ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 9, pp. 1378–1382. © Pleiades Publishing, Ltd., 2010. Original Russian Text © V.S. Grinev, O.A. Amal'chieva, A.Yu. Egorova, E.V. Lyubun', 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 9, pp. 1376–1379.

## Reaction of 4-Oxocarboxylic Acids and 5-Substituted 3*H*-Furan-2-ones with 1,2-Binucleophiles of Aromatic and Alicyclic Series

V. S. Grinev<sup>a</sup>, O. A. Amal'chieva<sup>b</sup>, A. Yu. Egorova<sup>b</sup>, and E. V. Lyubun'<sup>a</sup>

<sup>a</sup>Institute of Biochemistry and Physiology of Plants and Bacteria, Russian Academy of Sciences Saratov, 410049 Russia e-mail: grinev@ibppm.sgu.ru <sup>b</sup>Chernyshevskii Saratov State University, Saratov, Russia

Received July 27, 2009

**Abstract**— Based on reactions of 5-substituted 3*H*-furan-2-ones or 4-oxocarboxylic acids with 1,2-binucleophiles of aromatic and aliphatic series methods were developed for the synthesis of tricyclic structures containing a pyrrolidine fragment fused with imidazolidine or oxazolidine ring. The pathways of the reactions are considered. It was demonstrated that the nature of the substrate did not affect the reaction direction, but changed the scheme of the interaction. The structures of compounds obtained for the first time were proved using IR and <sup>1</sup>H NMR spectra.

DOI: 10.1134/S1070428010090198

The reactions of 3H-furan-2-ones containing aromatic and aliphatic substituents in the position C<sup>5</sup> with ethylenediamine and 2-aminoethanol was investigated before [1].

The target of this research is the study of reactions between 3H-furan-2-ones containing various substituents in the position C<sup>5</sup> with aromatic binucleophiles. We carried out the reactions of furan-2-ones with 1,2-phenylenediamine, 2-aminophenol, and 2-amino-4-methyphenol and thus obtained new tricyclic compounds containing in their structure an oxazolidine or imidazolidine ring fused with a benzene ring. This fact considerably extends the synthetic and applied possibilities of compounds obtained. We also studied the reaction with an alicyclic binucleophile, 1,2-diaminocyclohexane.

Besides the 3*H*-furan-2-ones we used as initial compounds 4-oxocarboxylic acids. Inasmuch as the 3*H*-furan-2-ones are cyclic internal esters of 4-oxocarboxylic acids, we have investigated the reactivity of these synthons and have compared the effect of the open or cyclic form of initial compounds on the structure of the obtained products.

4-Oxocarboxylic acids **Ia–Ic** and 5-substituted 3*H*-furan-2-ones **IIa–IIc** reacted with the aromatic 1,2-bi-



**I**, **II**,  $R = Ph(\mathbf{a})$ , 4-MeC<sub>6</sub>H<sub>4</sub>(**b**), 4-MeOC<sub>6</sub>H<sub>4</sub>(**c**); **III**, R' = H, X = NH,  $R = Ph(\mathbf{a})$ , 4-MeC<sub>6</sub>H<sub>4</sub>(**b**), 4-MeOC<sub>6</sub>H<sub>4</sub>(**c**); R' = H, X = O,  $R = Ph(\mathbf{d})$ , 4-MeC<sub>6</sub>H<sub>4</sub>(**e**), 4-MeOC<sub>6</sub>H<sub>4</sub>(**f**); R' = Me, X = O,  $R = Ph(\mathbf{g})$ , 4-MeC<sub>6</sub>H<sub>4</sub>(**h**).

nucleophiles (1,2-phenylenediamine, 2-aminophenol, and 2-amino-4-methyphenol) in protic and aprotic solvents (Scheme 1). The best results were obtained in benzene at continuous azeotropic distillation of the formed water.

The physicochemical characteristics of compounds **IIIa–IIIh** obtained using as initial substrates 4-oxoacids or furanones were completely identical. Therefore the synthesis of tricyclic systems from 4-oxoacids is more favorable from the preparative viewpoint for it reduces the process by one stage and eliminates the isolation of the intermediate 3*H*-furan-2-ones.

