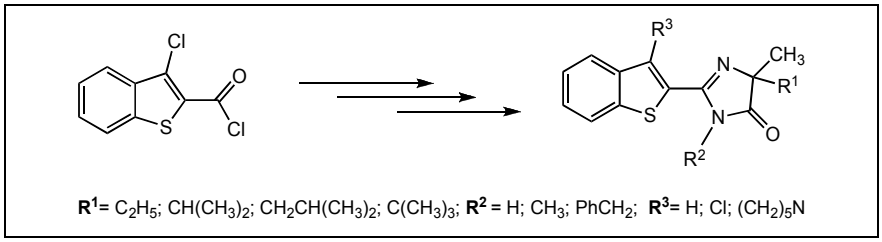
Synthesis and Characterization of Substituted (Benzo[*b*]thiophen-2-yl)-4-methyl-4,5-dihydro-1*H*-imidazol-5-ones

Miloš Sedlák*[a], Pavel Drabina[a], Václav Lánský[a] and Jiří Svoboda[b]

[a]Department of Organic Chemistry, Faculty of Chemical Technology, University of Pardubice, Čs. legií 565, 532 10 Pardubice, Czech Republic.
[b]Department of Organic Chemistry, Institute of Chemical Technology, Technická 5, 166 28 Prague 6, Czech Republic.

Received November 15, 2007



Reactions of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride with 2-alkyl-2-aminopropanamides have been used to prepare a series of carboxamides **1a-d** (yields 61-85 %). The products were submitted to base-catalysed ring closure reactions to give the corresponding 4,5-dihydro-1*H*-imidazol-5-ones **2a-d** (yields 69-97 %). By *N*-methylation and *N*-benzylation were prepared the corresponding 1-alkyl derivatives **3a** (91 %) and **3b** (85 %). These two alkyl derivatives were studied from the standpoint of potential replacement of 3-chlorine substituent by piperidine *via* the Buchwald–Hartwig reaction. It was found that the reaction gives besides except required products of C-N coupling **5a** (14 %) and **5b** (12 %) also products of reductive dechlorination **4a** (max. 57 %) and **4b** (max. 56 %). The reductive dechlorination product **4a** is formed exclusively (42 %) if butyl-di-(1-adamantyl)phosphine (BDAP) is used.

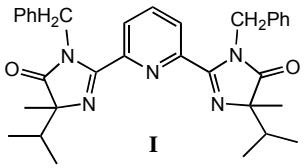
J. Heterocyclic Chem., **45**, 859 (2008).

INTRODUCTION

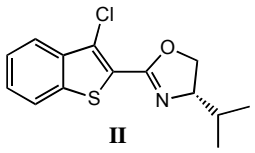
Our previous papers [1] dealt with synthesis and characterisation of substituted (4,5-dihydro-1*H*-imidazol-5-on-2-yl)pyridines. These heterocyclic systems were originally developed as selective and virtually non-toxic herbicides [2], which have been used up to now. Other application possibilities involve their use as ligands forming coordination compounds with selected metal ions [1i-m]. The rhodium complex of 2,6-bis(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on-2-yl)-pyridine (I) proved to be a considerably effective catalyst of deallylation reactions of diallyl malonates [1j].

Substituted benzo[*b*]thiophenes also represent the basic skeleton found in the molecules of biologically active substances, such as, *e.g.*, antiphlogistics, analgetics or antimicrobial substances [3a]. Even earlier published papers are dealing with preparation of heterocyclic systems formed by attaching another heterocyclic species to 3-chlorobenzo[*b*]thiophenes (II) [3b-g]. Such syntheses make use of the reactions of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride [4] with other fragments and subsequent ring closure reactions. Connecting of two or more heterocyclic compounds by means of ring fusion or single or double bond leads to new systems whose original properties may be modified.

The aim of this work is to synthesise and characterise new heterocyclic systems formed by combination of 3-chlorobenzo[*b*]thiophene with substituted 4,5-dihydro-



I



II

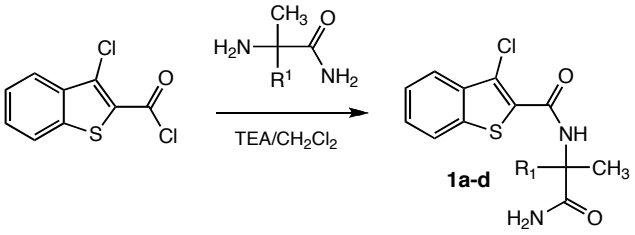
1*H*-imidazol-5-one. The aim was to use the reaction of 3-chlorbenzo[*b*]thiophene-2-carbonyl chloride [4] with 2-amino-2-alkylpropanamides [1a] for preparation of the corresponding aminoamides, and to use their ring closure reactions for preparation of a series of substituted 2-(3-chlorobenzo[*b*]thiophene-2-yl)-4-alkyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-ones. Another aim of this work was to test the possibility of application of the Buchwald–Hartwig reaction [5] to the chlorine-bearing carbon atom at 3-position of the benzo[*b*]thiophen skeleton, so that it would be possible to attach another nitrogen-bearing heterocyclic system.

