A New and Facile Synthesis of Imidazo[2,1-*b*]oxazoles

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An efficient and clean two step procedure for the synthesis of imidazo[2,1-*b*]oxazoles has been developed from 2-aminooxazoles using titanium(IV) chloride assisted cyclization, and a variety of imidazo[2,1-*b*]oxazoles have been synthesized in good yields. The structure of one of the products was confirmed by X-ray crystallographic analysis.

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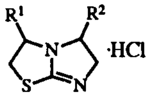
Due to considerable pharmacological interest the synthesis of heterocycles which contains a bicyclic fused [5,5] ring system with a bridgehead nitrogen atom, from the reactions of α-amino nitrogen heterocycles with bifunctional compounds, have been explored with significant success [1]. For instance, 2,3,5,6-tetrahydro-6-phenylimdazo[2,1-*b*]thiazole hydrochloride (**1a**) (tetramisole hydrochloride) is a broad spectrum anthelmintic agent, highly active at low doses against gastrointestinal and pulmonary nematodes in a variety of animals and also in humans [2,3]. The 3-(5-nitro-2-furyl) derivative **1b** (furazolium chloride) is available commercially under the trade name Novafur as a bactericide [4].



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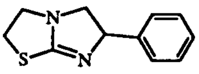
a $R^1 = H$, $R^2 = Ph$
b $R^1 = 5\text{-}NO_2\text{-}2\text{-furyl}$, $R^2 = H$

Levamisole (**2**), originally developed as an anthelmintic, was noted to exhibit a moderate antiinflammatory activity and to affect the immunomodulatory system [5,6]. Analgesic, antipyretic and antiimflammatory [7] activity is claimed for 2-aryl-1*H*-imidazo[1,2-*a*]imdazole derivatives **3**.



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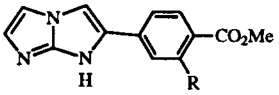

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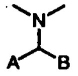
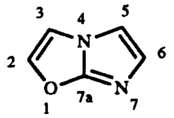
In general, many heterocyclic compounds which exhibit significant immunomodulatory or antiimflammatory activities [8-14] are discerned to have a common structural moiety, **4**, and this warrants additional detailed pharmacological investigation of compounds with this structural feature. The biological activities exhibited by these compounds stimulated our interest in synthesizing the hitherto little investigated imidazo[2,1-*b*]oxazoles.



4

A and B = CH, N, O, S.

Although there are some derivatives of the corresponding saturated systems such as 2,3-dihydro **6** and 2,3,5,6-tetrahydro **7**, only a few publications have appeared concerning the synthesis of the fully unsaturated imidazo[2,1-*b*]oxazole (**5**) system, notwithstanding an enormous amount of work accomplished in analogous fused heterocycles. For example, the synthesis and the associated chemical and biological properties of the analogous imdazo[2,1-*b*]thiazole (**8**) system have been studied quite exhaustively, owing to the commercial success of levamisole (**2**), depicted above.



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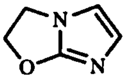
Imidazo[2,1-*b*]oxazole



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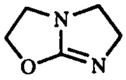

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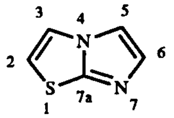

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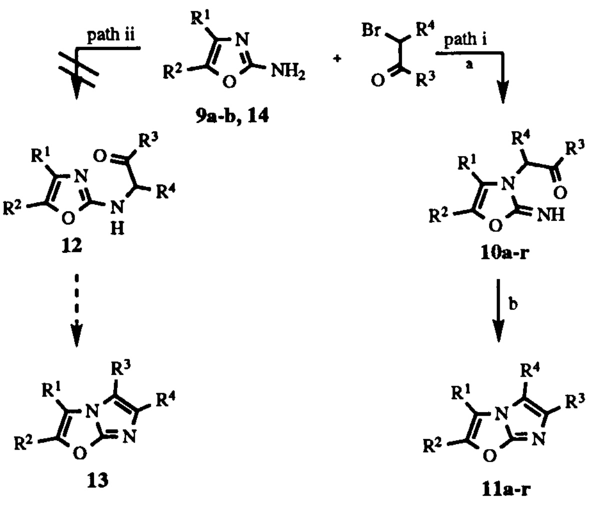
Imidazo[2,1-*b*]thiazole