However the routes of the products formation are different. 3*H*-Furan-2-ones **Ha–Hc** contain in their structure an electron-deficient carbon atom of the carbonyl group which serves as the point of the attack of the nitrogen atom of the binucleophile reagent resulting in the opening of the lactone ring (Scheme 2).

The formation of the pyrrolidone ring with water elimination results in the additional heterocyclization in compounds **IIIa–IIIh**.

The substrate nature does not affect the direction of the reaction, but the scheme of the interaction changes. At

the use of synthons **Ia–Ic** the nucleophilic attack of the nitrogen atom of the aromatic binucleophile is directed to the more electron-deficient carbon atom of the carbonyl group of the oxoacid (Scheme 3).

The stabilization of intermediate **A** probably occurs through the attack of the second nucleophilic site on the same carbon atom followed by intramolecular acylation and the formation of the tricyclic system **IIIa–IIIc** (Scheme 3).

Based on spectral data the structures of compounds obtained were identified as 3a-substituted 2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]-imidazol-1-ones **IIIa**– **IIIc**, 3a-substituted 3,3a-dihydrobenzo[*d*]pyrrolo[2,1-*b*] oxazol-1(2*H*)-ones **IIId**–**IIIf**, and 7-methyl-3a-substituted 3,3a-dihydro-benzo[*d*]pyrrolo[2,1-*b*]oxazol-1(2*H*)ones **IIIg**–**IIIh**.

The data of IR and <sup>1</sup>H NMR spectra confirm the fact of double heterocyclization. The IR spectra of tricyclic **IIIa–IIIh** contain an absorption band of the C=O group "Amide I" at 1690–1710 cm<sup>-1</sup>, a band of the C–N bond vibrations at 1320–1330 cm<sup>-1</sup>, and in the spectra of compounds **IIIa–IIIc** the absorption band of the N–H group





RUSSIAN JOURNAL OF ORGANIC CHEMISTRY Vol. 46 No. 9 2010

## Scheme 4.



**I**, R = Me (**d**), Pr (**e**); **IV**, R = Ph (**a**), 4-MeC<sub>6</sub>H<sub>4</sub> (**b**), Me (**d**), Pr (**e**).

appeared at 3290–3350 cm<sup>-1</sup>.

In the <sup>1</sup>H NMR spectra of obtained compounds **IIIa– IIIh** the multiplets of methylene protons at the atoms C<sup>3</sup> and C<sup>2</sup> are observed at  $\delta$  2.05–2.60, 2.20–2.90 ppm respectively, and the singlet of the proton of NH group, at  $\delta$  4.20–4.38 ppm in the spectra of compounds **IIIa–IIIc**. The proton signals from the fused benzene ring and the benzene ring in the substituent in the position *3*a appear at  $\delta$  6.15–7.45 ppm

We investigated the reaction of compounds **Id**, **Ie** and **IIa**, **IIb** with 1,2-binucleophile reagent of the alicyclic series, 1,2-cyclohexanediamine (Scheme 4).

The reaction with 1,2-cyclohexanediamine was performed by boiling in benzene equimolar amounts of reagents with azeotropic distillation of formed water. The 1,2-cyclohexanediamine was used as a mixture of *cis*- and *trans*-isomers.

With substrates **IIa**, **IIb** we obtained 3a-substituted decahydro-1*H*-benzo[*d*]pyrrolo[1,2-*a*]-imidazol-1-ones **IVa**, **IVb**, **IVd**, **IVe** characterized by elemental analyses, IR and <sup>1</sup>H NMR spectra.

IR spectra of compounds **IVa**, **IVb**, **IVd**, **IVe** contain the absorption bands of lactam carbonyl group in the region 1690–1710 cm<sup>-1</sup>, of the secondary amino group (3300–3350 cm<sup>-1</sup>), and of the cyclohexane ring (2800–2920 cm<sup>-1</sup>).