RESULTS AND DISCUSSION

The reactions of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride [4] with substituted 2-amino-2-alkylpropan-amides [1a] were adopted to prepare a series of

substituted *N*-(1-carbamoyl-1-alkylethyl)-3-chlorobenzo-[*b*]thiophene-2-carboxamides **1a–d** (**a**: $R^1 = C_2H_5$; **b**: $R^1 = CH(CH_3)_2$; **c**: $R^1 = CH_2CH(CH_3)_2$; **d**: $R^1 = C(CH_3)_3$) (Scheme 1). The acylation reactions were performed in anhydrous dichloromethane in the presence of triethylamine. The substituted carboxamides **3a–d** were obtained in the yields of 61-85 % after evaporation of the dichloromethane, washing with water, and recrystallization.

Scheme 1

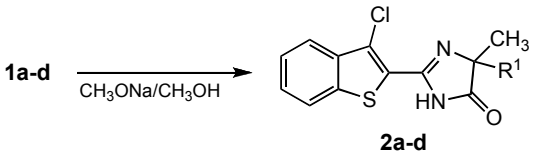


1a-d (**a:** $R^1 = C_2H_5$; **b**: $R^1 = CH(CH_3)_2$; **c**: $R^1 = CH_2CH(CH_3)_2$; **d**: $R^1 = C(CH_3)_3$)

The ring closure reactions of carboxamides **1a–d** giving substituted 2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-alkyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-ones **2a–d** (**a**: $R^1 = C_2H_5$; **b**: $R^1 = CH(CH_3)_2$; **c**: $R^1 = CH_2CH(CH_3)_2$; **d**: $R^1 = C(CH_3)_3$) (Scheme 2) were carried out in 1 mol·L^{-1} methanolic sodium methoxide at room temperature. Subsequent neutralization (HCl aq.; 5 mol·L^{-1}), evaporation, washing with water, and recrystallization gave products **2a–d** in the yields of 69-97 %. At the conditions described, only the ring closure reaction took place, and no nucleophilic substitution of chlorine substituent in the 3-chlorobenzo[*b*]thiophene skeleton by methoxide ion was observed. No nucleophilic substitution took place even in boiling methoxide solution or on heating with sodium hydroxide solution in an autoclave.

Further experiments concerned investigation of possible chemical modifications of the basic skeleton of 2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**2b**). This derivative was chosen because the substance can easily be prepared in both enantionerically pure forms *R* and *S* because of the availability of (*R*)-2-amino-2,3-dimethylbutanamide and (*S*)-2-amino-2,3-dimethylbutanamide [6]. First, a methyl group was introduced into the molecule of compound **2b** to give 2-(3-chlorobenzo[*b*]thiophen-2-yl)-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-one (**3a**) (91 %), and a benzyl group to give 2-(3-chlorobenzo[*b*]thiophene-2-yl)-1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**3b**) (85 %) (Scheme 3). The *N*-methylation and *N*-benzylation removed the easily separated acidic hydrogen atom that could unfavourably affect the subsequent reactions. Structures of the products prepared, **1a–d, 2a–d, 3a-b**, were verified by means of ^{1}H and ^{13}C NMR spectroscopy, EI-MS, and elemental analysis.

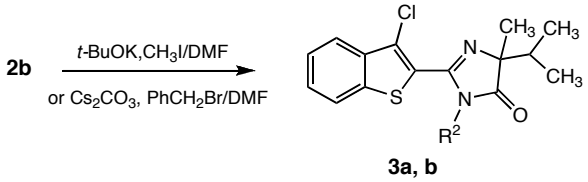
Scheme 2



Besides others, one of potential applications of substituted 2-(benzo[*b*]thiophene-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-ones could be based on their ability to coordinate atoms of transition metals and thus produce their coordination compounds. This was the reason why we studied the possibility of replacement of chlorine substituent at the 3-position by another, better coordinating group. Such well-coordinating groups include, e.g., the amino group with its free electron pair. Therefore, we tried to substitute the chlorine atom in ligands **3a-b** by piperidine. Since the benzo[*b*]thiophen skeleton belongs to systems with high electron density, this nucleophilic substitution cannot be carried out in usual classic way. One of the possibilities of activation of the chlorine atom lied in the oxidation of the sulphur atom in benzo[*b*]thiophene skeleton to the corresponding 1,1-dioxide. In contrast to the earlier-described uniform course of oxidation [3d], in our case the reaction always gave a complex mixture of products. Another possibility of replacement of the chlorine substituent at the 3-position consisted in the application of the Buchwald–Hartwig reaction [5]. This reaction requires application of a suitable palladium catalyst combined with a non-nucleophilic base. It is well-known that bromo derivatives are the best alternative for the Buchwald–Hartwig reaction [5a-c]. However, recent papers also describe syntheses starting from chloro derivatives and report very high yields, particularly with application of butyl-di-(1-adamantyl)phosphine (BDAP) as the palladium coordinating ligand [5d,e].

