Synthesis of 1-(2-Hydroxyphenyl)-2,4-imidazolidinedione Derivatives through Cyclic Transformations of Ethyl 2-Oxo-3(2*H*)-benzoxazoleacetate Derivatives

René Milcent*, Anna Akhnazarian and Nathalie Lensen

Laboratoire de Chimie Organique, Université Paris 7, 16, rue Henri-Huchard, 75018 Paris, France

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A series of ethyl 2-oxo-3(2*H*)-benzoxazoleacetate derivatives **2** have been synthesized. By reaction with ammonia, primary amines or hydrazine, these compounds **2** were transformed into 1-(2-hydroxyphenyl)-2,4-imidazolidinedione derivatives **4**, **5** and **6**, respectively. Some of these new hydantoins **4**, treated with phosphorus oxychloride, gave 3*H*-2-oxoimidazo[2,1-*b*]benzoxazole derivatives **9**. Ethyl 2-oxo-3(2*H*)-benzoxazolepropionate (**10**) was prepared by a Michaël reaction of ethyl acrylate with 2-benzoxazolone (**1a**). With **10**, no cyclic transformation was observed in the presence of ammonia or alkylamine.

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The known syntheses of 2,4-imidazolidinediones (hydantoins) [1-3] are not a convenient routes to 1-hydroxyphenyl-substituted derivatives. Only one synthesis of 1-(4-hydroxyphenyl)-2,4-imidazolidinedione by reaction of potassium isocyanate with an α-aminonitrile bearing a 4-hydroxyphenyl group has been reported [4].

Our purpose was the synthesis of unknown 1-(2-hydroxyphenyl)hydantoin derivatives. These interesting compounds have potential biological activities [1-4] and are synthons in the synthesis of 3*H*-2-oxoimidazo[2,1-*b*]-benzoxazole derivatives **10**, compounds known as bactericides, fungicides and virucides [5].

For the preparation of these hydantoin derivatives, a new cyclic transformation of ethyl 2-oxo-3(2*H*)-benzoxazoleacetate derivatives **2** has been studied. In the literature, some cyclic transformations of 3*H*-2-benzoxazolone derivatives into triazinones [6], *N*-(2-hydroxyphenyl)-2-oxazolidinones [7] or imidazolin-2-ones [8] have been reported. These cyclic transformations were in part the result of the easy "oxazolone" ring opening by various nucleophiles. For example, *N*-(2-hydroxyphenyl)-*N'*-alkylureas and 4-(2-hydroxyphenyl)semicarbazide were obtained by reaction of benzoxazolone with primary alkylamines [9] or hydrazine [10], respectively.

Esters **2** were prepared in good yields by alkylation in dimethylformamide of sodium salts of benzoxazolones **1**, with adequate α-halogenoesters (Table I). Treatment of esters **2** in ethanol with an aqueous ammonia solution at

