Research on Heterocyclic Compounds. XXI. Synthesis of Imidazo[2,1-*b*]benzothiazole and Imidazo[2,1-*b*]thiazole Derivatives

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The reaction of some 2-aminobenzothiazoles and 2-aminothiazoles with ethyl 3-bromo-4-oxopentanoate was investigated with the aim to obtain the corresponding imidazo[2,1-*b*]benzothiazole and imidazo[2,1-*b*]-thiazole derivatives, respectively. In some cases, two unexpected side products were obtained together with the required compound and their structures were elucidated: *e.g.*, 2-aminobenzothiazole reacted with ethyl 3-bromo-4-oxopentanoate to give ethyl 2-methylimidazo[2,1-*b*]benzothiazole-3-acetate together with ethyl imidazo[2,1-*b*]benzothiazole-2-propionate and ethyl 3-(benzothiazol-2-yl)amino-4-oxopentanoate.

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During our research on heterocyclic compounds with antiinflammatory activity, we synthesized a number of imidazo[2,1-*b*]thiazole and imidazo[2,1-*b*]benzothiazole derivatives bearing an acidic moiety on the imidazole ring [1-3]; most of these compounds showed interesting antiinflammatory activity. In the context of studies on structure-activity relationships, we have taken into consideration the possibility to improve the pharmacological activity of these compounds through structural modifications. In this respect we have considered interesting to synthesize some new compounds related to the structural models **1** and **2**.

As it can be seen in Figure 1, the imidazole ring of such derivatives bears a methyl group and an acetic moiety with a close similarity with the corresponding region of the indomethacin molecule. Such region is important for binding to the prostaglandin synthetase receptor site proposed by Gund and Shen for indomethacin and other antiinflammatory arylacetic acids [4].

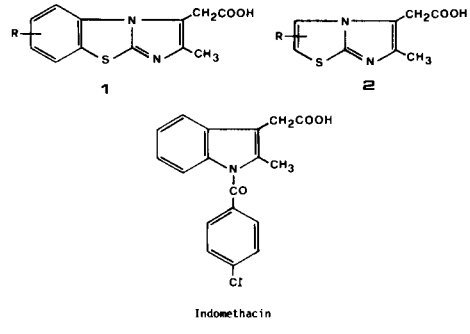

Figure 1

The synthetic method chosen to obtain the required compounds is closely related to the general procedure we have often employed to prepare many bicyclic imidazo-derivatives with a bridgehead nitrogen atom. In the present case, a first reaction was carried out refluxing 2-aminobenzothiazole with an equimolar amount of ethyl 3-bromo-4-oxopentanoate (**3**) in ethanolic solution. We have isolated in low yield from the reaction solution not only the required ethyl 2-methylimidazo[2,1-*b*]benzothiazole-3-acetate **4**, but also two other products to which the structures **5** and **6** were assigned, namely ethyl imidazo[2,1-*b*]benzothiazole-2-propionate and ethyl 3-(benzothiazol-2-yl)-amino-4-oxopentanoate, respectively (Figure 2); unreacted starting reagents were also recovered.

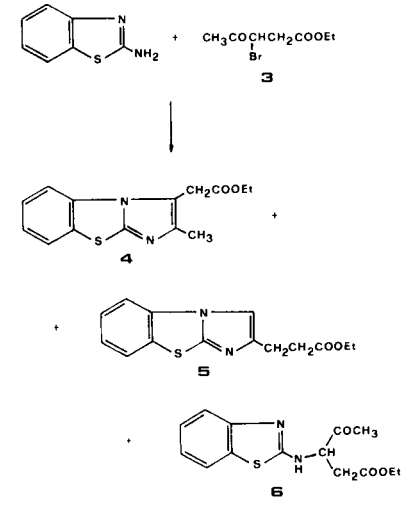

Figure 2

The structures assigned to products **4**, **5**, and **6** were supported by both elemental analytical data and spectral evidences. Compound **4** arose from the expected nucleophilic attack of the benzothiazole N-3 atom on C-3 of **3** and the subsequent cyclization between the amino and the CO groups; uv, ir, and ^{1}H-nmr spectra are coherent with the assigned structure, as detailed in the experimental section. Compound **6** clearly resulted from another reaction occurring simultaneously, that is the nucleophilic attack of the benzothiazole aminic N atom on C-3 of **3**, which was not