Several attempts were made to substitute the chlorine atom in compounds **3a** and **3b** by piperidine. The course of these Buchwald–Hartwig reactions carried out under

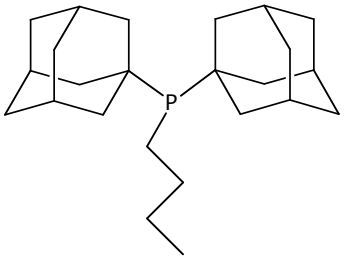
Scheme 3



3a, b (**a**: $R^2 = CH_3$, **b**: $R^2 = PhCH_2$)

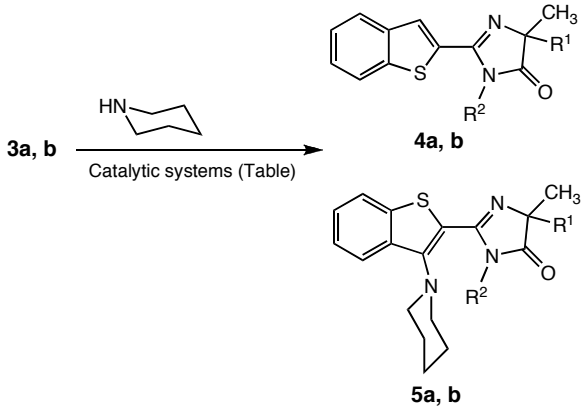
various conditions was monitored by means of GC-MS. (Table) (Scheme 4).

The individual experiments differed in the base used, the source of palladium, and the ligand adopted for coordination with palladium. The aim of these experiments was to optimize the substitution reaction and maximize the yield of the desired 2-[3-(1-piperidyl)-benzo[*b*]thiophene-2-yl]-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-one (**5a**) or 2-[3-(1-piperidyl) benzo[*b*]thiophene-2-yl]-1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one(**5b**) (Scheme 4) (Table).



BDAP

Scheme 4



4a, b; 5a, b (**a**: $R^1 = CH(CH_3)_2$,$R^2 = CH_3$; **b**: $R^1 = CH(CH_3)_2$, $R^2 = PhCH_2$)

The Table indicates that maximal conversion reached being 68 % (Table, Entry 6). The application of butyl-di-(1-adamantyl)phosphine (BDAP) gave conversion of 42 % (Table, Entry 2), but the only product was the product of reductive dechlorination of molecule **3a**, namely 2-(benzo[*b*]thiophene-2-yl)-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-on (**4a**), while the substitution product (**5a**) was not detected (Table, Entry 2). The experiments using BINAP (Table, Entries 3-6) gave the desired 2-[3-(1-piperidyl)benzo[*b*]thiophene-2-yl]-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-on (**5a**) or 2-[3-(1-piperidyl)benzo[*b*]thiophene-2-yl]-1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-on (**5b**), but these product were obtained as minor components: **5a** (14 %) **5b** (12 %), while the major components were products of reductive dechlorination: **4a** (15-57 %) and **4b** (56 %), which appeared in relatively high proportions (15-57 %) in all the experiments.

EXPERIMENTAL

The starting compounds were purchased from Sigma-Aldrich Comp. Butyl-di-(1-adamantyl)phosphine (BDAP) was purchased from ABCR GmBH & Co. KG Germany. The given melting temperatures were not corrected. Structures of the products prepared were verified by means of ^{1}H and ^{13}C NMR using a Bruker Avance 500 apparatus (500.13 MHz for ^{1}H and 125.77 MHz for ^{13}C). The samples were dissolved in hexadeuteriodimethyl sulphoxide (DMSO-d_6). The calibration used the residual signal of solvent (2.55 ppm ^{1}H, 39.51 ppm ^{13}C). The mass spectra were measured with apparatus set of Agilent Technologies Comp. (gas chromatograph 6890N with mass detector 5973 Network) (the samples were dissolved in ether or acetone). The elemental analyses were performed on an apparatus of FISONS Instruments, EA 1108 CHN.