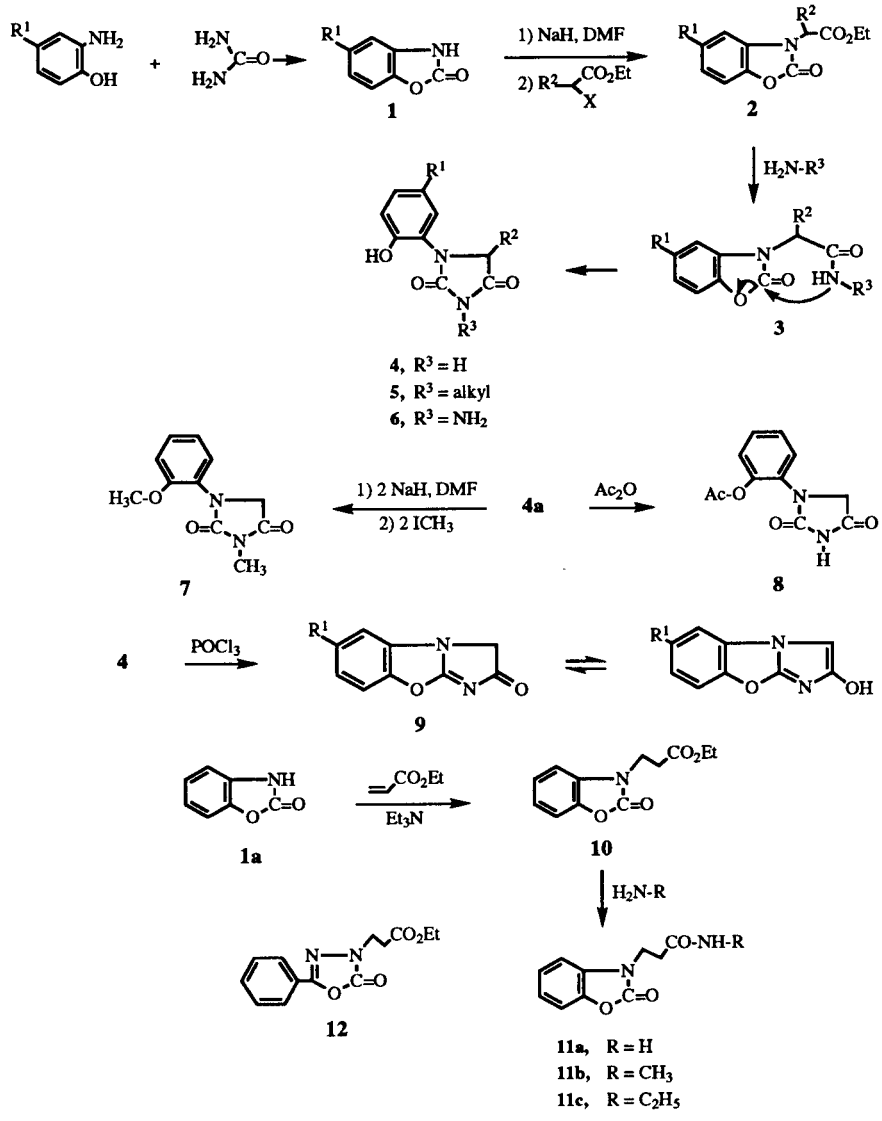
Table I

Ethyl 2-Oxo-3(2*H*)-benzoxazoleacetate Derivatives **2**

2	R^1	R^2	Yield % [a]	Mp °C	Formula (mol.wt.)	Analyses, % Calcd./Found C	H	N	IR ν cm^{-1}	^1H NMR [b] δ ppm
a	H	H	75	69 [c,d]					1770, 1730	1.2 (t, 3H), 4.2 (q, 2H), 4.75 (s, 2H), 7.05-7.5 (m, 4H)
b	H	Me	78	[e,f]					1770, 1730	1.15 (t, 3H), 1.65 (d, 3H), 4.2 (q, 2H), 5.25 (q, 1H), 7.1-7.5 (m, 4H)
c	H	Et	76	45 [g]	$C_{13}H_{15}NO_4$ (249.26)	62.64 / 62.74	6.07 / 6.04	5.62 / 5.57	1760, 1730	0.85 (t, 3H), 1.15 (t, 3H), 2.2 (quint, 2H), 4.2 (q, 2H), 5.05 (t, 1H), 7.1-7.6 (m, 4H)
d	Me	H	67	110 [c]	$C_{12}H_{13}NO_4$ (235.23)	61.27 / 61.12	5.57 / 5.55	5.95 / 5.99	1765, 1730	1.2 (t, 3H), 2.3 (s, 3H), 4.15 (q, 2H), 4.7 (s, 2H), 6.8-7.3 (m, 3H)
e	Me	Me	70	[e]	$C_{13}H_{15}NO_4$ (249.26)	62.64 / 62.40	6.07 / 6.04	5.62 / 5.68	1785, 1740	1.15 (t, 3H), 1.65 (d, 3H), 2.3 (s, 3H), 4.2 (q, 2H), 5.2 (q, 1H), 6.95-7.5 (m, 3H)
f	Me	Et	77	[e]	$C_{14}H_{17}NO_4$ (263.28)	63.86 / 63.97	6.51 / 6.50	5.32 / 5.35	1760, 1730	0.9 (t, 3H), 1.15 (t, 3H), 2.1-2.4 (m, 5H), 4.25 (q, 2H), 5.05 (t, 1H), 6.9-7.4 (m, 3H)
g	Cl	H	86	74 [c]	$C_{11}H_{10}ClNO_4$ (255.65)	51.68 / 51.88	3.94 / 3.95	5.48 / 5.43	1770, 1740	1.2 (t, 3H), 4.2 (q, 2H), 4.75 (s, 2H), 7.1-7.6 (m, 3H)
h	Cl	Me	57	56 [c]	$C_{12}H_{12}ClNO_4$ (269.68)	53.44 / 53.59	4.49 / 4.52	5.19 / 5.22	1770, 1730	1.15 (t, 3H), 1.65 (d, 3H), 4.2 (q, 2H), 5.3 (q, 1H), 7.2-7.7 (m, 3H)
i	Cl	Et	40	[e]	$C_{13}H_{14}ClNO_4$ (283.70)	55.03 / 54.88	4.97 / 4.94	4.94 / 4.98	1780, 1735	0.9 (t, 3H), 1.15 (t, 3H), 2.2 (quint, 2H), 4.15 (q, 2H), 5.1 (t, 1H), 7.1-7.6 (m, 3H)
j	NO_2	H	62	128 [c]	$C_{11}H_{10}N_2O_6$ (266.20)	49.63 / 49.85	3.79 / 3.77	10.52 / 10.50	1790, 1720	1.2 (t, 3H), 4.2 (q, 2H), 4.9 (s, 2H), 7.6-8.5 (m, 3H)

