SYNTHESIS OF *N*-(4,6-DIMETHYLPYRIDIN-2-YL)-BENZOXAZOLINONYL METHYLCARBOXAMIDES WITH POTENTIAL ANTIINFLAMMATORY ACTIVITY

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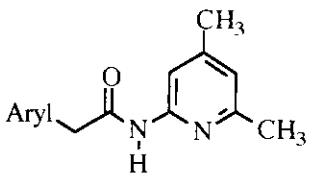
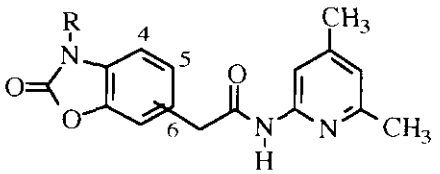
Abstract - New aryl(alkyl)carboxamides issued from 2-amino-4,6-dimethylpyridine and benzoxazolinone pharmacophores designed as antiinflammatory agents were synthesized from suitable methyl substituted *o*-aminophenols.

In recent years there has been a renewed interest for antiinflammatory agents endowed with either more selective mechanisms (COX-1 vs. COX-2 inhibition)[1] or novel modes of action. In this connection, recent studies[2-4] reported the interesting antiinflammatory profile of aralkylcarboxamides built around the 2-amino-4,6-dimethylpyridine template as shown in general structure (**A**) (Figure 1). This structure encoding a phenylacetyl moiety contains a methylene group when n is equal to 1. In an effort to emphasize this property, we planned the synthesis of compounds of general structure (**B**) (Figure 1) in which the central acetamide moiety will be linked on one side with a 2-amino-4,6-dimethylpyridine, an electron-deprived heterocycle, and on the other side by an electron-rich heterocycle, *i. e.* a 4, 5, or 6-substituted 2(3*H*)-benzoxazolone. This design was based on the following rationale: (1) the association on both ends of the acetamide connecting of electron-rich and electron-poor heterocycles is expected to promote the potential-

radical character *via* a capto-dative stabilization [5] and (2) the 2(3*H*)-benzoxazolone, a metabolically stabilized bioisoster of the pyrocatechol [6] is an heterocycle presenting *per se* with antiinflammatory activity.[7] This paper reports our synthesis endeavours along this line.



Structure A



Structure B

Figure 1

Results and discussion.

According to the retrosynthesis shown in Figure 2, isomeric 2(3*H*)-benzoxazolones bearing an acetyl side chain in either 4, 5, or 6-position were used as starting materials to prepare the target compounds of structure (**B**).

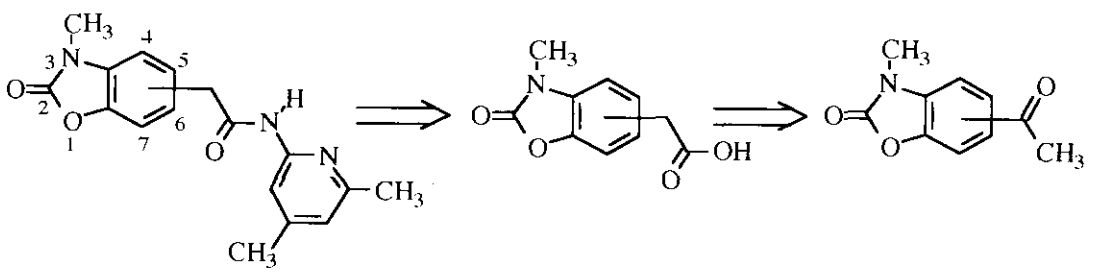
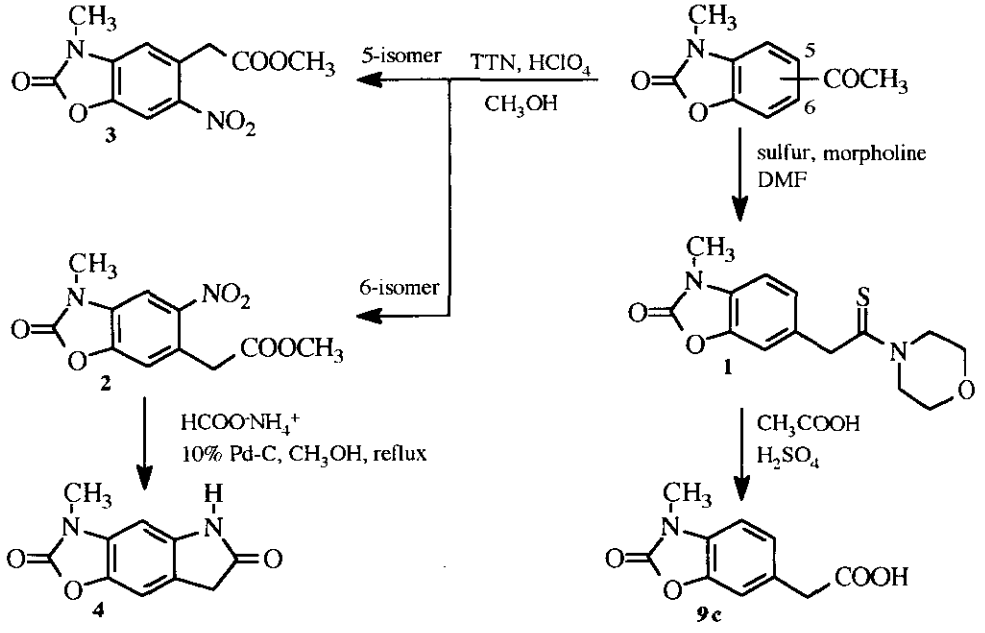