There is an isolated patented procedure [15] for the synthesis of a 5,6-diarylimidazo[2,1-*b*]oxazole, which was prepared by treating α-bromodesoxyanisoin with 2-aminooxazole. This compound has been found useful in the treatment of non-bacterial inflammations, for instance allergic inflammations [15]. To our knowledge, this is the only reported imidazo[2,1-*b*]oxazole synthesis in the literature to date. In one other communication 2-amino-4,5-dimethyloxazole has been reported to have failed to condense with α-bromoketones under a variety of experimental conditions to give the desired imidazo[2,1-*b*]oxazoles [16]. Likewise, in a similar approach using 2-aminooxazoles we investigated a number of conditions, including the method used successfully by Meakins and coworkers [18] to prepare the analogous imidazo[2,1-*b*]thiazoles, without success. In addition to their interesting biological properties, their potential for further elaborative chemistry using the π-excessive electron properties makes them an attractive target. In this paper, we wish to report an efficient and facile synthetic procedure of general scope for the imidazo[2,1-*b*]oxazoles ring system based on 2-aminooxazoles.

Results and Discussion.

The condensation of 2-aminooxazoles **9** and **14** with 2-haloketones can proceed in at least two possible ways, Scheme 1, whereby one of the two isomeric imidazo[2,1-*b*]-oxazoles **11** or **13** can be obtained as the final product.

Scheme 1



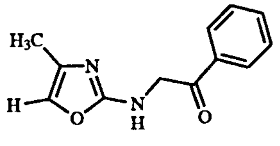
a) i) CH_3CN/THF, 24 hours, RT ii) $NH_4OH/5°$
b) $TiCl_4$/toluene, -10 to 120°/1-2 hours

Products resulting from *path i*, where the displacement of the halogen atom is by the endocyclic nitrogen, are represented by structure **11**, whereas product **13** would be formed if the nucleophilic attack on the carbon bearing the halogen atom, came from the exocyclic nitrogen, *path ii*.

The 2-aminooxazoles **9** and **14** were alkylated by the appropriate substituted or unsubstituted phenacyl bromide in a mixture of acetonitrile/tetrahydrofuran. In this reaction, phenacyl chloride is found to be much less effective than phenacyl bromide. The precipitated hydrobromide salt was worked up to give the intermediate compounds **10a-r** generally in good yields, Scheme 1. Unlike Meakins and coworkers [18], upon basification, we readily isolated these intermediates without a spontaneous cyclization which was observed in the analogous imidazo[2,1-*b*]thiazole synthesis.

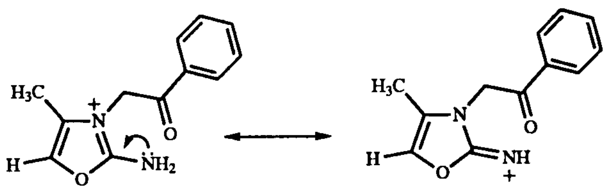
One of these intermediates, **10a** ($R^1 = CH_3$, $R^2 = H$, $R^3 = Ph$), which is assumed to have been formed *via* the accepted pathway, by the endocyclic nitrogen displacement of the bromine (*path i*), was characterized by standard spectroscopic methods. The ir spectrum shows a strong intense absorption band at 1690 cm^{-1} due to the carbonyl group and also a moderate absorption at 3350 cm^{-1} which can be attributed to the NH stretching. The ^1H nmr displays one proton at 4.27 ppm which was exchanged with deuterium oxide and assigned to the NH group, and a singlet corresponding to two protons at 5.03 ppm which is due to the methylene protons of the NCH_2CO group. The ^{13}C nmr spectrum is unambiguously assigned with complimentary information from a standard 2D-nmr experiment.

However, it was not possible to completely rule out the alternative plausible structure **12a** for this reaction intermediates, based only on this standard spectral data. Therefore, it was necessary to further scrutinize the nature of this intermediate using other techniques. A typical comparative uv analysis of **9a** and **10a** in acetonitrile has shown only a subtle difference which could be attributed solely for the disruption of conjugation in **9a**. Further investigations using ^{15}N nmr spectroscopy provided clear evidence [17] supporting the commonly assumed structure **10a**, the product of alkylation on the endocyclic nitrogen.