[a] Non optimized yields. [b] In DMSO-d_6. [c] Ethyl acetate-petroleum ether 40-60. [d] Lit [11] mp 67°. [e] This compound was obtained as an oil and was purified by column chromatography. [f] Lit [11] bp 165-170°/2 mm Hg. [g] Ethanol-water.

Scheme 1



room temperature gave hydantoins **4** (Table II). The reaction could proceed *via* a nucleophilic attack of ammonia at the ester function of **2** to form the nonisolated amide intermediate **3**. A subsequent intramolecular nucleophilic attack of the amido group at the cyclic benzoxazolone carbonyl group with a concomittant ring opening gave hydantoins **4** (Scheme 1).

Similarly, reaction of esters **2**, with alkyl primary amines in the place of ammonia afforded *N*-1, *N*-3-disubstituted hydantoins **5** (Table III). However, when R^1 was a methyl group, only the corresponding *N*-alkylamides **3a-c** were obtained. Replacement of alkyl amines by hydrazine hydrate in the reaction with esters **2a,d,g** gave 3-aminohydantoins **6a-c** (Table III). With other esters **2**, tars were obtained in the place of the corresponding compounds **6**.

In order to assure the structure of hydantoin **4a**, dimethylation of its disodium salt with methyl iodide was effected. It gave dimethylated hydantoin **7**.

With the aim to cyclize **4** into the corresponding 3*H*-2-oxoimidazo[2,1-*b*]benzoxazole derivatives **9**, intramolecular dehydration of hydantoin **4a** with acetic anhydride was tried but only the monoacetylhydantoin **8** was formed. However, on heating hydantoins **4a,d,g** in the presence of phosphorus oxychloride, the corresponding compounds **9** were obtained. The other hydantoins **4** gave tars. Syntheses of some heterocyclic compounds **9** have been reported by condensation of 2-aminooxazole with halocarbonyl compounds [5] or by treating *N*-Aryl-*S*,*S*-dimethylsulfilimines with diphenylketene [12].

The ethyl 2-oxo-3(2*H*)-benzoxazolepropionate (**10**) was synthesized in good yield by a Michael addition of ethyl