Figure 2

A first connection (Scheme 1) was based on the use of the readily available 5- and 6-substituted acetophenone *via* either the Willgerodt-Kindler route [8] (involving thioamide intermediates) or the more modern version using Th(III)-nitrate (TTN).[9] 5- And 6-acetophenones were synthesized as previously reported taking advantage of the $AlCl_3$-DMF complex used as Friedel-Crafts catalyst.[10-12] The classical Willgerodt-Kindler procedure using 6-acetyl-2(3*H*)-benzoxazolone, sulfur, and morpholine yielded the corresponding thiomorpholide in 42 % yield. However, acid hydrolysis was met with poor success due to the degradation of the oxazolinonic heterocycle and thus, arylacetic acid (**9c**) was produced in 10 % yield only. In view of this failure, the TTN route was explored. Treatment of either 5- or 6-acetyl-2(3*H*)-

benzoxazolone with TTN and perchloric acid in methanol gave surprisingly enough, the isomeric methyl nitrophenylacetate esters (**2** and **3**) in 70 % and 65 % yields, respectively. To our knowledge, this is the first case where the expected rearrangement is accompanied by a concomittent electrophilic substitution. This fact too emphasizes once again the high degree of activation of the 2(3*H*)-benzoxazolone heterocycle toward electrophiles, a consequence of the high electron density of the π-system. The position of the nitro group was confirmed by the ^{1}H NMR study and by heterocyclization taking place upon reduction with ammonium formate in the presence of 10% Pd-C at reflux to yield the interesting indolone (**4**) in 33 % yield.



Scheme 1

Having reached another unsuccessful, we explored another route based on the disconnection shown on Figure 3, and using commercially available *o*-hydroxytoluidines.

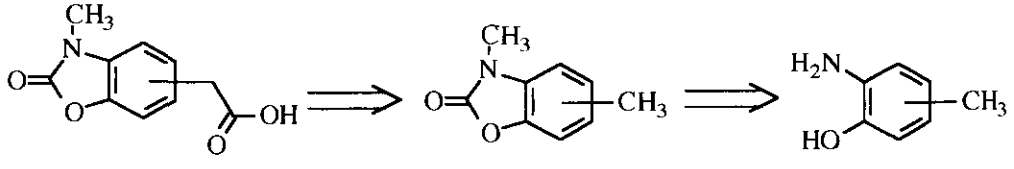
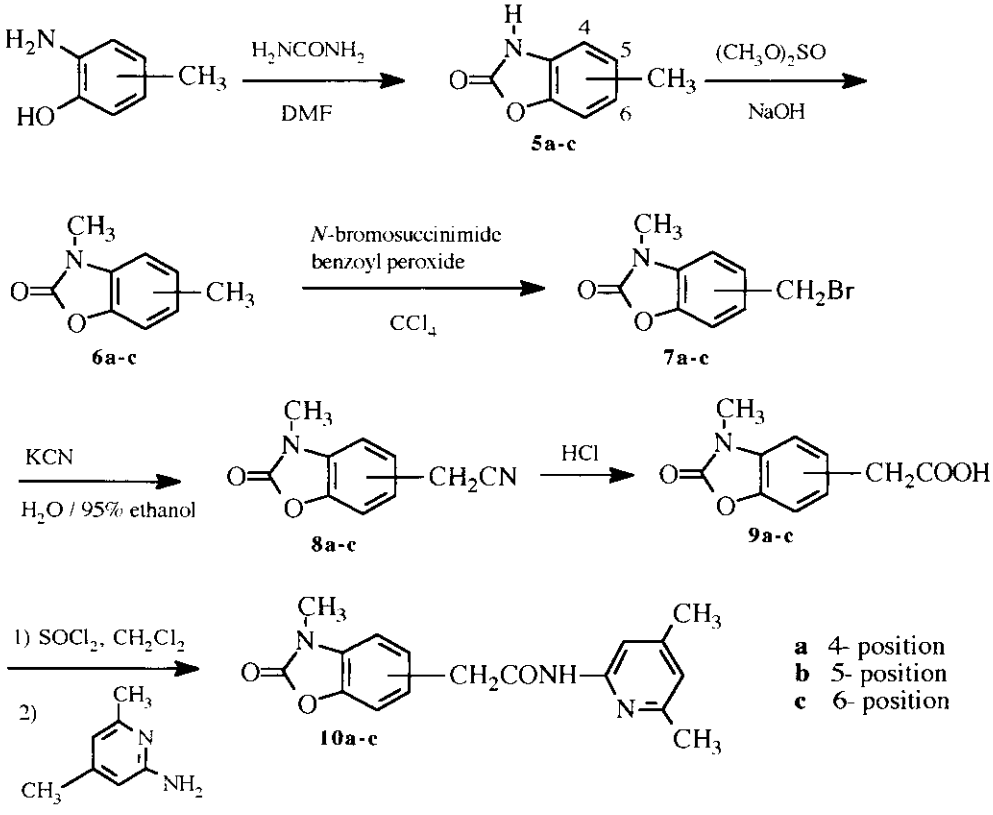


