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Multicomponent reactions for the synthesis of bis-heterocyclic pyrrole derivatives

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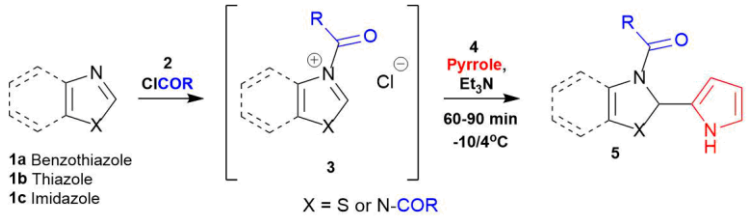
New pyrrole derivatives are synthesised in high yields (55–95%) by one-pot *α*-amidoalkylation reactions of various *N*-heterocycles (benzothiazole, thiazole and imidazole) and pyrrole. Further oxidation of the obtained derivatives leads to fully aromatic bis-heterocyclic products, bearing structural similarity to the natural product *Camalexin*.

Keywords: Camalexin, Pyrroles, One-pot amidoalkylation reactions

INTRODUCTION

The natural product *Camalexin* and its analogs have attracted a great deal of recent attention because of their interesting biological profile [1]. In a previous publication we reported a new and convenient synthesis of *Camalexin* and its benzo- and aza-analogs [2]. The underlying concept of this synthesis can be traced back to works of Bergman *et al*. [3] and is extendable to many other structurally related heterocyclic systems with potential biological activity. In the recent literature there are some interesting examples of biologically active pyrroles containing a thiazole fragment in their structure with prospects for their use as potential antifungal and antituberculosis agents [4]. Taking this into consideration, herein we describe the application of our previously published multicomponent approach for the synthesis of new pyrrole derivatives (Scheme 1).



Scheme 1. One-pot synthesis of 2-substituted pyrroles **5**

EXPERIMENTAL

General information

All reagents and solvents were obtained from commercial suppliers (Merck) and were used without further purification. Melting points were determined on a Boetius PHMKO5 hot stage apparatus and are uncorrected. IR and MS spectra were measured on VERTEX 70 FT-IR spectrometer (Bruker Optics, Germany) and HRMS "Q-Exactive Orbitrap" (Thermo Fisher Scientific, Waltham, MA, USA) spectrometer, respectively. NMR spectra were measured on Bruker Avance AV600 and DRX250 spectrometers in $CDCl_3$ and DMSO as solvents. Chemical shifts (δ, ppm) are downfield from TMS. To average out the rotamers observed in compounds **5** most of the NMR spectra were taken at 80°C in DMSO. TLC was done on precoated 0.2 mm Merck silica gel 60 plates. Neutral alumina was used for column chromatographic separation.

*Synthesis of amidoalkylated pyrroles **5aa-5ae, 5ba, 5bb**, general procedure*

The corresponding acyl chloride or alkyl chloroformate (1.2 equiv.) is slowly added with magnetic stirring to a solution of benzothiazole or thiazole (1 equiv.) in dry dichloromethane (4 – 8 mL/mmol) at the temperature indicated in Table 1. Immediately after that pyrrole is added (1 equiv.). Then, gradually, in the course of 30 min, triethylamine (1 equiv.), dissolved in dichloromethane (2 mL/mmol) is added. The reaction mixture is stirred for the time and at the temperature specified in Table 1. After completion

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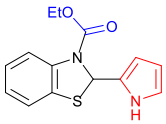
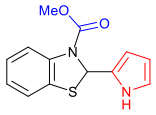
of the reaction, the mixture is transferred to a separatory funnel with dichloromethane (20 – 30 mL/mmol) and is consecutively extracted with equal volumes of aqueous Na_2CO_3 (3%), water and brine. The combined organic layers are dried (Na_2SO_4) and the solvent is removed under reduced pressure. Analytically pure samples were obtained by column chromatography on neutral alumina, using mixtures of diethyl ether/petroleum ether as eluents.



Ethyl 2-(1H-pyrrol-2-yl)benzo[d]thiazole-3(2H)-carboxylate **5aa**

Chromatographed on neutral alumina with petroleum/diethyl ether (8:1); Yield: 55%; Oil.