In the <sup>1</sup>H NMR spectra of compounds **IVa, IVb, IVd, IVe** the multiplets of the protons at atoms C<sup>3</sup> and C<sup>2</sup> were observed at  $\delta$  2.30–2.75, 2.55–2.95 ppm respectively, the protons at the atoms of C<sup>8</sup>a and C<sup>4</sup>a of the imidazolidine ring, at  $\delta$  2.22–2.45, 2.00–2.25 ppm, proton at the nitrogen atom, at  $\delta$  4.10–4.35 ppm, and the multiplets of the protons of the cyclohexane ring, in the region  $\delta$ 1.29–2.10 ppm.

The pathways of compounds IV formation are similar

to those described above (Schemes 2, 3).

Hence it was demonstrated that 5-substituted 3*H*-furan-2-ones and their precursors, 4-substituted 4-oxocarboxylic acids containing electron-deficient carbon atoms readily reacted with 1,2-binucleophile reagents both from alicyclic and aromatic series with the formation of tricyclic imidazolidine and oxazolidine structures. Notwithstanding different pathways of reactions involving substituted 3*H*-furan-2-ones and 4-oxocarboxylic acids, the final products have the same tricyclic structure.

## EXPERIMENTAL

IR spectra were recorded on a spectrophotometer FSM 1201 from pellets with KBr. <sup>1</sup>H NMR spectra were registered on a spectrometer Bruker MSL-400 (operating frequency 400 MHz), solvent CDCl<sub>3</sub>, internal reference TMS. The purity of compounds was checked by TLC on Silufol plates, eluent ethyl acetate–hexane–chloroform, 2:2:1, development in iodine vapor.

3a-Phenyl-2,3,3a,4-tetrahydro-1*H*-benzo[*d*]pyrrolo[1,2-a]imidazol-1-one (IIIa). A solution of 2 g (11 mmol) of compound Ia [or 1.76 g (11 mmol) of compound **Ha**] and 1.2 g (11 mmol) of 1,2-phenylenediamine in 30 ml of anhydrous benzene was boiled while continouosly distilling off azeotropic mixture with formed water over 5 h. The separated precipitate was washed with benzene, then with hexane, and reccrystallized from acetone. Yield 2.12 g (75%), light-yellow crystals, mp 156–159°C. IR spectrum, v, cm<sup>-1</sup>: 3330 (NH), 1710 (C=O, "Amide-I"), 1320 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.35–2.60 m (2H, C<sup>3</sup>H<sub>2 pvrrolidine</sub>), 2.70–2.90 m (2H, C<sup>2</sup>H<sub>2 pyrrolidine</sub>), 4.38 s (1H, NH), 6.50–6.90 m (4H<sub>arom</sub>), 7.25–7.60 m (5H<sub>arom</sub>, Ph). Found, %: C 76.56; H 5.73; N 11.56. C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O. Calculated, %: C 76.80; H 5.60; N 11.20.

Compounds **IIIb–IIIh**, **IVa–IVe** were obtained similarly.

**3a-(4-Methylphenyl)-2,3,3a,4-tetrahydro-1***H***benzo**[*d*]**pyrrolo**[**1,2**-*a*]**imidazol-1-one (IIIb)**. Yield 1.98 g (78%), light-yellow crystals, mp 158–160°C. IR spectrum, v, cm<sup>-1</sup>: 3350 (NH), 1690 (C=O, "Amide-I"), 1330 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.25 s (3H, CH<sub>3</sub>), 2.40–2.55 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.50–2.70 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 4.35 s (1H, NH), 6.50–6.85 m (4H<sub>arom</sub>), 7.15–7.35 d.d (4H<sub>arom</sub>). Found, %: C 76.16; H 6.15; N 10.10. C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O. Calculated, %: C 75.69; H 6.06; N 10.61.

**3a-(4-Methoxyphenyl)-2,3,3a,4-tetrahydro-1***H***benzo**[*d*]**pyrrolo**[**1,2**-*a*]**imidazol-1-one (IIIc)**. Yield 1.42 g (46%), orange crystals, mp 109–112°C. IR spectrum, v, cm<sup>-1</sup>: 3330 (NH), 1700 (C=O, "Amide-I"), 1330 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.40–2.59 m (2H, C<sup>3</sup>H<sub>2</sub> pyrrolidine), 2.50–2.70 m (2H, C<sup>2</sup>H<sub>2</sub> pyrrolidine), 3.35 s (3H, OCH<sub>3</sub>), 4.20 s (1H, NH), 6.40–6.90 m (4H<sub>arom</sub>), 7.20– 7.65 d.d (4H<sub>arom</sub>). Found, %: C 72.53; H 6.12; N 9.68. C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>. Calculated, %: C 72.86; H 5.71; N 10.00.