Figure 3

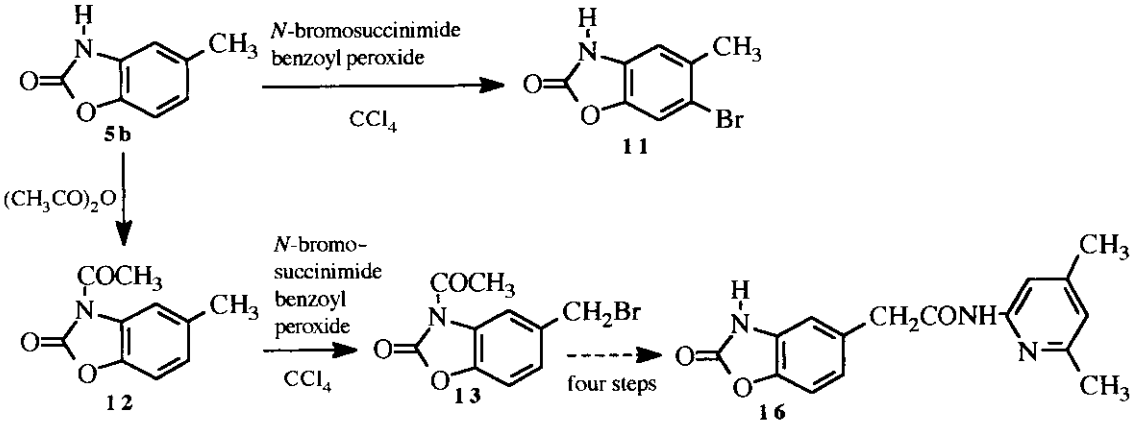
Scheme 2 illustrates the reactions finally adopted to synthezise 4-,5- and 6- substituted 2(3*H*)-benzoxazolinone derivatives (**10a-c**). The appropriate regioisomer methyl substituted *o*-aminophenols were reacted with urea in refluxing DMF [13, 14] leading to the formation of the corresponding 2(3*H*)-benzoxazolone derivatives (**5a-c**) that were *N*-methylated using dimethyl sulfate in basic medium. Bromination of the methyl group of **6a-c** with *N*-bromosuccinimide in carbon tetrachloride afforded the bromomethyl derivatives (**7a-c**). Nucleophilic displacement of the bromine atom of **7a-c** with KCN in 95% ethanol yielded the nitriles (**8a-c**) which were then hydrolyzed in acidic medium to the acids (**9a-c**). Treatment of these with thionyl chloride gave the intermediate acid chlorides which were coupled with 2-amino-4,6-dimethylpyridine to provide the target amides (**10a-c**).