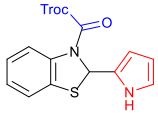
^{1}H-NMR (600 MHz, 20°C, $CDCl_3$, δ ppm, *J* Hz): 1.41 (t, *J* = 6, 3H, $CO_2CH_2\underline{CH_3}$), 4.34 – 4.40 (m, 2H, $CO_2\underline{CH_2}CH_3$), 6.12 (m, 1H), 6.33 (br s, 1H), 6.74 (m, 1H), 6.88 (s, 1H, *CH), 7.02 – 7.12 (m, 2H), 7.24 (m, 2H), 7.58 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 20°C, $CDCl_3$, δ ppm): 14.5, 60.6, 62.8, 107.9, 108.3, 117.8, 118.8, 122.3, 124.3, 125.5, 131.0, 132.1, 136.6, 152.5; IR (KBr, cm^{-1}): 3371, 2982, 1703, 1580, 1471, 1249, 747; HRMS *m/z* (ESI): calcd for $C_{14}H_{14}N_2NaO_2S^+$ $[M+Na]^+$ 297.0668, found 297.0660; calcd for $C_{14}H_{13}N_2O_2S^-$ $[M-H]^-$ 273.0703, found 273.0687.



Methyl 2-(1H-pyrrol-2-yl)benzo[d]thiazole-3(2H)-carboxylate **5ab**

Chromatographed on neutral alumina with petroleum/diethyl ether (8:1); Yield: 67%; mp = 111–113°C.

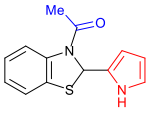
^{1}H-NMR (600 MHz, 20°C, $CDCl_3$, δ ppm, *J* Hz): 3.81 (s, 3H, $CO_2\underline{CH_3}$), 6.02 (m, 1H), 6.22 (br s, 1H), 6.63 (m, 1H), 6.77 (s, 1H, *CH), 6.92 – 7.02 (m, 2H), 7.12 (m, 2H), 7.51 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 20°C, $CDCl_3$, δ ppm): 53.5, 60.6, 107.9, 108.2, 108.3, 117.8, 118.9, 122.3, 124.4, 125.5, 130.9, 139.2, 151.1; IR (KBr, cm^{-1}): 3372, 2957, 1686, 1580, 1515, 1472, 1241, 745; HRMS *m/z* (ESI): calcd for $C_{13}H_{12}N_2NaO_2S^+$ $[M+Na]^+$ 283.0512, found 283.0507; calcd for $C_{13}H_{11}N_2O_2S^-$ $[M-H]^-$ 259.0547, found 259.0549.



2,2,2-trichloroethyl 2-(2-(1H-pyrrol-2-yl)benzo[d]thiazol-3(2H)-yl)-2-oxoacetate **5ac**

Chromatographed on neutral alumina with petroleum/diethyl ether (2:1 increasing polarity to 1:1); Yield: 93%; mp = 116–118°C.

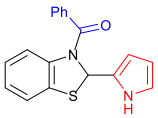
^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 4.96 (d, 2*J* = 12, 1H, $CO_2\underline{CH_2}CCl_3$) 5.06 (d, 2*J* = 12, 1H, $CO_2\underline{CH_2}CCl_3$), 5.88 (m, 2H), 6.67 (m, 1H), 6.96 (s, 1H, *CH), 7.09 (t, *J* = 8.2, 1H), 7.17 (t, *J* = 8.2, 1H), 7.28 (d, *J* = 7.6, 1H), 7.78 (d, *J* = 8.2, 1H) 10.56 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 61.9, 75.5, 105.9, 107.8, 117.9, 119.2, 123.3, 125.4, 125.7, 127.0, 129.2, 131.2, 137.3, 151.1; IR (KBr, cm^{-1}): 3382, 2992, 1698, 1576, 1480, 1260, 746; HRMS *m/z* (ESI): calcd for $C_{14}H_{11}Cl_3N_2NaO_2S^+$ $[M+Na]^+$ 398.9499, found 398.9497.



1-*(2-(1H-pyrrol-2-yl)benzo[d]thiazol-3(2H)-yl)ethan-1-one* **5ad**

Chromatographed on neutral alumina with petroleum/diethyl ether (4:1 increasing polarity to 2:1); Yield: 58%; mp = 118–120°C.