General method of preparation of acylated aminoamides (1a–d). A solution of 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride (2.31 g; 10 mmol) in dichloromethane (30 mL) was added drop by drop to a solution of the respective aminoamide (10 mmol) and triethylamine (TEA) (0.73 mL; 10 mmol) in dry dichloromethane (20 mL). After 24-hour stirring at room temperature, the suspension obtained was evaporated, and the dry evaporation residue was washed with distilled water (2 × 20 mL). The remaining solid was recrystallized from an ethanol/water mixture.

***N*-(2-Carbamoylbut-2-yl)-3-chlorobenzo[*b*]thiophen-2-carboxamide (1a).** Yield 2.54 g (82 %); mp 210-212 °C; ^{1}H NMR: δ 0.79 (t, J = 7.4 Hz, 3H, CH_2CH_3), 1.69 (s, 3H, CH_3), 1.92 (q, J = 6.9 Hz, 1H, CH_2CH_3), 2.46 (q, J = 6.8 Hz, 1H,

Table

Buchwald–Hartwig reaction of derivatives **3a,b** and piperidine[a]

Entry	Compound	Base	Phosphine	Catalyst	Product 4[b]	Product 5[b]
1	**3a**	*t*-BuOK	BDAP	$Pd(CH_3COO)_2$	0	0
2	**3a**	*t*-BuOK	BDAP	$Pd_2(DBA)_3$	42	0
3	**3a**	*t*-BuOK	BINAP	$Pd_2(DBA)_3$	57	9
4	**3a**	*t*-BuOK	BINAP	$Pd(CH_3COO)_2$	15	14
5	**3a**	Cs_2CO_3	BINAP	$Pd_2(DBA)_3$	42	11
6	**3b**	Cs_2CO_3	BINAP	$Pd_2(DBA)_3$	56	12

[a] Reaction conditions: 1.2 eq. piperidine, 1.4 eq. base, 0.1 eq. Pd-cat., 0.1 eq. phosphine, toluene (10 mL), 48 h reflux under Ar atmosphere; [b] Yields determined by GC-MS.

C*H*$_2$CH$_3$), 7.54 (bs, 1H, CON*H*$_2$), 7.62 (m, 2H, Ar), 7.73 (bs, 1H, CON*H*$_2$), 7.93 (m, 1H, Ar), 8.13 (m, 1H, Ar), 8.73 (bs, 1H, CON*H*); ^{13}C NMR: δ 12.8, 27.4, 32.6, 65.7, 122.2, 127.1, 127.8, 130.3, 132.0, 138.6, 140.8, 141.3, 162.6, 179.5; EI-MS: m/z 310, 266, 195 (100 %), 167, 132, 123. *Anal.* Calcd. for $C_{14}H_{15}ClN_2O_2S$ (310.8): C, 54.10; H, 4.86; Cl, 11.41; N, 9.01; S, 10.32. Found: C, 54.28; H, 5.06; Cl, 11.65; N, 8.83; S, 10.12.

***N*-(2-Carbamoyl-3-methylbut-2-yl)-3-chlorobenzo[*b*]thiophene-2-carboxamide (1b).** Yield 2.75 g (85 %); mp 186-187 °C; ^{1}H NMR: δ 0.94 (d, J = 6.8 Hz, 3H, iPrC*H*$_3$), δ 1.04 (d, J = 6.8 Hz, 3H, iPrC*H*$_3$), 1.57 (s, 3H, C*H*$_3$), 2.27 (sp, J = 6.8 Hz, 1H, *i*PrC*H*), 7.23 (bs, 1H, CON*H*$_2$), 7.40 (bs, 1H, CON*H*$_2$), 7.63 (m, 2H, Ar), 7.94 (m, 1H, Ar), 8.12 (m, 1H, Ar), 8.18 (bs, 1H, CON*H*); ^{13}C NMR: δ 17.6, 17.7, 34.8, 37.5. 64.1, 118.5, 123.1, 123.7, 126,4; 128.0, 134.3, 136.7, 137.1, 159.6, 174.9; EI-MS: m/z 324, 280, 195 (100 %), 167, 132, 123. *Anal.* Calcd. for $C_{15}H_{17}ClN_2O_2S$ (324.8): C, 55.46; H, 5.28; Cl, 10.91; N, 8.62; S, 10.32. Found: C, 55.56; H, 5.13; Cl, 10.96; N, 8.59; S, 10.07.