Scheme 2

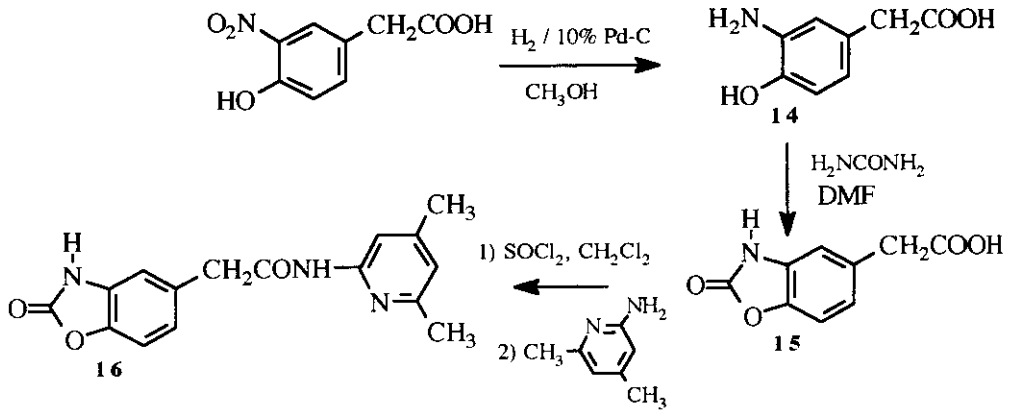
To access to the *N*-unsubtituted derivative (**15**) we initally planned to apply on **5b** the procedure described above for the methyl derivative (**6b**). However, NBS bromination afforded (Scheme 3) a mixture containing mainly the 6 - bromo compound (**11**). When the heterocycle was *N*-protected by acetylation, the

benzylic bromination proceeded cleanly to afford **12**, treatment of which with the potent nucleophile cyanide resulted in degradation of the heterocycle rather than nucleophilic substitution.



Scheme 3

Due to this negative result, we developped another synthetic strategy (Scheme 4): the commercially available 4-hydroxy-3-nitrophenylacetic acid was catalytically (10% Pd-C) reduced to the corresponding *o*-aminophenol (**14**) which was reacted with urea in refluxing DMF leading to the formation of the corresponding 2(3*H*)-benzoxazolone derivative (**15**). Treatment of **15** with thionyl chloride gave the intermediate acid chlorides which was coupled with 2-amino-4,6-dimethylpyridine to provide the amide (**16**).



Scheme 4

EXPERIMENTAL

Melting points were determined using a Büchi 530 melting point apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer and the ^{1}H NMR spectra were recorded using a Brüker AC 300 spectrometer. Chemical shifts (δ) are reported in ppm with tetramethylsilane as internal standard. Elemental analyses were performed by the "Service Central d'Analyses", CNRS, Vernaison, France and are within ± 0.4% of the calculated values.

3-Methyl-2(3*H*)-(benzoxazolinon-6-yl)acetothiomorpholide (1)

A mixture of 3-methyl-6-acetyl-2(3*H*)-benzoxazolinone (2.5 g, 0.013 mol), morpholine (1.70 mL, 0.019 mol), and sulfur (0.41 g, 0.013 mol) in DMF (10 mL), was heated under reflux for 18 h. The reaction mixture was then poured into ice water and acidified with an aqueous solution of 3M HCl. The precipitate was filtered, dried, and recrystallized from ethyl acetate to give **1** (1.60 g, 42 %). mp 108-110°C. IR ν CO 1780 cm^{-1}, ν CS 1270 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 3.25 (m, 4H); 3.35 (m, 4H); 3.38 (s, 3H); 4.20 (s, 2H); 7.16-7.22 (m, 2H); 7.30 (s, 1H). Anal. Calcd for $C_{14}H_{16}N_2O_3S$: C, 57.49; H, 5.51; N, 9.57. Found: C, 57.54; H, 5.46; N, 9.46.

Methyl 3-methyl-5-nitro-2(3*H*)-(benzoxazolinon-6-yl)acetate (2)

To a solution of 3-methyl-6-acetyl- 2(3*H*)-benzoxazolinone (1.91 g, 0.01 mol) in methanol (60 mL) were added 70 % perchloric acid (5.2 mL, 0.036 mol) and thallium (III) nitrate (5.57 g, 0.012 mol). The reaction mixture was stirred at rt for 18 h, poured into water and extracted with methylene chloride. The organic phase was washed with water, and then dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was recrystallized from 95 % ethanol (1.94 g, 70 %). mp 112°C. IR ν CO 1800, 1740 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 3.40 (s, 3H); 3.60 (s, 3H); 4.10 (s, 2H); 7.58 (s, 1H); 8.10 (s, 1H). Anal. Calcd for $C_{11}H_{10}N_2O_6$: C, 49.63; H, 3.78; N, 10.52. Found; C, 49.76; H, 3.75; N, 10.46 .

Methyl 3-methyl-6-nitro-2(3*H*)-(benzoxazolinon-5-yl)acetate (3)

Compound (**3**) was prepared by treatment of 3-methyl-5-acetyl-2(3*H*)-benzoxazolinone (1 g, 0.0052 mol) with perchloric acid (70 % aqueous) (2.60 mL, 0.018 mol) and thallium nitrate (2.78 g, 0.0062 mol) in methanol (20 mL) as described for compound (**2**). Recrystallization from 95 % ethanol gave **3** (1.33 g, 65 %). mp 115-117 °C. IR ν CO 1800, 1720 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 3.37 (s, 3H); 3.62 (s, 3H); 4.12

(s, 2H); 7.47 (s, 1H); 8.20 (s, 1H). Anal. Calcd for $C_{11}H_{10}N_2O_6$: C, 49.63; H, 3.78; N, 10.52. Found; C, 49.78; H, 3.67; N, 10.46.