followed by cyclization. This product is characterized by (a) an uv spectrum very similar to that of 2-aminobenzothiazole and considerably different from that of imidazobenzothiazole **4**, (b) an ir spectrum which shows two strong C=O bands, and (c) a nmr spectrum with the characteristic triplet-doublet system of signals related to $CHCH_2$ moiety, together with the broad singlet of the NH group which disappears after treatment with deuterium oxide. An alternative structure which could be coherent with the above set of experimental data is depicted in Figure 3. This is the intermediate compound resulting from the nucleophilic attack of the benzothiazole N-3 atom on C-3 of **3**; such intermediate should easily cyclize to afford compound **4**. On the contrary, it resulted impossible to turn compound **6** into **4**, also after prolonged heating in ethanolic solution.

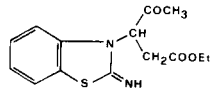

Figure 3

The structure of **5** is more intriguing. Such product could only arise from a hypothetic 5-bromo-4-oxopentanoate *via* a nucleophilic attack of the benzothiazole N-3 atom on C-5 of this bromo-derivative: however, the bromination of ethyl 4-oxopentanoate, which was carried out following Yoshida and Ishizuka [5], always afforded 3-bromo-4-oxopentanoate alone, and we never found the 5-bromo isomer in the reaction solution. On the other hand, the structure of compound **5** was unequivocally confirmed by the experimental data. Consequently, it is necessary to suppose ethyl 3-bromo-4-oxopentanoate underwent a rearrangement to 5-bromo isomer during the reaction. Such rearrangement probably occurs in a manner strictly similar to that proposed by Kharasch *et al.* [6] in the case of ethyl 2-bromoacetoacetate and 2-bromo-2-methylacetoacetate, which rearranged to the corresponding 4-bromo esters with a mechanism involving hydrogen bromide and oxygen.

Similar results were obtained when ethyl 3-bromo-4-oxopentanoate was reacted with 2-amino-6-methoxy- and 2-amino-6-ethoxybenzothiazole, respectively. In both cases we have isolated the required ethyl 2-methylimidazo[2,1-*b*]benzothiazole-3-acetate, products **7** and **10**, respectively, together with the unexpected ethyl imidazo[2,1-*b*]benzothiazole-2-propionate **8** and **11** and the open chain derivative **9** and **12**.

When the same reaction was performed starting from 2-amino-4-chlorobenzothiazole, a small amount of the open chain derivative **13** alone was obtained: the cyclization of the imidazole ring did not occur. The presence of a chlorine atom in the 4 position of the benzothiazole ring probably exerted a disactivating action on the N-3 atom rendering impossible its nucleophilic attack on both C-3 of 3-bromo-4-oxopentanoate and C-5 of the isomeric 5-bromo-4-oxopentanoate.

We also used 2-aminothiazole as starting material. This amine reacted with ethyl 3-bromo-4-oxopentanoate (**3**) affording the required ethyl 6-methylimidazo[2,1-*b*]thiazole-5-acetate (**14**) in very low yield, whereas only unisolable trace amounts of the side products were present in the reacted solution. On the contrary, when 2-amino-4-methylthiazole was reacted with **3** we were able to isolate significant amounts of three products closely similar to those obtained starting from 2-aminobenzothiazole and its 6-methoxy and 6-ethoxy derivative, namely ethyl 3,6-dimethylimidazo[2,1-*b*]thiazole-5-acetate (**15**), ethyl 3-methylimidazo-[2,1-*b*]thiazole-6-propionate (**16**), and ethyl-3-(4-methylthiazol-2-yl)amino-4-oxopentanoate (**17**) (Figure 4). In this case the methyl group apparently increased the nucleophilic reactivity of the thiazole nitrogen atoms.