**3a-Phenyl-3,3a-dihydrobenzo**[*d*]**pyrrolo**[**2,1-***b*]**oxazol-1(2***H***)-<b>one (IIId).** Yield 1.71 g (62%), yellow crystals, mp 153–155°C. IR spectrum, v, cm<sup>-1</sup>: 1710 (C=O, "Amide-I"), 1326 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.18–2.35 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.30–2.48 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 6.50–6.90 m (4H<sub>arom</sub>), 7.10–7.30 m (5H<sub>arom</sub>, Ph). Found, %: C 76.10; H 4.98; N 5.12. C<sub>16</sub>H<sub>13</sub>NO<sub>2</sub>. Calculated, %: C 76.49; H 5.18; N 5.58.

**3a-(4-Methylphenyl)-3,3a-dihydrobenzo**[*d*]pyrrolo[2,1-*b*]oxazol-1(2*H*)-one (IIIe). Yield 2.27 g (78%), greenish-yellow crystals, mp 116–117°C. IR spectrum, v, cm<sup>-1</sup>: 1700 (C=O, "Amide-I"), 1325 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.29–2.50 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.45–2.65 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.60 s (3H, CH<sub>3</sub>), 6.39–6.85 m (4H<sub>arom</sub>), 7.10–7.45 m (4H<sub>arom</sub>). Found, %: C 77.20; H 5.41; N 5.09. C<sub>17</sub>H<sub>15</sub>NO<sub>2</sub>. Calculated, %: C 76.98; H 5.66; N 5.28.

**3a-(4-Methoxyphenyl)-3,3a-dihydrobenzo**[*d*]pyrrolo[2,1-*b*]oxazol-1(2*H*)-one (IIIf). Yield 1.24 g (40%), greenish-yellow crystals, mp 110–112°C. IR spectrum, v, cm<sup>-1</sup>: 1695 (C=O, "Amide-I"), 1320 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.05–2.30 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.70–2.90 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 3.36 s (3H, OCH<sub>3</sub>), 6.15–6.60 m (4H<sub>arom</sub>), 7.25–7.55 m (4H<sub>arom</sub>). Found, %: C 75.39; H 5.91; N 4.77. C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>. Calculated, %: C 74.93; H 5.34; N 4.98. **7-Methyl-3a-phenyl-3,3a-dihydrobenzo**[*d*] **pyrrolo**[**2,1-***b***]<b>oxazol-1**(*2H*)-**one** (**HIg**). Yield 1.57 g (35%), greenish-yellow crystals, mp 122–124°C. IR spectrum, v, cm<sup>-1</sup>: 1710 (C=O, "Amide-I"), 1326 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.13–2.35 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.32 s (3H, CH<sub>3</sub>), 2.40–2.60 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 6.70–6.95 m (3H<sub>arom</sub>), 7.10–7.38 m (5H<sub>arom</sub>, Ph). Found, %: C 76.56; H 5.35; N 5.17. C<sub>17</sub>H<sub>15</sub>NO<sub>2</sub>. Calculated, %: C 76.96; H 5.70; N 5.28.

**7-Methyl-3a-(4-methylphenyl)-3,3a-dihydrobenzo**[*d*]pyrrolo[2,1-*b*]oxazol-1(2*H*)-one (IIIh). Yield 1.43 g (32%), greenish-yellow crystals, mp 123–124°C. IR spectrum, v, cm<sup>-1</sup>: 1705 (C=O, "Amide-I"), 1327 (C–N). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.15–2.37 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.42–2.67 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.62 s (3H, CH<sub>3</sub>), 2.36 s (3H, CH<sub>3</sub>), 6.60–7.05 m (3H<sub>arom</sub>), 7.10–7.45 m (4H<sub>arom</sub>). Found, %: C 77.15; H 5.97; N 4.91. C<sub>18</sub>H<sub>17</sub>NO<sub>2</sub>. Calculated, %: C 77.40; H 6.13; N 5.01.