12a

This was also proved by determining the X-ray structure of one of the final products **11n**. This was not unexpected, since the intermediate **10a** formed by reaction of the endocyclic nitrogen is expected to have a lower energy path in its transition state stabilized by resonance as illustrated below.

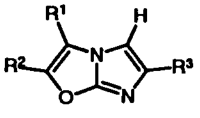


Resonance forms of Structure **10a**

Among a wide range of conditions we investigated, the cyclizations of the imino compounds, **10a-r**, which were effected efficiently only with titanium(IV) chloride in dry toluene. In addition to probing the scope of the procedure, we were also interested in making a range of compounds for biological screening. This protocol was then used to prepare all compounds listed in Table 1, almost all in good yield. At times, the main variations being the length of the time allowed for the reaction to go to completion, according to the nature of the individual substrates.

Table 1

Imidazo[2,1-*b*]oxazoles Prepared

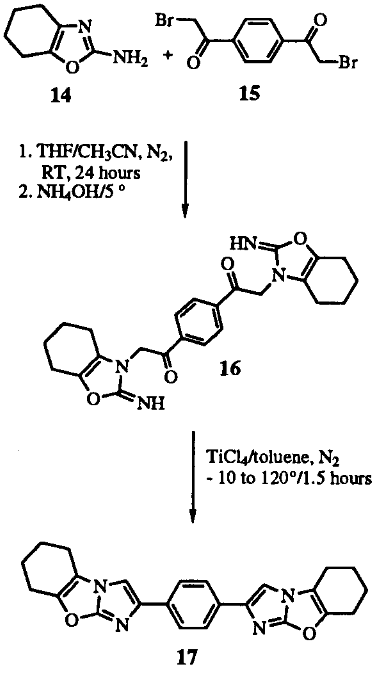


11a-r

Compound No. **11**	R^1	R^2	R^3	Yield %
a	CH_3	H	Ph	65
b	CH_3	H	4-BrPh	76
c	CH_3	H	4-PhPh	75
d	CH_3	H	4-ClPh	65
e	CH_3	H	4-CH_3OPh	70
f	CH_3	H	β-Naphthyl	57
g	CH_3	CH_3	Ph	82
h	CH_3	CH_3	4-BrPh	80
i	CH_3	CH_3	4-PhPh	74
j	CH_3	CH_3	4-ClPh	81
k	CH_3	CH_3	4-CH_3OPh	65
l	CH_3	CH_3	β-Naphthyl	74
m	-$(CH_2)_4$-		Ph	70
n	-$(CH_2)_4$-		4-BrPh	85
o	-$(CH_2)_4$-		4-PhPh	76
p	-$(CH_2)_4$-		4-ClPh	80
q	-$(CH_2)_4$-		4-CH_3OPh	75
r	-$(CH_2)_4$-		β-Naphthyl	85

The range of compounds synthesized by this method can be extended to examples like compound **17**, which was prepared in a similar manner using bis(bromoacetyl)benzene (**15**) as the bromoketone component, Scheme 2, in overall modest yield.

Scheme 2



X-Ray Crystal Structure.

In order to ascertain the exact structure of this class of imdazo[2,1-*b*]oxazoles one of the compounds was subjected to X-ray crystallographic analysis. Single crystals of compound **11n** suitable for X-ray crystallographic analysis were obtained by recrystallization from aqueous ethanol at room temperature. The atomic numbering scheme and molecular structure are depicted in Figure 1. Bond distances and angles are listed in Table 2 and Table 3. The final atomic coordinates and equivalent isotropic thermal parameters for the non-hydrogen atoms are given in Table 4.

The fused imidazo[2,1-*b*]oxazole moiety is planar and bond angles and lengths are in the normal ranges for heteroaromatic compounds.

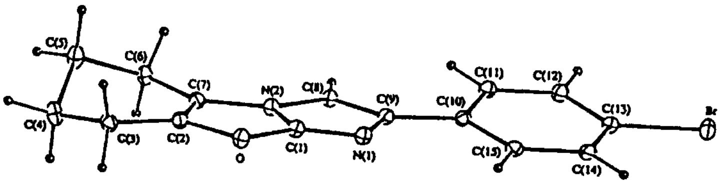


Figure 1. X-ray crystallographic structure of compound **11n**.