***N*-(2-Carbamoyl-4-methylpent-2-yl)-3-chlorobenzo[*b*]thiophene-2-carboxamide (1c).** Yield 2.21 g (65 %); mp 147-149 °C; ^{1}H NMR: 0.82 (d, J = 7.0 Hz 3H, *i*BuC*H*$_3$), 0.84 (d, J = 7.0 Hz 3H, *i*BuC*H*$_3$), 1.56 (sp, ^{3}J = 7.0 Hz, 1H, *i*BuC*H*), 1.62 (s, 3H, C*H*$_3$), 1.79 (m, 1H, *i*BuC*H*$_2$), 2.43 (m, 1H, *i*BuC*H*$_2$), 7.55 (bs, 1H, CON*H*$_2$), 7.58 (m, 2H, Ar), 7.74 (bs, 1H, CON*H*$_2$), 7.89 (m, 1H, Ar), 8.09 (m, 1H, Ar), 8.88 (bs, 1H, CON*H*); ^{13}C NMR: δ 23.0, 23.3, 24.4, 24.7, 43.0, 60.4, 117.5, 122.7, 123.3, 125.9, 127.6, 134.2, 136.4, 136.8, 158.0, 175.7; EI-MS: m/z 338, 294, 264, 207, 195 (100 %), 167, 132, 123. *Anal.* Calcd. for $C_{16}H_{19}ClN_2O_2S$ (338.9): C, 56.71; H, 5.65; Cl, 10.46; N, 8.27; S, 9.46. Found: C, 56.98; H, 5.76; Cl, 10.66; N, 8.39; S, 9.52.

***N*-(2-Carbamoyl-3,3-dimethylbut-2-yl)-3-chlorobenzo[*b*]-thiophene-2-carboxamide (1d).** Yield 2.08 g (61 %); mp 209-210 °C; ^{1}H NMR: δ 1.13 (s, 9H, C(C*H*$_3$)$_3$), 1.68 (s, 3H, C*H*$_3$), 7.25 (s, 1H, CON*H*$_2$), 7.36 (bs, 1H, CON*H*$_2$), 7.63 (m, 2H, Ar), 7.90 (bs, 1H, CON*H*), 7.94 (m, 1H, Ar), 8.14 (m, 1H, Ar), 8.36 (bs, 1H, CON*H*); ^{13}C NMR: δ 17.4, 26.2, 36.8, 66.2, 79.4, 117.8, 122.9, 123.6, 126.1, 127.8, 134.9, 136.6, 137.0, 159.3, 173.0; EI-MS: m/z 264 (100 %), 207, 194, 159, 114, 57. *Anal.* Calcd. for $C_{16}H_{19}ClN_2O_2S$ (338.9): C, 56.71; H, 5.65; Cl, 10.46; N, 8.27; S, 9.46. Found: C, 56.52; H, 5.62; Cl, 10.38; N, 8.30; S, 9.43.

General method of preparation of substituted 4,5-dihydro-1*H*-imidazol-5-ones (2a-d). The respective substituted aminoamide **1a–d** (5 mmol) was added to sodium methoxide solution (25 mL; 1 mol·L^{-1}). After 72-hour stirring at room temperature, the pH value of reaction mixture was adjusted at pH ~ 5-6 (HCl aq., 5 mol·L^{-1}). The suspension formed was evaporated, and the dry evaporation residue was washed with distilled water (2 × 10 mL). The remaining solid was recrystallized from ethanol or an ethanol/water mixture.

2-(3-Chlorobenzo[*b*]thiophene-2-yl)-4-ethyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (2a). Yield 1 g (69 %); mp 144-147 °C; ^{1}H NMR: δ 0.78 (t, J = 7.3 Hz, 3H, CH$_2$C*H*$_3$), 1.35 (s, 3H, C*H*$_3$), 1.78 (m, 2H, C*H*$_2$CH$_3$), 7.65 (m, 2H, Ar), 7.97 (m, 1H, Ar), 8.18 (m, 1H, Ar), 11.32 (bs, 1H, CON*H*); ^{13}C NMR: δ 7.9, 22.6, 30.3, 61.3, 117.8, 122.5, 123.3, 126.1, 127.6, 128.0, 136.0, 136.8, 158.2. 175.1; EI-MS: m/z 292, 277, 263, 229, 214, 194 (100 %), 159, 132, 114. *Anal.* Calcd. for $C_{14}H_{13}ClN_2OS$ (292.0): C, 57.43; H, 4.48; Cl, 12.11; N, 9.57; S, 10.95. Found: C, 57.66; H, 4.59; Cl, 12.23; N, 9.62; S, 10.74.

2-(3-Chlorobenzo[*b*]thiophene-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (2b). Yield 1.18 g (77 %); mp 152-153 °C; ^{1}H NMR: δ 0.78 (d, J = 6.8 Hz, 3H, iPrC*H*$_3$), δ 0.95 (d, J = 6.8 Hz, 3H, iPrC*H*$_3$), 1.24 (s, 3H, C*H*$_3$), 1.91 (sp, J = 6.8 Hz, 1H, *i*PrC*H*), 7.57 (m, 2H, Ar), 7.87 (m, 1H, Ar), 8.08 (m, 1H, Ar), 11.29 (bs, 1H, CON*H*); ^{13}C NMR: δ 21.0, 66.0, 117.8, 122.1, 125.2, 129.8, 133.7, 141.8, 145.7, 150.5, 153.2, 169.3; EI-MS: m/z 306, 263 (100 %),194, 159, 132, 114. *Anal.* Calcd. for $C_{15}H_{15}ClN_2OS$ (306.1): C, 58.72; H, 4.93; Cl, 11.56; N, 9.13; S, 10.45. Found: C, 58.86; H, 4.79; Cl, 11.41; N, 9.12; S, 10.34.