Table II

1-(2-Hydroxyphenyl)-2,4-imidazolidinedione Derivatives **4**

4	R^1	R^2	Time hours	Yield % [a]	Mp °C	Formula (mol.wt.)	Analyses, % Calcd./Found C	H	N	IR ν cm^{-1}	^1H NMR [b] δ ppm
a	H	H	1	87	249 [c]	$C_9H_8N_2O_3$ (192.17)	56.25 56.39	4.20 4.25	14.58 14.49	3360, 3140, 1750, 1680	4.4 (s, 2H), 7-7.5 (m, 4H arom. + 1H), 7.7 (s, 1H)
b	H	Me	12	45	209 [d,e]	$C_{10}H_{10}N_2O_3$ (206.19)	58.25 58.03	4.89 4.88	13.59 13.70	3440, 3170, 1770, 1675	1.15 (d, 3H), 4.5 (q, 1H), 6.7-7.4 (m, 4H), 9.9 (bs, 1H), 10.9 (bs, 1H)
c	H	Et	18	40	226 [d]	$C_{11}H_{12}N_2O_3$ (220.22)	59.99 59.91	5.49 5.46	12.72 12.78	3310, 3150, 1740, 1690	0.8 (t, 3H), 1.6 (m, 2H), 4.6 (t, 1H), 6.8-7-4 (m, 4H), 9.55 (bs, 1H), 11.2 (bs, 1H)
d	Me	H	8	80	206 [d]	$C_{10}H_{10}N_2O_3$ (206.19)	58.25 58.18	4.89 4.85	13.59 13.63	3420, 3300, 1760, 1670	2.35 (s, 3H), 4.45 (s, 2H), 6.9-7.5 (m, 3H arom. + 1H), 7.8 (bs, 1H)
e	Me	Me	12	55	242 [d,e]	$C_{11}H_{12}N_2O_3$ (220.22)	59.99 59.86	5.49 5.48	12.72 12.82	3350, 3220, 1755, 1700	1.2 (d, 3H), 2.25 (s, 3H), 4.5 (q, 1H), 6.85-7.15 (m, 3H), 9.55 (s, 1H), 11.1 (s, 1H)
f	Me	Et	24	30	202 [d,e]	$C_{12}H_{14}N_2O_3$ (234.25)	61.53 61.70	6.02 6.05	11.96 11.87	3315, 3180, 1750, 1700	0.8 (t, 3H), 1.6 (m, 2H), 2.3 (s, 3H), 4.65 (t, 1H), 6.85-7.15 (m, 3H), 9.6 (s, 1H), 11.3 (s, 1H)
g	Cl	H	12	58	238 [c]	$C_9H_7ClN_2O_3$ (226.61)	47.70 47.74	3.11 3.09	12.36 12.40	3310, 3200, 1770, 1670	4.5 (s, 2H), 7.2-7.5 (m, 3H arom. + 1H), 7.85 (s, 1H)
h	Cl	Me	12	23	240 [d,e]	$C_{10}H_9ClN_2O_3$ (240.64)	49.91 49.96	3.77 3.77	11.64 11.71	3220, 3140, 1760, 1680	1.15 (d, 3H), 4.55 (q, 1H), 6.85-7.4 (m, 3H), 10.05 (s, 1H), 11 (s, 1H)
i	Cl	Et	12	69	208 [f]	$C_{11}H_{11}ClN_2O_3$ (254.67)	51.88 51.91	4.35 4.38	11.00 11.00	3200, 3140, 1760, 1690	0.75 (t, 3H), 1.5 (m, 2H), 4.6 (t, 1H), 6.9-7.35 (m, 3H), 10 (s, 1H), 11 (s, 1H)
j	NO_2	H	12	78	239 [c]	$C_9H_7N_3O_5$ (237.17)	45.58 45.71	2.98 2.96	17.72 17.65	3400, 3200, 1770, 1670	4.55 (s, 2H), 7.45 (bs, 1H), 7.6 (d, 1H), 7.7 (bs, 1H), 8.15 (d, 2H)

[a] Non optimized yields. [b] In DMSO-d_6. [c] Ethanol-water. [d] Ethyl acetate. [e] Petroleum ether 40-60. [f] 1-Butanol.