Table 2

Bond Lengths (Å) for **11n**. Esd in parentheses

C(9)-N(1)	1.399(3)	C(7)-N(2)	1.400(3)
N(1)-C(1)	1.302(3)	N(2)-C(8)	1.390(3)
C(1)-N(2)	1.339(3)	C(8)-C(9)	1.375(3)
C(1)-O	1.368(3)	C(9)-C(10)	1.465(3)
O-C(2)	1.404(3)	C(10)-C(11)	1.400(3)
C(2)-C(3)	1.464(3)	C(11)-C(12)	1.380(3)
C(2)-C(7)	1.341(4)	C(12)-C(13)	1.392(3)
C(3)-C(4)	1.538(4)	C(13)-C(14)	1.379(4)
C(4)-C(5)	1.530(5)	C(14)-C(15)	1.386(4)
C(5)-C(6)	1.532(4)	C(15)-C(10)	1.391(3)
C(6)-C(7)	1.484(3)	C(13)-Br	1.899(2)

Table 3

Bond Angles (°) for **11n**. Esd in parentheses

C(1)-O-C(2)	104.2(2)	C(6)-C(7)-N(2)	129.5(2)
C(9)-N(1)-C(1)	101.4(2)	C(6)-C(7)-C(2)	125.0(2)
C(7)-N(2)-C(1)	108.7(2)	N(2)-C(8)-C(9)	104.5(2)
C(1)-N(2)-C(8)	105.4(2)	C(8)-C(9)-N(1)	112.1(2)
C(7)-N(2)-C(8)	145.8(2)	N(1)-C(9)-C(10)	120.5(2)
N(1)-C(1)-O	132.9(2)	C(8)-C(9)-C(10)	127.4(2)
O-C(1)-N(2)	110.3(2)	C(9)-C(10)-C(11)	120.5(2)
N(1)-C(1)-N(2)	116.7(2)	C(15)-C(10)-C(9)	121.0(2)
O-C(2)-C(3)	121.3(2)	C(15)-C(10)-C(11)	118.5(2)
O-C(2)-C(7)	111.2(2)	C(10)-C(11)-C(12)	121.1(2)
C(3)-C(2)-C(7)	127.5(2)	C(11)-C(12)-C(13)	119.0(2)
C(2)-C(3)-C(4)	107.5(2)	C(12)-C(13)-Br	119.1(2)
C(3)-C(4)-C(5)	112.8(2)	Br-C(13)-C(14)	119.8(2)
C(4)-C(5)-C(6)	112.4(3)	C(12)-C(13)-C(14)	121.1(2)
C(5)-C(6)-C(7)	107.6(2)	C(13)-C(14)-C(15)	119.3(2)
C(2)-C(7)-N(2)	105.5(2)	C(14)-C(15)-C(10)	121.0(2)

In conclusion, we have developed a new and efficient procedure for the synthesis of imidazo[2,1-*b*]oxazoles based on 4-substituted and 4,5-disubstituted 2-aminooxazoles. The structure of the precursor intermediate was unequivocally established by X-ray analysis of the product, and hence establishing the site of alkylations at the endo-nitrogen in 2-aminooxazoles.

Table 4

Non-hydrogen Atomic Parameters for **11n**. B_{eq}(Å^2) is the Isotropic Equivalent of the Anisotropic Temperature Factor