2-(3-Chlorobenzo[*b*]thiophene-2-yl)-4-isobutyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (2c). Yield 1.52 g (97 %); mp 150-151 °C; ^{1}H NMR: 0.86 (d, J = 6.5 Hz 3H, *i*BuC*H*$_3$), 1.03 (d, J = 6.5 Hz 3H, *i*BuC*H*$_3$), 1.27 (s, 3H, C*H*$_3$), 1.52 (sp, J = 6.5 Hz, 1H, *i*BuC*H*), 1.62 (m, 1H, *i*BuC*H*$_2$), 1.76 (m, 1H, *i*BuC*H*$_2$), 7.60 (m, 2H, Ar), 7.91 (m, 1H, Ar), 8.12 (m, 1H, Ar), 11.34 (bs, 1H, CON*H*); ^{13}C NMR: δ 23.3, 24.1, 24.4, 24.6, 46.5, 70.0, 122.4, 123.4, 126.1, 128.0, 136.1, 137.2, 148.5, 153.7, 185.6; EI-MS: m/z 320, 305, 277, 264, 249, 207, 194 (100 %), 159, 114, 84, 57. *Anal.* Calcd. for $C_{16}H_{17}ClN_2OS$ (320.1): C, 59.90; H, 5.34; Cl, 11.05; N, 8.73; S, 9.99. Found: C, 59.93; H, 5.40; Cl, 10.88; N, 9.12; S, 9.89.

2-(3-Chlorobenzo[*b*]thiophene-2-yl)-4-*tert*-butyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (2d). Yield 1.18 g (74 %); mp 197-200 °C; ^{1}H NMR: δ 1.04 (s, 9H, C(C*H*$_3$)$_3$), 1.31 (s, 3H, C*H*$_3$), 7.66 (m, 2H, Ar), 7.97 (m, 1H, Ar), 8.18 (m, 1H, Ar), 11.31 (bs, 1H, CON*H*); ^{13}C NMR: δ 18.4, 24.6, 36.2, 74.5, 95.0, 105.2, 122.5, 123.4, 125.7, 126.1, 127.8, 136.1, 152.6, 186.6, 191.8, 197.3; EI-MS: m/z 320, 264 (100 %), 194, 159, 114, 57. *Anal.* Calcd. for $C_{16}H_{17}ClN_2OS$ (320.1): C, 59.90; H, 5.34; Cl, 11.05; N, 8.73; S, 9.99. Found: C, 60.09; H, 5.44; Cl, 10.78; N, 8.67; S, 9.98.

Synthesis of 2-(3-chlorobenzo[*b*]thiophene-2-yl)-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-one (3a). The reaction was performed on a vacuum-argon line. 2-(3-Chlorobenzo[*b*]thiophen-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**2b**) (1.53 g; 5 mmol) was suspended in potassium *tert*-butyl alcoholate (20 mL; 0.50 mol·L^{-1}). After dissolution, the solvent *tert*-butyl alcohol was distilled off. The evaporation residue was dissolved in dry *N*,*N*-dimethylformamide (10 mL). After cooling to 0 °C, methyl iodide (0.63 ml; 10 mmol) was added and the temperature of the reaction mixture spontaneously increased up to 25 °C. After 24 hours, *N*,*N*-dimethylformamide was distilled off and the evaporation residue was mixed with distilled water and extracted with dimethyl ether (3 × 20 mL). The product was obtained by evaporating the combined dried diethyl ether extracts. Yield 1.45 g (91 %); mp 57-59 °C; ^{1}H NMR: δ 0.86 (d, J = 6.5 Hz 3H, *i*PrC*H*$_3$), 1.03 (d, J = 6.5 Hz 3H, *i*PrC*H*$_3$), 1.34 (s, 3H, C*H*$_3$), 1.96 (sp, J = 6.6 Hz, 1H, *i*PrC*H*), 3.03 (s, 3H, NC*H*$_3$), 7.68 (m, 2H, Ar), 7.98 (m, 1H, Ar), 8.24 (m, 1H, Ar); ^{13}C NMR: δ 16.6; 16.8, 20.9, 27.5, 34.2, 74.1, 121.4, 122.4, 123.6, 124.5, 126.2, 127.5, 135.3, 137.5, 154.7, 185.0; EI-MS: m/z 320, 277 (100 %), 208, 193, 158, 114. *Anal.* Calcd. for $C_{16}H_{17}ClN_2OS$ (320.1): C, 59.90; H, 5.34; Cl, 11.05; N, 8.73; S, 9.99. Found: C, 60.13; H, 5.43; Cl, 11.00; N, 8.74; S, 9.93.