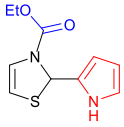
^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 2.23 (s, 3H, $CO\underline{CH_3}$), 5.83 (m, 1H), 5.89 (m, 1H), 6.69 (m, 1H), 6.99 (s, 1H, *CH), 7.05 (t, *J* = 7.6, 1H), 7.13 (t, *J* = 7.6, 1H), 7.25 (d, *J* = 7.6, 1H), 7.88 (d, *J* = 7.6, 1H) 10.60 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 23.7, 62.2, 106.0, 107.9, 119.0, 119.3, 123.2, 125.3, 125.4, 129.6, 131.6, 138.8, 169.1; IR (KBr, cm^{-1}): 3394, 2987, 1705, 1560, 1475, 1272, 749; HRMS *m/z* (ESI): calcd for $C_{13}H_{12}N_2NaOS^+$ $[M+Na]^+$ 267.0563, found 267.0563; calcd for $C_{13}H_{11}N_2OS^-$ $[M-H]^-$ 243.0598, found 243.0599.



(2-(1H-pyrrol-2-yl)benzo[d]thiazol-3(2H)-yl)(phenyl)methanone **5ae**

Chromatographed on neutral alumina with petroleum/diethyl ether (1:1); Yield: 57%; mp = 173–175°C.

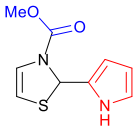
^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 5.87 (m, 2H), 6.67 (m, 1H), 6.77 (s, 1H, *CH), 7.03 (t, *J* = 7.6, 1H), 7.07 (t, *J* = 7.6, 1H), 7.29 – 7.31 (m, 2H), 7.39 – 7.43 (m, 4H), 7.50 – 7.53 (m, 1H), 10.46 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 64.0, 106.3, 107.8, 119.1, 119.7, 123.7, 125.1, 125.8, 127.5, 128.9, 130.4, 131.2, 131.4, 135.9, 138.8, 169.0; IR (KBr, cm^{-1}): 3362, 2966, 1625, 1572, 1468, 1282, 753; HRMS *m/z* (ESI): calcd for $C_{18}H_{14}N_2NaOS^+$ $[M+Na]^+$ 329.0719, found 329.0713; calcd for $C_{18}H_{13}N_2OS^-$ $[M-H]^-$ 305.0754, found 305.0748.



Ethyl 2-(1H-pyrrol-2-yl)thiazole-3(2H)-carboxylate **5ba**

Chromatographed on neutral alumina with petroleum/diethyl ether (8:1 increasing polarity to 4:1); Yield: 60%; mp = 85–87°C.

^{1}H-NMR (250 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 1.19 (t, *J* = 7.1, 3H, $CO_2CH_2\underline{CH_3}$), 4.13 (q, *J* = 7.1, 2H, $CO_2\underline{CH_2}CH_3$), 5.85 (d, *J* = 4.7, 1H), 5.93 – 5.96 (m, 1H), 5.99 – 6.02 (m, 1H), 6.53 (d, *J* = 4.7, 1H), 6.59 (s, 1H, *CH), 6.66 – 6.69 (m, 1H), 10.49 (br s, 1H, NH); ^{13}C-NMR (62.5 MHz, 80°C, DMSO-d_6, δ ppm): 14.1, 59.6, 61.7, 103.3, 105.4, 107.3, 118.2, 120.9, 131.6, 152.2; IR (KBr, cm^{-1}): 3312, 3086, 2981, 1685, 1597, 1564, 1467, 1382, 1251, 733; HRMS *m/z* (ESI): calcd for $C_{10}H_{12}N_2NaO_2S^+$ $[M+Na]^+$ 247.0512, found 247.0516; calcd for $C_{10}H_{11}N_2O_2S^-$ $[M-H]^-$ 223.0547, found 223.0555.



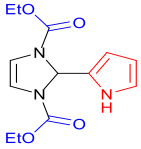
Methyl 2-(1H-pyrrol-2-yl)thiazole-3(2H)-carboxylate **5bb**

Chromatographed on neutral alumina with petroleum/diethyl ether (8:1 increasing polarity to 4:1); Yield: 63%; mp = 92–94°C.

^{1}H-NMR (250 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 3.69 (s, 3H, $CO_2\underline{CH_3}$), 5.87 (d, *J* = 4.7, 1H), 5.93 – 5.96 (m, 1H), 5.99 – 6.02 (m, 1H), 6.53 (d, *J* = 4.7, 1H), 6.60 (s, 1H, *CH), 6.67 – 6.69 (m, 1H), 10.53 (br s, 1H, NH); ^{13}C-NMR (62.5 MHz, 80°C, DMSO-d_6, δ ppm): 52.9, 59.6, 103.6, 105.4, 107.4, 118.3, 120.9, 131.5, 152.7; IR (KBr, cm^{-1}): 3332, 3093, 2957, 1691, 1597, 1561, 1449, 1366, 1250, 742; HRMS *m/z* (ESI): calcd for $C_9H_{10}N_2NaO_2S^+$ $[M+Na]^+$ 233.0355, found 233.0358; calcd for $C_9H_9N_2O_2S^-$ $[M-H]^-$ 209.0390, found 209.0396.