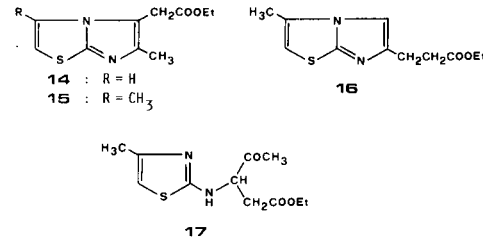

Figure 4

EXPERIMENTAL

Precoated silica gel 60 F254 plates from Merck were used for thin layer chromatographic controls; detection of components was made by either uv light or treatment with iodine vapors. Chromatographic separations were performed on columns packed with silica gel 60 Merck (70-230 mesh). Melting points were determined with a Kofler hot stage microscope and are uncorrected. The elemental analyses were performed by a Perkin-Elmer Elemental Analyzer mod. 240. The uv spectra were obtained with a Perkin-Elmer Coleman 575 spectrophotometer. The ir spectra were recorded with a Perkin-Elmer 177 spectrophotometer. The ^1H nmr spectra were recorded with a Bruker WM 250 apparatus; chemical shift values are reported in δ (parts per million) relative to an internal standard (tetramethylsilane).

Ethyl 3-Bromo-4-oxopentanoate (**3**).

This product was prepared starting from equimolar amounts of ethyl 4-oxopentanoate and bromine following Yoshida and Ishizuka [5]; nmr (deuteriochloroform): δ 1.19 (t, 3H, ethyl CH_3), 2.35 (s, 3H, CH_3CO), 2.81 (double d, 1H) and 3.18 (double d, 1H) (2-CH_2 geminal protons, J_{AB} = 16.8 Hz), 4.08 (q, 2H, ethyl CH_2), 4.59 (double d, 1H, CH_XBr; J_{AX} = 6.0 Hz, J_{BX} = 8.8 Hz).

Ethyl 2-Methylimidazo[2,1-*b*]benzothiazole-3-acetate (**4**).

A solution of 3.75 g (0.025 mole) of 2-aminobenzothiazole and 5.6 g (0.025 mole) of ethyl 3-bromo-4-oxopentanoate (**3**) in 100 ml of anhydrous ethanol was refluxed for 10 hours. The resulting solution was examined by tlc on silica gel plate (dichloromethane-diethyl ether 8:2), which showed the presence of three products with different Rf values together with unreacted starting compounds. The solution was evaporated to dryness

in vacuo; the residue was redissolved in sodium bicarbonate saturated solution and then extracted three times with chloroform. The combined extracts were washed with water, dried on anhydrous sodium sulfate, concentrated to a small volume and then chromatographed on a silica gel column eluting first with dichloromethane and then with dichloromethane-methanol 95:5. This procedure allowed us to eliminate the unreacted starting materials; the fractions containing mixtures of the three above mentioned products were combined and chromatographed again on a second silica gel column. The best separation was obtained eluting first with dichloromethane and then with dichloromethane-diethyl ether 8:2. The required compound **4** was eluted last from this column. It was recrystallized from *n*-hexane to obtain 1.55 g (23%) of colorless crystals, mp 123-125°; Rf 0.45 (dichloromethane-diethyl ether 8:2); uv (methanol): λ max 208, 220 (sh), 240 (sh) nm; ir (chloroform): cm^{-1} 2960, 1730 strong, 1580, 1480 strong; nmr (deuteriochloroform): δ 1.22 (t, 3H, ethyl CH_3), 2.36 (s, 3H, 2-CH_3), 4.00 (s, 2H, CH_2), 4.18 (q, 2H, ethyl CH_2), 7.20-7.75 (series of peaks, 4H, aromatic).