	x	y	z	B_{eq}
Br	-0.1585(1)	-0.1881(1)	0.9463(1)	5.40(1)
O	0.6150(2)	0.3127(3)	0.4458(1)	3.74(5)
N(1)	0.4368(3)	0.1666(3)	0.5835(2)	3.38(6)
N(2)	0.2996(3)	0.3278(3)	0.4231(2)	3.06(6)
C(1)	0.4582(4)	0.2626(4)	0.4911(2)	3.29(7)
C(2)	0.5413(4)	0.4127(3)	0.3438(2)	3.37(7)
C(3)	0.6671(4)	0.4890(4)	0.2685(2)	3.83(8)
C(4)	0.5296(5)	0.6229(5)	0.1728(3)	5.07(10)
C(5)	0.3771(5)	0.5386(5)	0.1439(2)	4.84(10)
C(6)	0.2314(4)	0.5126(4)	0.2281(2)	3.60(7)
C(7)	0.3515(4)	0.4221(3)	0.3281(2)	3.04(6)
C(8)	0.1514(3)	0.2681(3)	0.4767(2)	3.10(6)
C(9)	0.2392(4)	0.1702(3)	0.5741(2)	3.05(6)
C(10)	0.1473(3)	0.0803(3)	0.6628(2)	2.88(6)
C(11)	-0.0390(4)	0.0593(4)	0.6505(2)	3.36(7)
C(12)	-0.1303(4)	-0.0195(4)	0.7339(2)	3.47(7)
C(13)	-0.0329(4)	-0.0808(3)	0.8314(2)	3.38(7)
C(14)	0.1516(4)	-0.0633(4)	0.8456(2)	3.63(7)
C(15)	0.2415(4)	0.0158(3)	0.7611(2)	3.29(7)

EXPERIMENTAL

Melting points were recorded on a Leitz hot stage microscope and are uncorrected. Elemental analysis were carried out by the Microanalytical Laboratory, University of New South Wales. Infrared spectra were obtained from a Perkin Elmer 298 Infrared Spectrophotometer and mass spectra from an AEI MS 12 mass spectrometer at 70 eV. The ^{1}H and ^{13}C nmr spectra were recorded on a Bruker CXP 300 (300 MHz) or a Bruker AM 500 (500 MHz) spectrometer. The ^{1}H nmr data was reported as follows: chemical shift measured in parts per million (ppm) downfield from TMS (δ), multiplicity, observed coupling constant (J) in Hertz (Hz), proton count. Multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q) and multiplet (m). The ^{13}C nmr chemical shifts (δ) are reported in ppm downfield from TMS and identifiable carbons are given.

Column chromatography was carried out using Merck silica gel 7736 60H, whilst preparative thin layer chromatography (tlc) was performed using Merk silica gel 7730 60 GF$_{254}$. Starting materials were analytical grade reagents and were checked for purity before use and all solvents were distilled before use.

2-Amino-4-methyloxazole [19a], 2-amino-4,5-dimethyloxazole [19a], 2-amino-4,5,6,7-tetrahydrobenzooxazole [19b], and 2-amino-4,5-diphenyloxazole [19b] were prepared as described in the literature. Most substituted phenacyl bromides were commercially available except 2-bromoacetophenone (phenacyl bromide) [20]. Those prepared according to a modified literature procedure are described herein.

1,4-Bis(2'-bromoacetyl)benzene (**15**) [21].

1,4-Diacetylbenzene (15.0 g, 0.093 mole) was suspended in glacial acetic acid (120 ml), warmed gently on a water bath until a clear solution was formed, then cooled as far as possible without the formation of crystals (~15°). To this solution was added bromine (29.80 g, 0.186 mole) dropwise over 30 minutes; the internal temperature was not allowed to rise above 30° during the addition. The brominated product started to separate from the solution when about three-quarters of the bromine had been added. After two hours the flask was cooled in a bath of ice-salt, filtered, washed with a little cold glacial acetic acid, followed by small volumes of water until all the acetic acid had been removed. The crude material was crystallized from aqueous tetrahydrofuran. It formed off-white crystals (23.0 g, 77%) mp 179-181°; ir (potassium bromide): 1698 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 4.99 (s, 4H, CH$_2$), 8.13 (s, 4H, aromatic H); ^{13}C nmr (dimethyl sulfoxide-d$_6$): δ 34.6 (CH$_2$), 129.3 (C-2 and C-3, aromatic C), 137.9 (C-1 and C-4, aromatic C), 191.7 (CO).

Anal. Calcd. for $C_{10}H_8O_2Br_2$: C, 37.54; H, 2.52. Found: C, 37.80; H, 2.74.

Synthesis of 2-Imino-3-[4-substitutedphenacyl]-2,3-dihydrooxazoles **10a-10r**.