3-Methyl-5,7-dihydro-3*H*-oxazolo[5,4-*f*]indole-2,6-dione (4)

To a solution of **2** (0.3 g, 0.0011 mol) in methanol (30 mL), were added 10 % Pd-C (35 mg) and ammonium formate (0.35 g, 0.0055 mol). The reaction mixture was refluxed for 16 h, filtered and evaporated *in vacuo*. The residue was taken with 1M HCl, and extracted with ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$ and evaporated. Recrystallization from 2-propanol gave **4** (0.08 g, 35 %). mp > 260 °C. IR ν CO 1768, 1685 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.29 (s, 2H); 3.34 (s, 3H); 6.68 (s, 1H); 7.51 (s, 1H); 10. 57 (s, 1H). Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.94; N, 13.72. Found; C, 58.97; H, 3.87; N, 13.68.

General Procedure for the Synthesis of x-Methyl-2(3*H*)-benzoxazolinone Derivatives (5a-c)

To a solution of the appropriate substituted methyl 2-aminophenol (12.3 g, 0.1 mol) in dimethylformamide (150 mL) was added urea (30 g, 0.5 mol). The reaction mixture was refluxed for 5 h. After cooling, the mixture was

quenched with ice water, acidified with concentrated HCl and the resulting precipitate was filtered, washed with water, dried and recrystallized from an appropriate solvent (Table I).

General Procedure for the Synthesis of 3-Methyl-x-methyl-2(3*H*)-benzoxazolinone Derivatives (6a-c)

The appropriate derivative (**5**) (29.8 g, 0.2 mol) was dissolved in 1M aqueous solution of sodium hydroxyde (250 mL). The solution was stirred at 0°C and dimethyl sulfate (21 mL, 0.22 mol) was added dropwise over 30 min. After stirring for 3 h, the solid was filtered, washed with water and recrystallized from an appropriate solvent (Table II).

General Procedure for the Synthesis of 3-Methyl-x-bromomethyl-2(3*H*)-benzoxazolinone Derivatives (7a-c)

To a solution of the appropriate derivative (**6**) (9.3 g, 0.056 mol) in carbon tetrachloride (300 mL) was added *N*-bromosuccinimide (10.32 g, 0.058 mol), and dibenzoyl peroxide (1.11 g, 0.0046 mol). The

mixture was heated at reflux for 4 h, and then immediately filtered. After evaporating the solvent *in vacuo*, trituration with ether afforded the crude product which was recrystallized from an appropriate solvent (Table III).

General Procedure for the Synthesis of 3-Methyl-x-cyanomethyl-2(3*H*)-benzoxazolinone Derivatives (8a-c)

A solution of potassium cyanide (2.34 g, 0.036 mol) in water (25 mL) was added to a solution of the appropriate bromomethyl derivative (**7**) (7.26 g, 0.03 mol) in ethanol (50 mL). The reaction mixture was stirred at 45 °C for 18 h. After cooling, the precipitate was filtered, dried, and recrystallized from an appropriate solvent (Table IV).

General Procedure for the Synthesis of [3-Methyl-2(3*H*)-benzoxazolinon-x-yl]acetic Acids (9a-c) (Method A)

A suspension of the appropriate nitrile (**8**) (1.88 g, 0.01 mol) in a 6M solution of aqueous HCl (50 mL) was refluxed for 5h. After cooling, water was added, and the resulting precipitate was filtered, dried, and recrystallized from an appropriate solvent (Table V).

3-Methyl-2(3*H*)-(benzoxazolinon-6-yl)acetic Acid (9c) (Method B)

Sulfuric acid (3 mL), and water (4.9 mL) were added to a solution of **1** (5.26 g, 0.018 mol) in acetic acid (20 mL). After refluxing for 6 h, the cooled reaction mixture was poured into water and extracted with ethyl acetate. The organic phase was washed with water, dried over $MgSO_4$ and evaporated *in vacuo*. The residue was recrystallized from an appropriate solvent (Table V).

