## A STUDY OF FURAN COMPOUNDS

XL. Synthesis of Some Derivatives of N-Aryl-Substituted Pyrrole- $\alpha$ -Carboxylic Acids\*

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The ethyl esters of N-phenyl-, N-p-tolyl-, and N-ethoxyphenyl- $\alpha$ -pyrrolecarboxylic acid have been synthesized by the reaction of ethyl 2,5-dimethoxytetrahydrofuran-2-carboxylate with aniline, p-toluidine, and p-phenetidine in the presence of p-toluenesulfonic acid. The reaction of the same ester with benzylamine gives N-benzyl-pyrrole- $\alpha$ -carboxybenzylamine or 2,5-dimethoxytetrahydrofuran-2-carboxybenzylamide, depending on the ratio of the reactants.

Clauson-Kaas, Elming, et al. [2-4] have described a method for the synthesis of pyrrole and some of its derivatives starting from 2,5-dimethoxytetrahydrofurans. Among the substances which they obtained were the methyl esters of pyrrole- $\alpha$ -carboxylic, Nphenylpyrrole- $\alpha$ -carboxylic, and N-phenyl-tert-butylpyrrole- $\alpha$ -carboxylic acids.

Later, Gross [5] obtained N-substituted pyrroles from 2,5-dichloro-, 2,5-dialkoxy-, and 2,5-diacyloxytetrahydrofurans and various primary amines. He used p-toluenesulfonic acid as catalyst for this reaction.

We have effected the synthesis of several derivatives of N-aryl-substituted pyrrole- $\alpha$ -carboxylic acids required for further investigation.

The experiments showed that the reaction of ethyl 2,5-dimethyltetrahydrofuran-2-carboxylate (I) with aniline, p-toluidine, and p-phenetidine in the presence of p-toluenesulfonic acid forms the ethyl esters of N-phenyl- (II), N-p-tolyl- (III), and N-p-ethoxyphenyl-pyrrole- $\alpha$ -carboxylic (IV) acids respectively.

$$CH_{3}O - \bigcirc OCH_{3} + R - C_{6}H_{4} - NH_{2} - \bigcap \bigvee_{\substack{N \\ COOC_{2}H_{5}}} - COOC_{2}H_{5}$$
  
if R=H; fill R = CH\_{3}; IV R = OC\_{2}H\_{5}

The IR spectra form a partial confirmation of the structure of compounds II-IV. A strong absorption band at  $1725 \text{ cm}^{-1}$  corresponds to the stretching vibrations of a C=O bond in an ester grouping conjugated with the double bonds of the pyrrole ring. Bands with frequencies of 1522 and 1593 cm<sup>-1</sup> correspond to the stretching vibrations of the double bonds in the benzene and pyrrole rings [6].

The reaction of I with benzylamine takes place in two directions according to the molar ratios of the reactants [1:1.5 (a) or 1:3 (b)] and leads to the formation of 2,5-dimethoxytetrahydrofuran-2-carboxybenzylamide (V) or N-benzylpyrrole- $\alpha$ -carboxybenzylamide (VI).



The structures of V and VI are confirmed by their IR spectra, in addition to the usual analytical data. The IR spectrum of V has: the band of the stretching vibrations of a C=O bond of a secondary amide grouping (1700 cm<sup>-1</sup>), a band at 1038 cm<sup>-1</sup> characteristic for the C-O-C link of a tetrahydrofuran ring [7], and a band at 2832 cm<sup>-1</sup> confirming the presence of methoxyl groups. The IR spectrum of compound VI lacks a band in the 2830-2850 cm<sup>-1</sup> region. A band at 1641 cm<sup>-1</sup> shows the presence of the C=O of a secondary amide grouping conjugated with the pyrrole ring. The stretching vibrations of the C=C of the pyrrole and benzene rings are represented by bands at 1525 and 1596 cm<sup>-1</sup>.

Compounds III-VI have not been described previously, and the constants of compound II have been refined.

## EXPERIMENTAL

Ethyl 2, 5-dimethoxytetrahydrofuran-2-carboxylate (I) was obtained by the catalytic hydrogenation of ethyl 2, 5-dimethoxy-2, 5-dihydrofuran-2-carboxylate (VIII) [8] under a pressure of hydrogen of 90 atm at room temperature in the presence of Raney nickel. Yield 76.5%. Bp 88-92° C (8 mm);  $d_4^{20}$  1,1204;  $n_D^{20}$  1.4352. Found, %: C 52.60, 52.58; H 8.08, 7.95; MRD 47.54. Calculated for C<sub>9</sub>H<sub>16</sub>O<sub>5</sub>, %: C 52.93; H 7.90; MRD 47.58.