Table III

1-(2-Hydroxyphenyl)-2,4-imidazolidinedione Derivatives **5** and **6**

No.	R^1	R^2	R^3	Time hours	Yield % [a]	Mp °C	Formula (mol.wt.)	Analyses, % Calcd./Found C	H	N	IR ν cm^{-1}	^1H NMR [b] δ ppm
5a	H	H	Me	12	52	168 [c]	$C_{10}H_{10}N_2O_3$ (206.19)	58.25 58.33	4.89 4.89	13.59 13.68	3190, 1760, 1670	2.95 (s, 3H), 4.3 (s, 2H), 6.7-7.4 (m, 4H), 9.85 (s, 1H)
5b	H	H	Et	12	41	98 [d]	$C_{11}H_{12}N_2O_3$ (220.20)	59.99 60.08	5.49 5.48	12.72 12.65	3170, 1760, 1680	1.15 (t, 3H), 3.5 (q, 2H), 4.35 (s, 2H), 6.75-7.4 (m, 4H), 9.85 (s, 1H)
5c	H	H	Pr	18	30	131 [d]	$C_{12}H_{14}N_2O_3$ (234.25)	61.53 61.39	6.02 6.03	11.96 11.99	3160, 1760, 1670	0.9 (t, 3H), 1.4-1.7 (m, 2H), 3.4 (t, 2H), 4.3 (s, 2H), 6.75-7.4 (m, 4H), 9.85 (s, 1H)
5d	H	H	Bu	24	13	111 [d]	$C_{13}H_{16}N_2O_3$ (248.27)	62.89 62.67	6.50 6.51	11.28 11.35	3160, 1760, 1670	0.9 (t, 3H), 1.1-1.7 (m, 4H), 3.45 (t, 2H), 4.3 (s, 2H), 6.8-7.4 (m, 4H), 9.8 (bs, 1H)
5e	H	Et	Me	24	35	110 [c]	$C_{12}H_{14}N_2O_3$ (234.25)	61.53 61.67	6.02 6.00	11.96 11.96	3200, 1740, 1665	0.75 (t, 3H), 1.4-1.8 (m, 2H), 2.95 (s, 3H), 4.6 (t, 1H), 6.8-7.4 (m, 4H), 9.9 (s, 1H)
5f	Cl	H	Me	24	42	210 [c]	$C_{10}H_9ClN_2O_3$ (240.64)	49.91 49.77	3.77 3.81	11.64 11.56	3150, 1765, 1665	2.95 (s, 3H), 4.3 (s, 2H), 6.9-7.5 (m, 3H), 10.1 (bs, 1H)
5g	Cl	H	Et	24	40	158 [c]	$C_{11}H_{11}ClN_2O_3$ (254.67)	51.88 51.60	4.35 4.36	11.00 11.09	3290, 1760, 1680	1.15 (t, 3H), 3.5 (q, 2H), 4.3 (s, 2H), 6.9-7.55 (m, 3H), 10.15 (s, 1H)
6a	H	H	NH_2	24	43	204 [e]	$C_9H_9N_3O_3$ (207.18)	52.17 52.49	4.38 4.28	20.28 20.43	3330, 3260, 1755, 1680	4.25 (s, 2H), 4.85 (bs, 2H), 6.7-7.4 (m, 4H), 9.85 (s, 1H)
6b	Me	H	NH_2	24	51	245 [e]	$C_{10}H_{11}N_3O_3$ (221.21)	54.29 54.08	5.01 4.99	19.00 19.13	3310, 3210, 1760, 1695	2.2 (s, 3H), 4.25 (s, 2H), 4.85 (bs, 2H), 6.6-7.25 (m, 3H), 9.6 (s, 1H)
6c	Cl	H	NH_2	8	71	265 [e]	$C_9H_8ClN_3O_3$ (241.63)	44.73 44.66	3.34 3.35	17.39 17.29	3315, 3200, 1760, 1695	4.25 (s, 2H), 4.7 (bs, 2H), 6.8-7.5 (m, 3H), 10.35 (s, 1H)

[a] Non optimized yields. [b] In DMSO-d_6. [c] 1-Butanol. [d] Diethyl ether-petroleum ether 40-60. [e] Water.

acrylate, used as the solvent, with benzoxazolone **1a** (R^1 = H) in the presence of triethylamine. Compound **10**, the homologue of **2a** did not give a cyclic transformation with ammonia or alkylamines but reacted only as an ester with formation of the corresponding amides **11a-c.** The same conduct was observed with ethyl 2-oxo-5-phenyl-1,3,4-oxadiazole-3(2*H*)-propionate (**12**) which was prepared from 5-phenyl-1,3,4-oxadiazol-2(3*H*)-one by the same reaction as **10** [13], whereas its acetate homologue gave several cyclic transformations [14].

Physicochemical data of new compounds **2,4-6** are listed in Tables I-III. Assignment for the structures of new products was provided by elemental analysis, ir and ^{1}H nmr spectra.