Anal. Calcd. for $C_{14}H_{14}N_2O_2S$: C, 61.3; H, 5.1; N, 10.2. Found: C, 61.0; H, 5.2; N, 10.2.

Ethyl Imidazo[2,1-*b*]benzothiazole-2-propionate (**5**).

The second product eluted from the above mentioned column was **5**. Recrystallization from *n*-hexane afforded 0.5 g (7.5%) of colorless crystals, mp 83-85°; Rf 0.55; nmr (deuteriochloroform): δ 1.26 (t, 3H, CH_3), 2.79 (t, 2H) and 3.07 (t, 2H) (CH_2CH_2, J = 7 Hz), 4.16 (q, 2H, ethyl CH_2), 7.32 (split t, 1H), 7.43 (split t, 1H), 7.53 (m, 2H) and 7.69 (d, 1H) (aromatic and 3-H).

Anal. Calcd. for $C_{14}H_{14}N_2O_2S$: C, 61.3; H, 5.1; N, 10.2. Found: C, 61.2; H, 4.9; N, 10.0.

Ethyl 3-(Benzothiazol-2-yl)amino-4-oxopentanoate (**6**).

This product was the first one obtained *via* the chromatographic procedure already described. It was recrystallized from *n*-hexane obtaining 1.4 g (19%) of colorless crystals, mp 102-104°; Rf 0.65; uv (methanol): λ max 208 (sh), 224, 267 nm; ir (chloroform): cm^{-1} 3420, 2980, 1740 and 1718 strong, 1602, 1538 strong; nmr (deuteriochloroform): δ 1.38 (t, 3H, ethyl CH_3), 2.20 (s, 3H, $COCH_3$), 3.31 (d, 2H, CH_2), 4.25 (q, 2H, ethyl CH_2), 4.95 (t, 1H, CH), 6.10 (broad s, 1H, NH; exchanges with deuterium oxide), 7.12 and 7.31 (split triplets, 1H each) and 7.57 (split t, 2H) (aromatic), J_{CH,CH_2} = 4.5 Hz.

Anal. Calcd. for $C_{14}H_{16}N_2O_3S$: C, 57.5; H, 5.5; N, 9.6. Found: C, 57.3; H, 5.2; N, 9.7.

Ethyl 7-Methoxy-2-methylimidazo[2,1-*b*]benzothiazole-3-acetate (**7**).

The required product **7** was obtained with the same procedure described for **4**, starting from 4.5 g (0.025 mole) of 2-amino-6-methoxybenzothiazole and 5.6 g (0.025 mole) of ethyl 3-bromo-4-oxopentanoate (**3**) in 100 ml of anhydrous ethanol. The product obtained last in the chromatographic separation was recrystallized from *n*-hexane to yield 0.4 g (5.2%) of colorless crystals, mp 130-132°; Rf 0.40 (dichloromethane-diethyl ether 8:2); nmr (deuteriochloroform): δ 1.20 (t, 3H, ethyl CH_3), 2.30 (s, 3H, 2-CH_3), 3.85 (s, 3H, 7-OCH_3), 3.95 (s, 2H, CH_2), 4.15 (q, 2H, ethyl CH_2), 6.98 (double d, 1H, H-6), 7.21 (d, 1H, H-8), 7.65 (d, 1H, H-5), $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.5 Hz.

Anal. Calcd. for $C_{15}H_{16}N_2O_3S$: C, 59.2; H, 5.3; N, 9.2. Found: C, 59.0; H, 5.0; N, 9.3.

Ethyl 7-Methoxyimidazo[2,1-*b*]benzothiazole-2-propionate (**8**).

The second product obtained starting from 2-amino-6-methoxybenzothiazole *via* the chromatographic procedure previously described was recrystallized from *n*-hexane to afford 0.55 g (7.4%) of colorless crystals, mp 88-90°; Rf 0.53; nmr (deuteriochloroform): δ 1.25 (t, 3H, ethyl CH_3), 2.76 (t, 2H) and 3.05 (t, 2H) (CH_2CH_2, J = 7 Hz), 3.88 (s, 3H, 7-OCH_3), 4.15 (q, 2H, ethyl CH_2), 6.98 (double d, 1H, H-6), 7.20 (d, 1H, H-8), 7.42 (d, 1H, H-5), 7.46 (s, 1H, H-3), $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.5 Hz.

