether. Then the reaction mixture was boiled for 5 h and further it was worked up as above. According to $^1$H NMR and IR spectra, boiling points, and refractive indices the compounds obtained were identical to pyrrole derivatives synthesized by procedure a.

**2-Alkyl-1-(2-morpholinoethyl)pyrroles (IIIa–d).** A solution of 0.1 mol of pyrrole **II** and 28 ml (0.2 mol) of triethylamine in 100 ml of dioxane was brought to boiling, and then at vigorous stirring was added dropwise within 3 h 14.4 g (0.1 mol) of 2,2′-dichlorodiethyl ether dissolved in 25 ml of dioxane. Then the reaction mixture was boiled for 4 h more, cooled, washed with diluted solution of sodium carbonate, the water layer was separated and extracted with ether, the combined ether solutions were dried with $MgSO_4$, and on removing the solvent the residue was subjected to vacuum distillation.

**2-Alkyl-1-(2-acetoamidoethyl)pyrroles (IVa–d).** To a solution of 0.025 mol of pyrrole **II** in 50 ml of anhydrous ether was added dropwise at stirring 2.5 ml (0.025 mol) of acetic anhydride. Then the reaction mixture was boiled for 4 h and on cooling was washed with diluted solution of sodium carbonate, the water layer was separated and extracted with ether, the combined ether solutions were dried with $MgSO_4$, and on removing the solvent the residue was subjected to vacuum distillation.

***N*-(2-Methylpyrrol-1-yl)ethylmaleinamic-(phthalamic) acid (Va, b).** To a solution of 0.05 mol of the corresponding acid anhydride in 50 ml of acetone at 20–25°C while stirring was added dropwise 6.8 g (0.055 mol) of pyrrole **IIa** dissolved in 50 ml of acetone. Then the reaction mixture was stirred at room temperature for 3 h, the crystals formed were filtered off, washed with ether, and recrystallized from heptane.

***N*-(2-Methylpyrrol-1-yl)ethylmale(phthal)imide (VIa, b).** (a) A solution of 0.025 mol of the corresponding acid anhydride and 3.4 g (0.027 mol) of pyrrole **IIa** in 50 ml of DMF was boiled for 5 h. On cooling the reaction mixture was poured into ice water, and the mixture was left standing for 2 h. The separated crystals were filtered off, washed with water, died, and recrystallized from heptane.

(b) A mixture of 0.025 mol of acid **Va, b** and 50 ml of DMF was boiled for 3 h. The workup and purification of the product was done as above. According to $^1$H NMR and IR spectra and boiling points the imides of dicarboxylic acids prepared by procedures (a) and (b) were identical.

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