EXPERIMENTAL

Melting points were determined on a Büchi 510 oil heated apparatus and are uncorrected. Column chromatography was performed on Macherey-Nagel silica gel 60 (0.05-0.2 mm). The ir spectra were recorded on a Perkin Elmer 1310 spectrometer as potassium bromide disks. The ^{1}H nmr spectra were obtained in DMSO-d_6 or deuteriochloroform on a Bruker WP 80 spectrometer and are reported as δ values (ppm) relative to tetramethylsilane as an internal standard.

Ethyl 2-Oxo-3(2*H*)-benzoxazoleacetate Derivatives **2a-j**.

To a stirred solution of the corresponding benzoxazolone **1** (0.01 mole) in dry dimethylformamide (40 ml) was added sodium hydride (0.24 g, 0.01 mole) at 0°. When hydrogen gas evolution has ceased, the mixture was heated at 60° for 30 minutes. After cooling at 0°, the corresponding commercial α-halogenoester (0.01 mole) was added dropwise. After heating at 60° for 1 hour, the mixture was cooled and poured into ice-water (100 ml). The mixture was left at 0° for 1 hour. When **2** was a solid, it was filtered, washed with water (20 ml), dried and recrystallized from adequate solvent. If **2** was greasy or an oil, it was extracted with diethyl ether and purified by column chromatography using ethyl acetate-petroleum ether (1:1) as the eluent (Table I).

1-(2-Hydroxyphenyl)-2,4-imidazolidinedione Derivatives **4a-j**.

To a solution of benzoxazolinone **2a-j** (0.01 mole) in ethanol (20 ml) was added a 28% aqueous ammonia solution (20 ml). The mixture was stirred at room temperature for one to 24 hours (Table II). After removal of the solvent *in vacuo*, the resulting crop was treated with ice-water (10 ml). The insoluble compound **4** was filtered, washed with water (5 ml), dried and recrystallized from a suitable solvent (Table II).

N-1, *N*-3-Disubstituted 2,4-Imidazolidinediones Derivatives **5a-g** and *N*-Alkyl-5-methyl-2-oxo-3(2*H*)-benzoxazoleacetamide **3a-c**.

To a solution of ester **2** (0.01 mole) in ethanol (20 ml) was added a 40% methylamine or 70% ethylamine aqueous solution (10 ml), or propylamine (3.55 g, 0.06 mole) or butylamine (4.39 g, 0.06 mole). The mixture was stirred at room temperature for 12 to 24 hours (Table III). After removal of the excess of amine and solvent *in vacuo*, the resulting greasy mixture was treated with ice-water (25 ml) and diethyl ether (5 ml). After standing at 0°, a precipitate of **5** appeared. It was filtered, dried and recrystallized from a suitable solvent (Table III).

With ester **2d**, only *N*-alkylamides **3** were obtained by the same procedure.

N-Methyl-5-methyl-2-oxo-3(2*H*)-benzoxazoleacetamide (**3a**).

This compound was recrystallized from 1-butanol giving 1.3 g (59%), mp 240°; ir: 3280, 1760, 1635 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.35 (s, 3H), 2.65 (d, 3H), 4.45 (s, 2H), 6.9-7.4 (m, 3H), 8.25 (m, 1H).

Anal. Calcd. for $C_{11}H_{12}N_2O_3$ (220.22): C, 59.99; H, 5.49; N, 12.72. Found: C, 59.86; H, 5.55; N, 12.79.

N-Ethyl-5-methyl-2-oxo-3(2*H*)-benzoxazoleacetamide (**3b**).

This compound was recrystallized from 1-butanol giving 1.2 g (51%), mp 198°; ir: 3295, 1770, 1645 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.05 (t, 3H), 2.3 (s, 3H), 3.15 (quint, 2H), 4.4 (s, 2H), 6.9-7.35 (m, 3H), 8.3 (m, 1H).

Anal. Calcd. for $C_{12}H_{14}N_2O_3$ (234.25): C, 61.53; H, 6.02; N, 11.96. Found: C, 61.74; H, 6.03; N, 11.90.

N-Propyl-5-methyl-2-oxo-3(2*H*)-benzoxazoleacetamide (**3c**).