Synthesis of amidoalkylated pyrroles ***5ca-5cd****, general procedure*

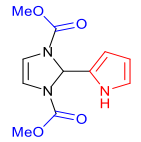
The corresponding acyl chloride or alkyl chloroformate (4.4 mmol) is slowly added to a cooled (0°C) and magnetically stirred solution of imidazole (2 mmol, 0.136 mg) and Et_3N (2 mmol, 0.28 mL) in dry 1,2-dichloroethane (10 mL). Immediately after that, pyrrole (2 mmol, 0.139 mL) is added. In the course of the next 30 minutes Et_3N (2 mmol) in 1,2-dichloroethane (4 mL) is gradually added. After completion of the reaction (Table 1), the mixture is transferred to a separatory funnel with dichloromethane (50 mL) and is successively extracted with equal volumes of aqueous HCl (1:4), Na_2CO_3 (3%), water and brine. The combined organic layers are dried (Na_2SO_4) and the solvent is removed under reduced pressure. The solid residue is then triturated and washed with small amount of hexane and petrol/diethyl ether (4:1) to remove any unreacted pyrrole. This sequence induces crystallization of the products. The material obtained in this way is usually sufficiently clean to be taken to the next stage without further purification. Analytically pure samples of **5cc** and **5cd** were obtained by column chromatography on neutral alumina, using mixtures of diethyl ether/petroleum ether as eluents.



Diethyl 2-(1H-pyrrol-2-yl)-1H-imidazole-1,3(2H)-dicarboxylate **5ca**

Yield: 81%; mp = 104–106°C.

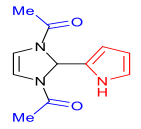
^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 1.16 (t, *J* = 7.0, 6H, 2×$CO_2CH_2\underline{CH_3}$), 4.06 – 4.11 (m, 4H, 2×$CO_2\underline{CH_2}CH_3$), 5.95 – 5.97 (m, 1H), 6.02 – 6.03 (m, 1H), 6.35 (s, 2H), 6.61 (s, 1H, *CH), 6.65 (m, 1H), 10.60 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 14.7, 61.9, 69.4, 106.3, 107.8, 112.8, 118.4, 129.2, 150.8; IR (KBr, cm^{-1}): 3385, 3154, 2988, 1706, 1627, 1561, 1463, 1410, 1383, 1265; HRMS *m/z* (ESI): calcd for $C_{13}H_{17}N_3NaO_4^+$ $[M+Na]^+$ 302.1111, found 302.1101; calcd for $C_{13}H_{16}N_3O_4^-$ $[M-H]^-$ 278.1146, found 278.1147.



Dimethyl 2-(1H-pyrrol-2-yl)-1H-imidazole-1,3(2H)-dicarboxylate **5cb**

Yield: 95%; mp = 123–125°C.

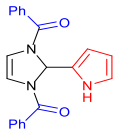
^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 3.65 (s, 6H, 2×$CO_2\underline{CH_3}$), 5.95 – 5.97 (m, 1H), 6.02 – 6.03 (m, 1H), 6.35 (s, 2H), 6.63 (s, 1H, *CH), 6.65 (m, 1H), 10.56 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 53.1, 69.4, 106.3, 107.9, 112.9, 118.5, 129.0, 151.2; IR (KBr, cm^{-1}): 3331, 3133, 2958, 1689, 1626, 1562, 1450, 1402, 1392, 1272; HRMS *m/z* (ESI): calcd for $C_{11}H_{13}N_3NaO_4^+$ $[M+Na]^+$ 274.0798, found 274.0797; calcd for $C_{11}H_{12}N_3O_4^-$ $[M-H]^-$ 250.0833, found 250.0829.



1,1'-(2-(1H-pyrrol-2-yl)-1H-imidazole-1,3(2H)-diyl)bis(ethan-1-one) **5cc**

Chromatographed on neutral alumina with petroleum/diethyl ether (1:1 increasing polarity to diethyl ether); Yield: 66%; mp = 141–143°C.