General Procedure for the Synthesis of 3-Methyl-*N*-(4,6-dimethylpyridin-2-yl)-2(3*H*)-(benzoxazolinon-x-yl)methylcarboxamide Derivatives (10a-c)

A solution of the appropriate acid (**9**) (2 g, 0.0096 mol) in chloroform (30 mL) was cooled to 0°C. Under stirring, thionyl chloride (3.50 mL, 0.048 mol) was added dropwise and the reaction mixture was heated at reflux for 5 h. After evaporation, the oil was dissolved in methylene chloride (30 mL), and added dropwise to a cooled mixture of 2-amino-4, 6-dimethylpyridine (1.18 g, 0.0096 mol) and triethylamine (1.60 mL, 0.0115 mol) in methylene chloride (50 mL). The reaction mixture was then stirred at rt for 18 h. After

evaporation of methylene chloride under *vacuum*, the residue was treated with water, and the resulting precipitate filtered, washed with water, dried and recrystallized from an appropriate solvent (Table VI).

5-Methyl-6-bromo-2(3*H*)-benzoxazolinone (11)

Compound (**11**) was prepared by treatment of compound (**5b**) (5 g, 0.033 mol) in carbon tetrachloride (300 mL) with *N*-bromosuccinimide (7.11 g, 0.04 mol), and dibenzoyl peroxide (0.62 g, 0.0026 mol) as described for compounds (**7a-c**). Recrystallization from toluene gave **11** (0.15 g, 60 %). mp 143-145 °C. IR ν NH 3150 cm^{-1}, ν CO 1770 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.57 (s, 3H); 7.10 (s, 1H); 7.57 (s, 1H); 11.76 (br s, 1H, exchanged with D_2O). Anal. Calcd for $C_8H_6NO_3Br$: C, 42.11; H, 2.65; N, 6.14. Found: C, 42.17 , H, 2.46; N, 6.23.

3-Acetyl-5-methyl-2(3*H*)-benzoxazolinone (12)

A solution of 5-methyl-2(3*H*)-benzoxazolinone (3.72 g, 0.025 mol) in acetic anhydride (25 mL) was refluxed for 3 h. After cooling, the precipitate was filtered and recrystallized from cyclohexane to give 3.33 g (70 %) of **12**. mp 93-95 °C. IR ν CO 1790, 1720 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.36 (s, 3H); 2.60 (s, 3H); 7.10 (dd, J=8.20 and 0.85 Hz, 1H); 7.28 (d, J=8.20 Hz, 1H); 7.78 (s, 1H). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 6.14. Found; C, 62.96; H, 4.67; N, 6.23.

3-Acetyl-5-bromomethyl-2(3*H*)-benzoxazolinone (13)

Compound (**13**) was prepared by treatment of **12** (3.30 g, 0.017 mol) with *N*-bromosuccinimide (3.50 g, 0.02 mol) in the presence of dibenzoyl peroxide (0.35 g, 0.0013 mol) in carbon tetrachloride (200 mL) as described for compounds (**7a-c**). Recrystallization from 95 % ethanol gave **13** (2.70 g, 58 %). mp 212-214 °C. IR ν CO 1770, 1720 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.64 (s, 3H); 4.82 (s, 2H); 7.38-7.40 (m, 2H); 8.05 (s, 1H). Anal. Calcd for $C_{10}H_8BrNO_3$: C, 44.47; H, 2.98; N, 5.18. Found; C, 44.54; H, 2.86; N, 5.23.

3-Amino-4-hydroxyphenylacetic Acid (14; HCl)

A solution of 3-nitro-4-hydroxyphenylacetic (6.9 g, 0.034 mol) in methanol (100 mL) containing 10 % palladium on charcoal (1.36 g) was hydrogenated at 1 atm for 6 h. After filtration of the catalyst, the solution was acidified with concentrated HCl. The resulting solution was evaporated *in vacuo* and the residue recrystallized from 95% ethanol-ether (1-1) (3.8 g, 65%). mp 195-197°C. IR ν OH, NH_3^+ 3450-

2500 cm^{-1}, ν CO 1700 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 3.49 (s, 2H); 6.10 (dd, J=8.25 and 1.80 Hz, 1H); 6.98 (d, J= 8.25 Hz, 1H); 7.22 (s, 1H); 9.90 (br s, 3H, exchanged with D_2O); 10.68 (br s, 1H, exchanged with D_2O). Anal. Calcd for $C_8H_{10}NO_3Cl$: C, 47.00; H, 4.93; N, 6.85. Found; C, 47.12; H, 4.86; N, 6.75 .