This compound was recrystallized from 1-butanol giving 1 g (40%), mp 160°; ir: 3350, 1740, 1670 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 0.85 (t, 3H), 1.3-1.7 (m, 2H), 2.3 (s, 3H), 3.1 (q, 2H), 4.4 (s, 2H), 6.8-7.3 (m, 3H), 8.25 (m, 1H).

Anal. Calcd. for $C_{13}H_{16}N_2O_3$ (248.27): C, 62.89; H, 6.50; N, 11.28. Found: C, 62.72; H, 6.48; N, 11.39.

3-Amino-1-(2-hydroxyaryl)-2,4-imidazolidinediones **6**.

To esters **2a,d,g** (5 mmoles) in propanol (15 ml) was added hydrazine hydrate (0.3 g, 6 mmoles). The mixture was heated at reflux for 48, 24 or 8 hours for **6a**, **6b** or **6c**, respectively. After removal of the solvent *in vacuo*, the resulting crop was treated with ice-water (10 ml). The insoluble compound **6** was filtered and recrystallized from water (Table III).

1-(2-Methoxyphenyl)-3-methyl-2,4-imidazolidinedione (**7**).

To a stirred solution of **4a** (1.92 g, 0.01 mole) in dry dimethylformamide (40 ml) at 0°, was added sodium hydride (0.48 g, 0.02 mole). When hydrogen gas evolution has ceased, the mixture was heated at 60° for 10 minutes. After cooling at 0°, methyl iodide (2.9 g, 0.02 mole) was added dropwise. After heating at 60° for 2 hours, the mixture was cooled and poured into ice-water (100 ml) and **7** was extracted with diethyl ether. The organic solution was washed with water, dried over magnesium sulfate, filtered and evaporated. Compound **7** was purified by column chromatography using ethyl acetate-cyclohexane (3:1) as the eluent, then recrystallized from ethanol to give 1.32 g (60%), mp 122°; ir: 1760, 1685 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.95 (s, 3H), 3.8 (s, 3H), 4.3 (s, 2H), 6.9-7.5 (m, 4H).

Anal. Calcd. for $C_{11}H_{12}N_2O_3$ (220.22): C, 59.99; H, 5.49; N, 12.72. Found: C, 59.83; H, 5.52; N, 12.82.

1-(2-Acetyloxyphenyl)-2,4-imidazolidinedione (**8**).

Hydantoin **4a** (1.92 g, 0.01 mole) and a catalytic amount of sulfuric acid were added to acetic anhydride (10 ml). The mixture was stirred at 60° for 30 minutes. After removal of 66% of excess of acetic anhydride *in vacuo*, the mixture was cooled and poured into ice-water (50 ml). Compound **8** precipitated. It was washed twice with water, filtered and recrystallized from

ethanol to give 1.4 g (60%), mp 196°; ir: 3295, 1760, 1725, 1690 cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.1 (s, 3H), 4.85 (s, 2H), 7-7.4 (m, 4H), 11.15 (s, 1H).

Anal. Calcd. for $C_{11}H_{10}N_2O_4$ (234.20): C, 56.41; H, 4.30; N, 11.96. Found: C, 56.51; H, 4.32; N, 11.84.

3*H*-2-Oxoimidazo[2,1-*b*]benzoxazole Derivatives **9a,d,g**.

To a stirred solution of **4a,d,g** (0.01 mole) in dry toluene (40 ml) at 0° was added freshly redistillated phosphorus oxychloride (10 ml). The mixture was heated at reflux for 60, 30 or 15 minutes for **9a**, **9d** or **9g**, respectively. After that time, some tar appeared. Solvent and excess of phosphorus oxychloride were evaporated *in vacuo*. The residue was treated with ice-water (20 ml) and the insoluble compound **9** was filtered, dried and recrystallized from a suitable solvent.

3*H*-2-Oxoimidazo[2,1-*b*]benzoxazole (**9a**).

This compound was recrystallized from ethanol-water giving 1.2 g (69%), mp 178°; ir: 1760, 1600 cm^{-1}; ^1H nmr (DMSO-d_6): δ 5.15 (s, 2H), 7.15-7.45 (m, 4H).

Anal. Calcd. for $C_9H_6N_2O_2$ (174.15): C, 62.07; H, 3.47; N, 16.09. Found: C, 62.21; H, 3.52; N, 15.90.