^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 2.07 (s, 6H, 2×CO$\underline{CH_3}$), 5.93 – 5.95 (m, 1H), 6.01 (br s, 1H), 6.33 (s, 2H), 6.63 (m, 1H), 6.94 (s, 1H, *CH), 10.34 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 24.2, 70.1, 106.8, 108.0, 112.8, 117.5, 128.8, 152.5; IR (KBr, cm^{-1}): 3406, 3119, 1646, 1612, 1551, 1442, 1399, 1260; HRMS *m/z* (ESI): calcd for $C_{11}H_{13}N_3NaO_2^+$ $[M+Na]^+$ 242.0900, found 242.0890; calcd for $C_{11}H_{12}N_3O_2^-$ $[M-H]^-$ 218.0935, found 218.0927.



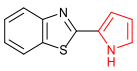
(2-(1H-pyrrol-2-yl)-1H-imidazole-1,3(2H)-diyl)bis(phenylmethanone) **5cd**

Chromatographed on neutral alumina with petroleum/diethyl ether (1:1); Yield: 65%; mp = 153–155°C.

^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 5.96 (s, 1H), 6.06 (br s, 1H), 6.45 (s, 2H), 6.68 (s, 1H, *CH), 7.29 – 7.55 (m, 11H), 10.59 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 70.5, 106.9, 107.8, 115.2, 118.8, 127.0, 128.5, 129.0, 131.2, 134.9, 165.0; IR (KBr, cm^{-1}): 3372, 3137, 1653, 1615, 1577, 1447, 1392, 1281; HRMS *m/z* (ESI): calcd for $C_{21}H_{17}N_3NaO_2^+$ $[M+Na]^+$ 366.1213, found 366.1212; calcd for $C_{21}H_{16}N_3O_2^-$ $[M-H]^-$ 342.1248, found 342.1257.

Oxidation of amidoalkylated pyrroles **5aa, 5ab, 5ba, 5bb** *to 2-(1H-pyrrol-2-yl)benzo[d]thiazole 6a and 2-(1H-pyrrol-2-yl)thiazole* **6b**

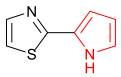
The corresponding compound **5** (0.5 mmol) is dissolved in CH_3CN (8 mL), then the oxidant (*o*-chloranil) (2 equiv. for the benzothiazole derivatives **5a** or 1 equiv. for thiazole derivatives **5b**) is added and the reaction mixture is magnetically stirred under the conditions specified in Table 2. After completion of the reaction the solvent is evaporated under reduced pressure and the mixture is then dry-loaded onto neutral alumina. Chromatography on a short alumina column with diethyl ether/petroleum as the eluent gave 2-(1H-pyrrol-2-yl)benzo[d]thiazole **6a** or 2-(1H-pyrrol-2-yl)thiazole **6b** in yields indicated in Table 2.



2-(1H-pyrrol-2-yl)benzo[d]thiazole **6a**

Chromatographed on neutral alumina with petroleum/diethyl ether (8:1 increasing polarity to 4:1); Yield: 91%, 86%; mp = 158–159°C; lit. 151–154°C [5^a], 155–156°C [5^b].

^{1}H-NMR (600 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 6.24 (m, 1H), 6.84 (m, 1H), 7.02 (m, 1H), 7.35 (t, *J* = 7.6, 1H), 7.47 (t, *J* = 7.6, 1H), 7.88 (d, *J* = 8, 1H), 7.99 (d, *J* = 8, 1H), 11.82 (br s, 1H, NH); ^{13}C-NMR (150 MHz, 80°C, DMSO-d_6, δ ppm): 110.5, 112.7, 122.0, 122.3, 123.6, 124.9, 126.2, 126.7, 134.1, 154.1, 160.3; IR (KBr, cm^{-1}): 3125, 2854, 1572, 1559, 1113, 742; HRMS *m/z* (ESI): calcd for $C_{11}H_7N_2S^-$ $[M-H]^-$ 199.0335, found 199.0330.



2-(1H-pyrrol-2-yl)thiazole **6b**

Chromatographed on neutral alumina with petroleum/diethyl ether (4:1); Yield: 89%, 82%; mp = 74–76°C; lit. mp = 75°C [4^a].