**3a-Phenyldecahydro-1***H***-benzo**[*d*]**pyrrolo**[1,2*a*]-imidazol-1-one (IVa). Yield 1.35 g (48%), lightbrown crystals, mp 165°C (decomp.). IR spectrum, v, cm<sup>-1</sup>: 3330 (NH), 1710 (C=O, "Amide-I"), <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.35–1.89 m (8H, 4 CH<sub>2</sub>), 2.00 m (1H), 2.22 m (1H), 2.42–2.60 m (2H, C<sup>3</sup>H<sub>2</sub> pyrrolidine), 2.70–2.85 m (2H, C<sup>2</sup>H<sub>2</sub> pyrrolidine), 4.39 s (1H, NH), 7.20–7.60 m (5H<sub>arom</sub>). Found, %: C 74.85; H 8.05; N 11.12. C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O. Calculated, %: C 75.00; H 7.81; N 10.94.

**3a-(4-Methylphenyl)decahydro-1***H***-benzo**[*d*] **pyrrolo**[1,2-*a*]**imidazol-1-one (IVb).** Yield 1.54 g (52%), light-brown crystals, mp 177°C (decomp.). IR spectrum, v, cm<sup>-1</sup>: 3300 (NH), 1710 (C=O, "Amide-I"), <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.40–2.00 m (8H, 4 CH<sub>2</sub>), 2.25 m (1H), 2.30–2.42 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.45 m (1H), 2.55 s (3H, CH<sub>3</sub>), 2.55–2.75 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 4.25 s (1H, NH), 7.30–7.60 m (4H<sub>arom</sub>). Found, %: C 75.37; H 8.00; N 10.61. C<sub>17</sub>H<sub>22</sub>N<sub>2</sub>O. Calculated, %: C 75.56; H 8.15; N 10.37.

**3a-Methyldecahydro-1***H***-benzo**[*d*]**pyrrolo**[1,2-*a*]**imidazol-1-one (IVd).** Yield 1.26 g (59%), light-brown crystals, mp 152°C (decomp.). IR spectrum, *v*, cm<sup>-1</sup>: 3350 (NH), 1700 (C=O, "Amide-I"), <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.50–2.10 m (8H, 4 CH<sub>2</sub>), 2.35 m (3H, CH<sub>3</sub>), 2.40 m (1H), 2.50 m (1H), 2.55–2.75 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.60–2.95 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 4.15 s (1H, NH). Found, %: C 67.95; H 9.59; N 14.68. C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O. Calculated, %: C 68.04; H 9.28; N 14.43.

RUSSIAN JOURNAL OF ORGANIC CHEMISTRY Vol. 46 No. 9 2010

**3a-Propyldecahydro-1***H***-benzo**[*d*]**pyrrolo**[1,2-*a*]**imidazol-1-one (IVe).** Yield 1.34 g (55%), light-brown crystals, mp 159°C (decomp.). IR spectrum, v, cm<sup>-1</sup>: 3335 (NH), 1695 (C=O, "Amide-I"), <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 0.90–1.65 m (7H, C<sub>3</sub>H<sub>7</sub>), 1.50–2.10 m (8H, 4 CH<sub>2</sub>), 2.29 m (1H), 2.35 m (1H), 2.45–2.60 m (2H, C<sup>3</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 2.70–2.85 m (2H, C<sup>2</sup>H<sub>2</sub> <sub>pyrrolidine</sub>), 4.15 s (1H, NH). Found, %: C 70.08; H 10.16; N 12.82. C<sub>13</sub>H<sub>22</sub>N<sub>2</sub>O. Calculated, %: C 70.27; H 9.91; N 12.61.

The study was carried out under a financial support of the Russian Foundation for Basic Research (grant no. 10-03-00640-a).

## REFERENCES

1. Amaml'chieva, O.A. and Egorova, A.Yu., *Zh. Org Khim.*, 2006, vol. 42, p. 1358.