2(3*H*)-Benzoxazolinon-5-yl-acetic Acid (15)

Compound (**15**) was prepared by treatment of compound (**14**) (1.38 g, 0.0083 mol) with urea (2.51 g, 0.041 mol) in DMF (20 mL) as described for compounds (**5a-c**). Recrystallization from 95% ethanol gave **17** (0.5 g, 31 %). mp 228-230 °C. IR ν NH 3300 cm^{-1}, ν OH 3000-2500 cm^{-1}, ν CO 1750, 1720 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 3.60 (s, 2H); 6.95 (dd, J=8.20 and 1.54 Hz, 1H); 7.00 (d, J=1.54 Hz, 1H); 7.20 (d, J=8.20 Hz, 1H); 11.60 (br s, 1H, exchanged with D_2O); 12.35 (br s, 1H, exchanged with D_2O). Anal. Calcd for $C_9H_7NO_4$: C, 55.97; H, 3.65; N, 7.25. Found; C, 56.12, H, 3.58 N, 7.14.

***N*-(4,6-Dimethylpyridin-2-yl)-(2(3*H*)-benzoxazolinon-5-yl)methylcarboxamide (16)**

Compound (**16**) was prepared by treatment of compound (**15**) (0.70 g, 0.0036 mol) with thionyl chloride (1.32 mL, 0.018 mol) and 2-amino-4,6-dimethylpyridine (0.44 g, 0.0036 mol) as described for compounds (**10a-c**). Recrystallization from 95% ethanol gave **16** (0.15 g, 15 %). mp 245-247 °C. IR ν NH 3250 cm^{-1}, ν CO 1765, 1670 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ 2.23 (s, 3H); 2.35 (s, 3H); 3.68 (s, 2H); 6.80 (s, 1H); 7.00-7.20 (m, 3H); 7.70 (s, 1H); 10.58 (br s, 1H, exchanged with D_2O); 11.60 (br s, 1H, exchanged with D_2O). Anal. Calcd for $C_{16}H_{15}N_3O_3$: C, 64.64; H, 5.08; N, 14.13. Found: C, 64.76 , H, 5.15; N, 14.24 .

Table I. Physical and spectral data of compounds (5)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6), δ	Molecular formula	Analysis (%) Calcd / Found C	H	N
5a	1790	70 Toluene	153-155	2.29 (s, 3H); 6.98 -7.00 (m, 3H).	$C_8H_7NO_2$	64.42 64.56	4.73 4.65	9.39 9.23
5b	1785	55 Toluene	123-125	2.31 (s, 3H); 6.86 (s, 1H); 6.87 (d, J=8.25 Hz, 1H); 7.14 (d, J=8.25 Hz, 1H); 11.54 (br s, 1H).	$C_8H_7NO_2$	64.42 64.45	4.73 4.61	9.39 9.45
5c	1785	55 Toluene	143-145	2.30 (s, 3H); 6.85 (dd, J=8.00 and 1.30 Hz, 1H); 6.90 (s, 1H); 7.12 (d, J=8.00 Hz, 1H); 11.54 (br s, 1H).	$C_8H_7NO_2$	64.42 64.52	4.73 4.62	9.39 9.34

Table II. Physical and spectral data of compounds (6)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6), δ	Molecular formula	Analysis (%) Calcd / Found C	H	N
6a	1755	85 Cyclohexane	70-72	2.28 (s, 3H); 3.56 (s, 3H); 6.05-7.24 (m, 3H).	$C_8H_9NO_2$	66.25 66.14	5.55 5.62	8.58 8.42
6b	1770	92 Toluene	83-85	2.35 (s, 3H); 3.36 (s, 3H); 6.90 (d, J=7.90 Hz, 1H); 7.06 (s, 1H); 7.18 (d, J=7.90 Hz, 1H).	$C_8H_9NO_2$	66.25 66.36	5.55 5.42	8.58 8.48
6c	1750	90 Cyclohexane	103-105	2.39 (s, 3H); 3.38 (s, 3H); 6.83 (d, J=7.74 Hz, 1H); 7.06 (d, J=7.74 Hz, 1H); 7.18 (s, 1H).	$C_8H_9NO_2$	66.25 66.17	5.55 5.38	8.58 8.45

Table III. Physical and spectral data of compounds (7)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6), δ	Molecular formula	Analysis (%) Calcd / Found C	H	N
7a	1760	85 Cyclohexane	59-60	3.69 (s, 3H); 5.00 (s, 2H); 7.10 (m, 1H); 7.27 (d, J=8.0 Hz, 1H); 7.33 (d, J=8.0 Hz, 1H).	$C_9H_8NO_2Br$	44.65 44.56	5.78 5.68	3.33 3.42
7b	1765	55 Cyclohexane	93-95	3.33 (s, 3H); 4.77 (s, 2H); 7.23 (d, J=8.20 Hz, 1H); 7.30-7.55 (m, 2H).	$C_9H_8NO_2Br$	44.65 44.57	5.78 5.68	3.33 3.23
7c	1750	63 Toluene	153-155	3.35 (s, 3H); 4.50 (s, 2H); 6.90 (d, J=8.40 Hz, 1H); 7.16 (s, 1H); 7.20 (d, J=8.40 Hz, 1H).	$C_9H_8NO_2Br$	44.65 44.56	5.78 5.62	3.33 3.19