Anal. Calcd. for $C_{15}H_{16}N_2O_3S$: C, 59.2; H, 5.3; N, 9.2. Found: C, 58.9; H, 5.2; N, 9.2.

Ethyl 3-(6-methoxybenzothiazol-2-yl)amino-4-oxopentanoate (**9**).

The first product obtained in the chromatographic separation was recrystallized from *n*-hexane to afford 0.8 g (10%) of colorless crystals, mp 150-152°; Rf 0.70; nmr (deuteriochloroform): δ 1.25 (t, 3H, ethyl CH_3), 2.18 (s, 3H, $COCH_3$), 3.28 (d, 2H, CH_2), 3.82 (s, 3H, 6-OCH_3), 4.24 (q, 2H, ethyl CH_2), 4.90 (t, 1H, CH), 5.98 (broad s, 1H, NH, exchanges with deuterium oxide), 6.89 (double d, 1H, H-5), 7.12 (d, 1H, H-7), 7.45 (d, 1H, H-4), J_{CH,CH_2} = 4.5 Hz, $J_{4,5}$ = 9 Hz, $J_{5,7}$ = 2.5 Hz.

Anal. Calcd. for $C_{15}H_{18}N_2O_4S$: C, 55.9; H, 5.6; N, 8.7. Found: C, 56.0; H, 5.5; N, 8.5.

Ethyl 7-Ethoxy-2-methylimidazo[2,1-*b*]benzothiazole-3-acetate (**10**).

The required product **10** was obtained *via* the same procedure described for **4**, starting from 4.9 g (0.025 mole) of 2-amino-6-ethoxybenzothiazole and 5.6 g (0.025 mole) of **3** in 100 ml of anhydrous ethanol. The last product obtained in the chromatographic separation was recrystallized from *n*-hexane to afford 0.4 g (5.1%) of colorless crystals, mp 142-144°; Rf 0.30 (dichloromethane-diethyl ether 8:2); nmr (deuteriochloroform): δ 1.22 (t, 3H) and 1.45 (t, 3H), (two ethyl CH_3), 2.35 (s, 3H, 2-CH_3), 3.98 (s, 2H, CH_2), 4.08 (q, 2H) and 4.18 (q, 2H) (two ethyl CH_2), 6.95 (double d, 1H, H-6), 7.28 (d, 1H, H-8), 7.63 (d, 1H, H-5), $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.5 Hz.

Anal. Calcd. for $C_{16}H_{18}N_2O_3S$: C, 60.3; H, 5.7; N, 8.8. Found: C, 60.0; H, 5.5; N, 8.6.

Ethyl 7-Ethoxyimidazo[2,1-*b*]benzothiazole-2-propionate (**11**).

Compound **11** was the second product obtained starting from 2-amino-6-ethoxybenzothiazole *via* the chromatographic procedure previously described. After recrystallization from *n*-hexane, we have obtained 0.35 g (4.5%) of colorless crystals, mp 85-87°; Rf 0.51; nmr (deuteriochloroform): δ 1.26 (t, 3H) and 1.44 (t, 3H) (two ethyl CH_3), 2.76 (t, 2H) and 3.04 (t, 2H) (CH_2CH_2, J = 7 Hz), 4.06 (q, 2H) and 4.15 (q, 2H) (two ethyl CH_2), 6.95 (double d, 1H, H-6), 7.17 (d, 1H, H-8), 7.40 (m, 2H, H-3 and H-5), $J_{5,6}$ = 8.5 Hz, $J_{6,8}$ = 2.5 Hz.