Synthesis of 1-benzyl-2-(3-chlorobenzo[*b*]thiophene-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (3b). The reaction was performed on a vacuum-argon line. Benzyl bromide (1.2 ml; 10 mmol) was added to a mixture of 2-(3-chlorbenzo[*b*]thiophen-2-yl)-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**2b**) (1.85 g; 6 mmol) and cesium carbonate (1.38 g; 10 mmol) in dry *N*,*N*-dimethylformamide (15 mL).

After 48-hour heating at 150 °C, the content of the flask was cooled and filtered. The separated solid was washed with *N*,*N*-dimethylformamide (50 mL), and the filtrate was evaporated in vacuum. The evaporation residue was dissolved in ethyl acetate (20 mL) and filtered through a silica gel layer (2 cm). The product was obtained by evaporating the ethyl acetate. Yield 1.56 g (85 %), mp 80-82 °C; ^{1}H NMR: δ 0.89 (d, J = 6.8 Hz 3H, *i*PrC*H*$_3$), 0.98 (d, J = 6.8 Hz 3H, *i*PrC*H*$_3$), 1.39 (s, 3H, C*H*$_3$), 2.09 (sp, J = 6.8 Hz, 1H, *i*PrC*H*), 4.7 (s, 2H, C*H*$_2$Ph), 6.94 (m, 2H, CH$_2$*Ph*), 7.21 (m, 3H, CH$_2$*Ph*), 7.65 (m, 2H, Ar), 7.93 (m, 1H, Ar) 8.15 (m, 1H, Ar); ^{13}C NMR: 16.9, 17.1, 21.4, 34.4, 37.4, 44.1, 74.4, 122.0, 122.6, 123.7, 126.5, 127.0, 127.7, 127.8, 128.7, 135.1, 136.2, 137.6, 154.2, 185.0; EI-MS**:** m/z 396, 353, 263, 194, 91 (100 %). *Anal***.** Calcd. for $C_{16}H_{17}ClN_2OS$ (396.9): C, 66.57; H, 5.33; Cl, 8.93; N, 7.06; S, 8.08. Found: C, 66.32; H, 5.40; Cl, 8.86; N, 7.17; S, 7.99.

Investigation of C-N coupling reaction of 3a, b with piperidine. The reaction was performed on a vacuum-argon line. A solution of piperidine (1.2 mmol) in dry toluene (10 mL) was added to a mixture of the substrate (**3a**, **3b**) (1 mmol), ligand (BINAP, BDAP) (0.1 mmol), base (*t*-BuOK, Cs_2CO_3) (1.4 mmol) and palladium source ($Pd(CH_3COO)_2$, $Pd_2(DBA)_3$) (0.1 mmol) in toluene (20 mL). After 72-hour refluxing, the toluene solvent was evaporated in vacuum, the evaporation residue was mixed with diethyl ether (30 mL), and the mixture formed was poured through a silica gel layer (2 cm). The oil obtained after evaporating diethyl ether was analysed by means of GC-MS (Table).

2-(Benzo[*b*]thiophene-2-yl)-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-one (**4a**). EI-MS m/z 286, 271, 257, 243 (100%), 174, 159, 133, 115, 102, 89.

2-[3-(1-Piperidyl)benzo[*b*]thiophene-2-yl]-4-isopropyl-1,4-dimethyl-4,5-dihydro-1*H*-imidazol-5-one (**5a**) EI-MS m/z: 369, 326 (100 %), 285, 267, 257, 243, 226, 215, 201, 186, 173, 159, 147, 84.

2-(Benzo[*b*]thiophene-2-yl)-l-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**4b**) EI-MS : m/z 362, 347, 319 (100 %), 281, 249, 229, 207, 187, 173, 159, 132, 115, 91.

2-[3-(1-Piperidyl)benzo[*b*]thiophene-2-yl]-1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1*H*-imidazol-5-one (**5b**) EI-MS m/z: 445, 402, 354 (100 %), 319, 267, 249, 226, 186, 159, 91.

Acknowledgments The authors acknowledge the financial support from the MSM 002 162 7501.