Ethyl N-phenylpyrole- $\alpha$ -carboxylate (II). A round-bottomed flask fitted with a descending condenser was charged with 0.02 mole of I, 0.03 mole of aniline, and a few small crystals of p-toluenesulfonic acid. The mixture was boiled on a sand bath for 10 min. The methanol formed in the process was partially distilled off. After cooling, dilute acetic acid (1:1) was added to the reaction mixture. This precipitated an oil which crystallized on cooling. Yield 72%, Bp 88-89° C (from 65% ethanol). Found, %: C 72.87, 72.44; H 6.06, 5.83; N 6.81, 6.77. Calculated for C<sub>13</sub>H<sub>13</sub>NO<sub>2</sub>, %: C 72.53; H 6.07; N 6.51. According to the literature [9], bp 289° C.

Compound III was obtained from I and p-toluidine in a similar manner to that described above. After the addition of the dilute acetic acid, the oil was separated off. The aqueous layer was extracted with ether. The ethereal extracts and the oil were combined and dried with magnesium sulfate. The ether was distilled off from the water bath and the residue was distilled in vacuum. Yield 68%. Bp 140-142° C (2 mm);  $d_4^{20}$  1.2582;  $n_D^{20}$  1.5681. Found, %: C 72.98, 72.83; H 6.38, 6.58; N 6.36, 6.38; MRD 59,63. Calculated for C<sub>14</sub>H<sub>15</sub>NO<sub>2</sub>, %: C 73.30; H 6.59; N 6.11; MRD 59.94.

Compound IV was obtained similarly from I and p-phenetidine. The resulting viscous oily product crystallized on being triturated with ether. Yield 68%. Mp 110° C (from 70% ethanol). Found, % C 69.02,

<sup>\*</sup>For part XXXIX, see [1].

69,28; H 6.46, 6.38; N 5.51, 5.55. Calculated for  $\rm C_{15}H_{17}NO_3,$  %: C 69.47; H 6.60; N 5.40.

2,5-Dimethoxytetrahydrofuran-2-carboxybenzylamide (V). As described above, a round-bottomed flask was charged with 0.02 mole of I and 0.03 mole of benzylamine and a few small crystals of p-toluenesulfonic acid. The mixture was boiled on the sand bath for 50 min. After cooling, a small amount of water was added to the reaction mixture. The oil that deposited was separated off and the aqueous layer was extracted with ether. The oil and the ethereal extracts were combined and dried over calcined magnesium sulfate. The ether was distilled off on the water bath and the residue was distilled in vacuum. Yield 41%. Bp 164-167° C (2 mm);  $n_{\rm D}^{20}$  1.5275. Found, %: C 63.37, 63.94; H 7.37, 7.92; N 5.23, 5.52. Calculated for C<sub>14</sub>H<sub>19</sub>NO<sub>4</sub>, %: C 63.38; H 7.21; N 5.28.

Compound VI was obtained similarly from 0.02 of I and 0.06 mole of benzylamine. The viscous oily product obtained crystallized on being triturated with ether or methanol. Yield 89%, mp 108-109° C (from 50% ethanol). Found, %: C 78.79, 78.84; H 6.44, 6.62; N 9.22, 9.56. Calculated for C<sub>19</sub>H<sub>18</sub> N<sub>2</sub>O, %: C 78.59; H 6.21; N 9.64.

The IR spectra were recorded on an H-800 (Hilger) double-beam spectrometer. The crystalline substances were examined in the form of mulls with paraffin oil and the liquid substances as layers of capillary thickness between NaCl plates.

## REFERENCES

1. A. A. Ponomarev, N. I. Martem'yanova, and N. Popkova, KhGS, collection 2 (in press).

2. N. Clauson-Kass and Z. Tyle, Acta Chem. Scand., 6, 667, 1952.

3. N. Elming and N. Clauson-Kaas, Acta Chem. Scand., 6, 867, 1952.

4. P. Nedenskov, N. Elming, J. T. Nielsen, and N. Clauson-Kaas, Acta Chem. Scand., 9, 17, 1955.

5. H. Gross, Ber., 9, 2270, 1962.

6. A. Cross, An Introduction to Practical Infrared Spectroscopy [Russian translation], IL, Moscow, pp. 86, 100, 1961.

7. H. Tschamler and R. Leutner, Mon., 83, 1502, 1952.

8. W. R. Boehme and N. J. Somerville, British patent 2907794; C., 16260, 1960.

9. A. Pictet and Steinmann, Ber., 35, 2530, 1902.

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