Anal. Calcd. for $C_{16}H_{18}N_2O_3S$: C, 60.3; H, 5.7; N, 8.8. Found: C, 60.2; H, 5.8; N, 8.5.

Ethyl 3-(6-Ethoxybenzothiazol-2-yl)amino-4-oxopentanoate (**12**).

Compound **12** was the first product obtained starting from 2-amino-6-ethoxybenzothiazole using the chromatographic procedure previously described. After recrystallization from *n*-hexane, we have obtained 0.8 g (9.6%) of colorless crystals, mp 145-148°; Rf 0.74; nmr (deuteriochloroform): δ 1.26 (t, 3H) and 1.43 (t, 3H) (two ethyl CH_3), 2.18 (s, 3H, $COCH_3$), 3.29 (d, 2H, CH_2), 4.04 (q, 2H) and 4.24 (q, 2H) (two ethyl CH_2), 4.91 (t, 1H, CH), 6.00 (broad s, 1H, NH, exchanges with deuterium oxide), 6.90 (double d, 1H, H-5), 7.11 (d, 1H, H-7), 7.45 (d, 1H, H-4); J_{CH,CH_2} = 4.5 Hz, $J_{4,5}$ = 9 Hz, $J_{5,7}$ = 2.5 Hz.

Anal. Calcd. for $C_{16}H_{20}N_2O_4S$: C, 57.1; H, 6.0; N, 8.3. Found: C, 56.8; H, 5.9; N, 8.3.

Ethyl 3-(4-Chlorobenzothiazol-2-yl)amino-4-oxopentanoate (**13**).

A solution of 4.6 g (0.025 mole) of 2-amino-4-chlorobenzothiazole and 5.6 g (0.025 mole) of ethyl 3-bromo-4-oxopentanoate (**3**) in 100 ml of anhydrous ethanol was refluxed for 20 hours. The reacted solution was evaporated to dryness *in vacuo*; the residue was treated with sodium bicarbonate saturated solution and filtered to remove the unreacted starting amine which is insoluble in alkaline medium. The aqueous filtrate was extracted with chloroform. The organic extract was washed with water, dried on anhydrous sodium sulfate, concentrated to a small volume and then chromatographed on a silica gel column eluting with *n*-hexane-diethyl ether (95:5) to afford 0.2 g (2.5%) of **13** (recrystallized from *n*-hexane), mp 68-70°; uv (methanol): λ max 231, 273 nm; ir (chloroform): cm^{-1} 3410, 2980, 1740 and 1715 strong, 1590, 1535 strong; nmr (deuteriochloroform): δ 1.30 (t, 3H, ethyl CH_3), 2.24 (s, 3H, $COCH_3$), 3.36 (d, 2H, CH_2), 4.28 (q, 2H, ethyl CH_2), 4.97 (t, 1H, CH), 6.46 (broad s, 1H, NH; exchanges with deuterium oxide), 7.07 (t, 1H), 7.35 (d, 1H) and 7.51 (d, 1H) (aromatic), J_{CH,CH_2} = 4.5 Hz.

Anal. Calcd. for $C_{14}H_{15}ClN_2O_3S$: C, 51.5; H, 4.6; N, 8.6. Found: C, 51.2; H, 4.5; N, 8.6.

Ethyl 6-Methylimidazo[2,1-*b*]thiazole-5-acetate (**14**).

A solution of 2.5 g (0.025 mole) of 2-aminothiazole and 5.6 g (0.025 mole) of **3** in 60 ml of anhydrous ethanol was refluxed for 8 hours. The solution was then evaporated to dryness *in vacuo*; the residue was redissolved in sodium bicarbonate saturated solution and extracted with chloroform. The extract was washed with water, dried on anhydrous sodium sulfate, concentrated to a small volume and then chromatographed on a silica gel column eluting with dichloromethane. The only product isolated was a colorless oily liquid (0.2 g, 3.7%); nmr (deuteriochloroform): δ 1.22 (t, 3H, ethyl CH_3), 2.29 (s, 3H, 6-CH_3), 3.74 (s, 2H, CH_2), 4.12 (q, 2H, ethyl CH_2), 6.73 (d, 1H, H-2), 7.38 (d, 1H, H-3), $J_{2,3}$ = 4.5 Hz.