REFERENCES AND NOTES

[1] (a) Sedlák, M.; Halama, A.; Kaválek, J.; Macháček, V.; Štěrba, V. *Collect. Czech. Chem. Commun*. **1995**, *60*, 150; (b) Sedlák, M.; Halama, A.; Kaválek, J.; Macháček, V.; Mitaš, P.; Štěrba V. *Collect. Czech. Chem. Commun*. **1996**, *61*, 910; (c) Sedlák, M.; Halama, A.; Mitaš, P.; Kaválek, J.; Macháček, V. *J. Heterocyclic Chem*. **1997,** *34*, 1227; (d) Mitaš, P.; Sedlák, M.; Kaválek, J. *Collect. Czech. Chem. Commun*. **1998**, *63*, 85; (e) Sedlák, M.; Kaválek, J.; Mitaš, P.; Macháček, V. *Collect. Czech. Chem. Commun*. **1998**, *63*, 394; (f) Sedlák, M.; Hanusek, J.; Bína, R.; Kaválek, J.; Macháček, V. *Collect. Czech. Chem. Commun*. **1999**, *64*, 1629; (g) Sedlák, M.; Hanusek, J. *Molecules* **2000,** 5, M177; (h) Sedlák, M.; Drabina, P.; Hanusek, J. *Heterocycl. Commun*. **2003**, *9*, 129; (i) Sedlák, M.; Drabina, P.; Císařová, I.; Růžička, A.; Hanusek, J.; Macháček, V. *Tetrahedron Lett*. **2004**, *45*, 7723; (j) Turský, M.; Nečas, D.; Drabina, P.; Sedlák, M.; Kotora, M. *Organometallics* **2006**, *25*, 901; (k) Sedlák, M.; Drabina, P.; Keder, R.; Hanusek, J.; Císařová, I.;.Růžička, A. *J. Organomet. Chem*. **2006**, *691*, 2623; (l) Drabina, P.; Hanusek, J.; Jiráska, R.; Sedlák, M. *Transition Met. Chem*. **2006**, *31*, 1052; (m) Nečas, D.; Drabina, P.; Sedlák, M.; Kotora, M. *Tetrahedron Lett*. **2007**, *45*, 4539.

[2] (a) Wepplo, P. *J. Pestic. Sci*. **1990**, *31*, 293; (b) Harris, J. E.; Gagne, J. A.; Fischer. J. E.; Sharma, R. R.; Traul, K. A.; Scot, J. D.; Hess F. G. In *The Imidazole Herbicides*; Shaner, D. L.; O'Connor, S. L. Eds., CRC Press, Boca Raton, FL, USA **1991**, 179.

[3] (a) Nič, M.; Havelková, M.; Terinek, M.; Paleček, J.; Svoboda, J.; Jandera, A.; Panajotová, V. *Česk. Slov. Farm* **1999**, *48*, 281; (b) Kutschy, P.; Imrich. J.; Bernát, J. *Synthesis* **1983**, 929; (c) Kutschy, P.; Imrich. J.; Bernát, J.; Kristian, P.; Hritzová, O.; Schöffmann, T. *Collect. Czech. Chem. Commun*. **1986**, *51*, 2839; (d) Svoboda, J.; Štádler, M.; Jandera, A.; Panajotová, V.; Kuchař, M. *Collect. Czech. Chem. Commun*. **2000**, *65*, 1082; (e) Mezlová, M.; Petříková, H.; Maloň, P.; Kozmík, V.; Svoboda. V. *Collect. Czech. Chem. Commun*. **2003**, *68*, 1020; (f) Rejnak, J.; Klíma, J.; Svoboda, J.; Ludvík, J. *Collect. Czech. Chem. Commun*. **2004**, *69*, 242; (g) El Ashry, E. S. H.; Kassem, A. A.; Abdel-Hamid, H.; Louis, F. F.; Khattab, Sh. A. N.; Aouad, M. R. *J. Heterocyclic Chem*. **2006**, *43*, 1421.

[4] (a) Krubsack, A. J.; Higa, T. *Tetrahedron Lett*. **1968**, *49*, 5149; (b) Higa, T., Krubsack, A. *J. Org. Chem*. **1975**, *40*, 3037.

[5] (a) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem*. **1999**, *576*, 125; (b) Hartwig J. F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*, Negishi, E.-I. Ed., Wiley-Interscience, New York, **2002**, Vol. 1, 1051; (c) Neumann, H.; Brennführer, A.; Gross, P.; Riermeier, J. A.; Beller, M. *Adv. Synth. Catal*. **2006**, *348*, 1255; (d) Tewari. A.; Hein, M.; Zapf, A.; Beller, M. *Tetrahedron* **2005**, *61*, 9705; (e) Fleckenstein, C. A.; Plenio, H. *Chem. Eur. J*. **2007**, *13*, 2701.

[6] (a) Gastrok, W. H.; Wepplo, P. J. U.S. 4,683,324, 1987. American Cyanamid Company, *Chem. Abstr*. **1987**, *107*, 198332; (b) Shoemaker, P. J. H.; Kamphius J. *Tetrahedron*: *Asymmetry* **1993**, *6*, 113.