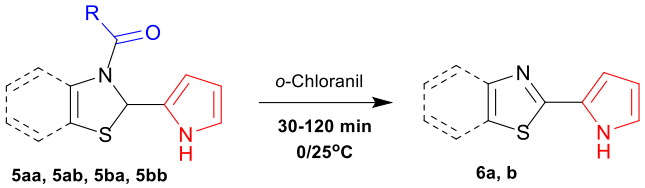
^{1}H-NMR (250 MHz, 80°C, DMSO-d_6, δ ppm, *J* Hz): 6.18 (t, *J* = 3.1, 1H), 6.64 – 6.66 (m, 1H), 6.90 – 6.91 (m, 1H), 7.47 (d, *J* = 3.4, 1H), 7.72 (d, *J* = 3.4, 1H), 11.46 (br s, 1H, NH); ^{13}C-NMR (62.5 MHz, 80°C, DMSO-d_6, δ ppm): 109.3, 109.4, 116.8, 121.2, 126.2, 142.5, 165.3; IR (KBr, cm^{-1}): 3108, 2964, 1572, 1487, 1098, 738; HRMS *m/z* (ESI): calcd for $C_7H_5N_2S^-$ $[M-H]^-$ 149.0179, found 149.0170.

RESULTS AND DISCUSSION

Our primary aim was to develop an efficient multicomponent one-pot procedure for the synthesis pyrrole derivatives through the reaction of benzothiazole, thiazole or imidazole **1a-c**, acid chlorides **2** and pyrrole **4**. The aforementioned azoles react with acyl chlorides or alkyl chloroformates to give acyliminium reagents **3** which further react with pyrrole in the presence of triethylamine as HCl scavenger. In this way a range of 2-substituted pyrroles **5** were obtained in good yields (55–95%, Table 1). The reaction conditions were optimized by varying the solvent, temperature and time. Low temperature (-10 to +4 °C) was beneficial in all cases. At higher temperature there were competing reactions which led to complicated mixtures of products and lowered the yields of the targeted monosubstituted pyrrole derivatives. Although in principle the amidoalkylation of aromatic rings can take place in the absence of base, the presence of Et_3N was of crucial importance in all of the examples studied here, because both pyrrole and its amydoalkylated products **5** were adversely affected by the HCl released in the course of the reaction. Dichloromethane was found to be the optimal solvent for the reactions with thiazoles, while in the case of imidazole dichloroethane performed better.

Table 1. Reaction conditions and yields of amidoalkylated pyrroles **5**

N-heterocycle	Product	R	Conditions	Yield, %
Benzothiazole **1a**	**5aa**	CH_3CH_2O	0 – 4°C, 1.5h	55
	5ab	CH_3O	0 – 4°C, 1.5h	67
	5ac	CCl_3CH_2O	0 – 4°C, 1.5h	93
	5ad	CH_3	0 – 4°C, 1.5h	58
	5ae	C_6H_5	0 – 4°C, 1.5h	57
Thiazole **1b**	**5ba**	CH_3CH_2O	-10 – -5°C, 1h	60
	5bb	CH_3O	-10 – -5°C, 1h	63
Imidazole **1c**	**5ca**	CH_3CH_2O	0 – 4°C, 1.5h	81
	5cb	CH_3O	0 – 4°C, 1.5h	95
	5cc	CH_3	0 – 4°C, 1.5h	66
	5cd	C_6H_5	0 – 4°C, 1.5h	65



Scheme 2. Oxidation of **5aa**, **5ab**, **5ba**, **5bb** to products **6a**, **6b**

Table 2. Reaction conditions and yields of **6a**, **6b**, obtained according to Scheme 2

Starting material	Product	*o*-Chloranil oxidation		
		T, °C	Time, h	Yield 6, %
5aa	**6a**	25	2	91
5ab	**6a**	25	2	86
5ba	**6b**	0 – 4	0.5	89
5bb	**6b**	0 – 4	0.5	82

After the optimization of the conditions for the coupling of the heterocyclic rings we proceeded with experiments to remove the alkoxycabonyl groups and rearomatize the thiazole moiety in the obtained products **5a**, **5b**. This was successfully accomplished by oxidation with *o*-chloranil (Scheme 2, Table 2).

All products were purified by column chromatography and characterized by IR, ^{1}H-NMR, ^{13}C-NMR and ESI-MS analysis.

CONCLUSIONS

An efficient one-pot method for the synthesis of bis-heterocyclic pyrrole derivatives has been developed. Thirteen new derivatives bearing structural similarity to the natural product *Camalexin* were successfully synthesized.

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