6-Methyl-3*H*-2-Oxoimidazo[2,1-*b*]benzoxazole (**9d**).

This compound was recrystallized from 1-propanol giving 1.2 g (64%), mp 134°; ir: 1760, 1610 cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.35 (s, 3H), 5.15 (s, 2H), 6.9-7.35 (m, 3H).

Anal. Calcd. for $C_{10}H_8N_2O_2$ (188.18): C, 63.82; H, 4.29; N, 14.89. Found: C, 63.64; H, 4.26; N, 14.97.

6-Chloro-3*H*-2-Oxoimidazo[2,1-*b*]benzoxazole (**9g**).

This compound was recrystallized from ethanol giving 1.15 g (55%), mp 164°; ir: 1760, 1600 cm^{-1}; ^1H nmr (DMSO-d_6): δ 5.15 (s, 2H), 7.2-7.8 (m, 3H).

Anal. Calcd. for $C_9H_5ClN_2O_2$ (208.60): C, 51.82; H, 2.42; N, 13.43. Found: C, 52.19; H, 2.46; N, 13.53.

Ethyl 2-Oxo-3(2*H*)-benzoxazolepropionate (**10**).

A stirred mixture of benzoxazolone **1a** (6.75 g, 0.05 mole), ethyl acrylate (20 ml) and triethylamine (0.2 ml) was heated at reflux for one hour. After cooling at 0°, petroleum ether (150 ml) was added. The mixture was left at -20° for 2 hours. Compound **10** crystallized. It was filtered and recrystallized from diethyl ether-petroleum ether 40-60 to give 10 g (85%) of pure product, mp 36°; ir: 1770, 1710 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.2 (t, 3H), 2.8 (t, 2H), 3.9-4.3 (m, 4H), 7.15 (bs, 4H).

Anal. Calcd. for $C_{12}H_{13}NO_4$ (235.23): C, 61.27; H, 5.57; N, 5.95. Found: C, 61.51; H, 5.54; N, 5.87.

Reaction of Ammonia or Alkylamines with Ester **10**.

A mixture of ester **10** (2.35 g, 0.01 mole) and of a 28% ammonia, 40% methylamine or 70% ethylamine aqueous solution (20 ml) for **11a**, **11b** or **11c**, respectively, was stirred at room temperature for 2 hours. After removal under reduced pressure of the excess of ammonia (or amine) and water, the resulting crop was treated with ice-water (5 ml). The mixture was left at 4° for one day. The insoluble compound **11** was filtered, washed with water (1 ml) and recrystallized from a suitable solvent.

2-Oxo-3(2*H*)-benzoxazolepropionamide (**11a**).

This compound was recrystallized from propanol giving 0.8 g (39%), mp 169°; ir: 3400, 3200, 1740, 1655 cm^{-1}; ^1H nmr (DMSO-d_6): δ 2.4 (t, 2H), 3.85 (bs, 2H), 4 (t, 2H), 7-7.5 (m, 4H).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$ (206.19): C, 58.25; H, 4.89; N, 13.59. Found: C, 58.42; H, 4.83; N, 13.80.

N-Methyl-2-oxo-3(2*H*)-benzoxazolepropionamide (**11b**).

This compound was recrystallized from water giving 0.55 g (25%), mp 160°; ir: 3300, 3100, 1760, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.6-2.9 (m, 5H), 4.25 (t, 2H), 6.1 (bs, 1H), 7.1-7.4 (m, 4H).

Anal. Calcd. for $C_{11}H_{12}N_2O_3$ (220.22): C, 59.99; H, 5.49; N, 12.72. Found: C, 59.86; H, 5.55; N, 12.79.

N-Ethyl-2-oxo-3(2*H*)-benzoxazolepropionamide (**11c**).

This compound was recrystallized from ethanol-water giving 0.7 g (30%), mp 142°; ir: 3300, 3080, 1755, 1620 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.05 (t, 3H), 2.75 (t, 2H), 3.25 (quint, 2H), 4.25 (t, 2H), 6.4 (bs, 1H), 7-7.4 (m, 4H).

Anal. Calcd. for $C_{12}H_{14}N_2O_3$ (234.25): C, 61.53; H, 6.02; N, 11.96. Found: C, 61.40; H, 6.08; N, 12.08.

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