Anal. Calcd. for $C_{10}H_{12}N_2O_2S$: C, 53.5; H, 5.4; N, 12.5. Found: C, 53.1; H, 5.5; N, 12.2.

Ethyl 3,6-Dimethylimidazo[2,1-*b*]thiazole-5-acetate (**15**).

A solution of 4 g (0.035 mole) of 2-amino-4-methylthiazole and 7.8 g (0.035 mole) of **3** in 100 ml of anhydrous ethanol was refluxed for 7 hours. The reacted solution was subjected to tlc testing on silica gel plate, using *n*-hexane-diethyl ether (1:1) as eluent: three different products together with unreacted starting compounds were found. Consequently, the solution was worked up in the same manner already described for **4**, with the difference that the first column chromatographic separation was carried out using *n*-hexane-diethyl ether (1:1) as eluent, whereas the second one was effected with dichloromethane-methanol (98:2). The required compound **15** was eluted last from the latter column. The solvent was removed *in vacuo* to afford 0.5 g (5.8%) of a colorless oil; Rf 0.32; nmr (deuteriochloroform): δ 1.20 (t, 3H, ethyl CH_3), 2.24 (s, 3H) and 2.42 (s, 3H) (3- and 6-CH_3), 3.78 (s, 2H, CH_2), 4.10 (q, 2H, ethyl CH_2), 6.21 (s, 1H, H-2).

Anal. Calcd. for $C_{11}H_{14}N_2O_2S$: C, 55.4; H, 5.9; N, 11.7. Found: C, 55.3; H, 6.0; N, 11.8.

Ethyl 3-Methylimidazo[2,1-*b*]thiazole-6-propionate (**16**).

The second product obtained *via* the chromatographic procedure already described starting from 2-amino-4-methylthiazole was **16**. This compound was a colorless oil (0.6 g, 7.3%); Rf 0.48; nmr (deuteriochloroform): δ 1.25 (t, 3H, ethyl CH_3), 2.35 (split s, 3H, 3-CH_3), 2.76 (t, 2H) and 3.03 (t, 2H) (CH_2CH_2, J = 7 Hz), 4.15 (q, 2H, ethyl CH_2), 6.37 (split s, 1H, H-2), 7.17 (s, 1H, H-5) [7].

Anal. Calcd. for $C_{11}H_{14}N_2O_2S$: C, 55.4; H, 5.9; N, 11.7. Found: C, 55.1; H, 5.7; N, 11.6.

Ethyl 3-(4-Methylthiazol-2-yl)amino-4-oxopentanoate (**17**).

The first product obtained by the chromatographic procedure already described starting from 2-amino-4-methylthiazole was **17**, in form of colorless oil (0.9 g, 10%); Rf 0.72; uv (methanol): λ max 200, 259 nm; ir (chloroform): cm^{-1} 3405, 2980, 1738 and 1712 strong, 1518 strong; nmr (deuteriochloroform): δ 1.23 (t, 3H, ethyl CH_3), 2.18 (s, 3H, $COCH_3$), 2.22 (split s, 3H, 4-CH_3), 3.18 (d, 2H, CH_2), 4.21 (q, 2H, ethyl CH_2), 4.70 (t, 1H, CH), 5.90 (broad s, 1H, NH; exchanges with deuterium oxide), 6.10 (split s, 1H, H-5) [7], J_{CH,CH_2} = 4.5 Hz.

Anal. Calcd. for $C_{11}H_{16}N_2O_3S$: C, 51.5; H, 6.3; N, 10.9. Found: C, 51.4; H, 6.1; N, 10.9.

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[7] Signals related to the methyl group and the adjacent proton on the thiazole ring are significantly split in consequence of longe range coupling.