Table IV. Physical and spectral data of compounds (8)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6), δ	Molecular formula	Analysis (%) Calcd / Found C	H	N
8a	1760	62 Toluene	177-180	3.57 (s, 3H); 4.45 (s, 2H); 7.15 (m, 1H); 7.20 (d, J=6.96 Hz, 1H); 7.33 (d, J=6.96 Hz, 1H).	$C_{10}H_8N_2O_2$	63.82 63.95	14.88 14.75	4.28 4.36
8b	1765	63 Isopropanol	125-127	3.34 (s, 3H); 4.07 (s, 2H); 7.10 (dd, J=8.40 and 1.17 Hz, 1H); 7.24 (d, J=1.17 Hz, 1H); 7.33 (d, J=8.40 Hz, 1H).	$C_{10}H_8N_2O_2$	63.82 63.74	14.88 14.68	4.28 4.32
8c	1750	33 Ethanol	168	3.33 (s, 3H); 4.05 (s, 2H), 7.22 (d, J=8.00 Hz, 1H); 7.27 (d, J=8.00 Hz, 1H); 7.35 (s, 1H).	$C_{10}H_8N_2O_2$	63.82 63.75	14.88 14.92	4.28 4.16

Table V. Physical and spectral data of compounds (9)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6) δ	Molecular formula	Analysis (%) Calcd / Found C H N
9a	1650 and 1750	28 Isopropanol-Cyclohexane (1-3)	155-157	3.50 (s, 3H); 3.93 (s, 2H); 7.07 (m, 1H); 7.10 (m, 1H); 7.33 (m, 1H); 12.74 (br s, 1H).	$C_{10}H_9NO_4$	58.0 6.76 4.38 58.12 6.65 4.42
9b	1625 and 1750	74 Water	168-170	3.33 (s, 3H); 3.60 (s, 2H); 7.00 (d, J=8.20 Hz, 1H); 7.15 (s, 1H); 7.24 (d, J=8.20 Hz, 1H); 7.33 (d, J=8.40 Hz, 1H); 10.40 (br s, 1H).	$C_{10}H_9NO_4$	58.0 6.76 4.38 58.15 6.72 4.46
9c	1640 and 1755	55 (Method A) 10 (Method B) Ethanol	210-212	3.32 (s, 3H); 3.60 (s, 2H); 7.10 (d, J=7.62 Hz, 1H); 7.17 (d, J=7.62 Hz, 1H); 7.24 (s, 1H); 12.37 (br s, 1H).	$C_{10}H_9NO_4$	58.0 6.76 4.38 58.14 6.63 4.29

Table VI. Physical and spectral data of compounds (10)

Compd	IR, ν CO (cm^{-1})	Yield (%) Solvent	mp (°C)	^1H NMR (DMSO-d_6), δ	Molecular formula	Analysis (%) Calcd / Found C	H	N
10a	1660 and 1760	50 Ethanol	235-237	2.22 (s, 3H); 2.35 (s, 3H); 3.35 (s, 3H); 4.05 (s, 2H), 6.80 (s, 1H); 7.08 (m, 1H); 7.14 (d, J=7.80 Hz, 1H), 7.26 (d, J=7.80 Hz, 1H); 7.70 (s, 1H); 10.75 (br s, 1H).	$C_{17}H_{17}N_3O_3$	65.59 65.30	5.50 5.73	13.49 13.49
10b	1685 and 1775	34 Ethanol	155	2.20 (s, 3H); 2.33 (s, 3H); 3.30 (s, 3H); 3.70 (s, 2H), 6.77 (s, 1H); 7.20-7.30 (m, 3H); 7.70 (s, 1H); 10.54 (br s, 1H).	$C_{17}H_{17}N_3O_3 \cdot 1\ H_2O$	61.99 62.12	5.81 5.86	12.76 12.65
10c	1685 and 1775	47 Ethanol	85	2.20 (s, 3H); 2.33 (s, 3H); 3.30 (s, 3H); 3.70 (s, 2H); 6.77 (s, 1H); 7.07 (d, J=8.20 Hz, 1H); 7.18 (s, 1H); 7.24 (d, J=8.20 Hz, 1H); 7.70 (s, 1H); 10.75 (br s, 1H).	$C_{17}H_{17}N_3O_3 \cdot 0.5\ H_2O$	63.73 63.85	5.66 5.56	13.11 13.21

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