All imines were prepared following the general procedure illustrated by the preparation of 2-imino-4-methyl-3-phenacyl-2,3-dihydrooxazole (**10a**), using the appropriate 2-aminooxazole and *p*-substituted or *p*-unsubstitutedphenacyl bromide. Analogues are listed after this representative procedure with their physical characteristics and variations noted under the individual products. These products were of high purity and used directly for subsequent cyclization without further purification.

2-Imino-4-methyl-3-phenacyl-2,3-dihydrooxazole (**10a**).

A solution of phenacyl bromide (2.03 g, 0.01 mole) in freshly distilled dry tetrahydrofuran (20 ml) was added during 20 minutes to a stirred solution of 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) in freshly distilled dry acetonitrile (20 ml) at room temperature under a nitrogen atmosphere, and the mixture was stirred for 24 hours. The precipitate was collected and washed with cold acetonitrile (20 ml). The solid product was slurried in ice-cold water (30 ml), and basified with 2 *M* ammonium hydroxide solution to *p*H 9-10. The resulting crystals were filtered off, washed with a small amount of cold water, and dried *in vacuo* over phosphorus pentoxide. This gave 2-imino-4-methyl-3-phenacyl-2,3-dihydrooxazole (**10a**) as yellow crystals (1.20 g, 54%) mp 111-112°; ir (potassium bromide): 1670, 1690, 3140, 3350 cm^{-1}; ms: m/z (%) 216 (M$^+$, 42), 199 (8), 188 (M-CO, 50), 187 (20), 11 (M-PhCO, 100), 105 (PhCO, 75), 91 (31), 77 (46), 51 (18), 41 (35); ^{1}H nmr (deuteriochloroform): δ 1.85 (d, J = 1.70 Hz, 3H, CH$_3$), 4.27 (bs, 1H, exchanged with deuterium oxide, NH), 5.03 (s, 2H, CH$_2$), 6.49 (q, J = 1.70 Hz, 1H, H-5), 7.46-7.61 (m, 3H, aromatic H), 8.01 (d, J = 8.50 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.2 (CH$_3$), 48.4 (CH$_2$), 124.6 (C-4', aromatic C), 125.3 (C-1', aromatic C), 128.2 (C-3', aromatic C), 128.9 (C-2', aromatic C), 129.5 (C-4), 134.1 (C-5), 159.3 (C-2), 192.5 (CO).

2-Imino-4-methyl-3-(4'-bromophenacyl)-2,3-dihydrooxazole (**10b**).

This was prepared by a similar procedure from 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) and 4-bromophenacyl bromide (2.83 g, 0.01 mole) as a yellow solid (2.2 g, 73%) mp 97-99°;

ir (potassium bromide): 1635, 1680, 3300, 3330 cm^{-1}; ms: m/z (%) 296 (M+2, 5), 294 (M$^+$, 6), 266 (M-28, 8), 185 (15), 183 (BrPhCO, 16), 157 (11), 155 (12), 111 (M-BrPhCO, 100), 89 (13), 75 (21), 55 (10); ^{1}H nmr (deuteriochloroform): δ 1.87 (d, J = 1.62 Hz, 3H, CH$_3$), 4.15 (bs, 1H, exchanged with deuterium oxide, NH), 5.00 (s, 2H, CH$_2$CO), 6.51 (q, J = 1.62 Hz, 1H, H-5), 7.63 (d, J = 8.58 Hz, 2H, aromatic H), 7.87 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.3 (CH$_3$), 48.0 (CH$_2$), 123.81 (C-5), 124.7 (C-4), 129.3 (C-4', aromatic C), 129.6 (C-3', aromatic C), 132.2 (C-2', aromatic C), 133.1 (C-1', aromatic C), 159.2 (C-2), 193.2 (CO).

2-Imino-4-methyl-3-(4'-phenylphenacyl)-2,3-dihydrooxazole (**10c**).

This was prepared in the same way from 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) and 4-phenylphenacyl bromide (2.81 g, 0.01 mole) as a light yellow solid (1.9 g, 64%) mp 216-218°; ir (potassium bromide): 1650, 1680, 3325 cm^{-1}; ms: m/z (%) 292 (M$^+$, 13), 274 (M-H$_2$O, 7), 264 (M-28, 10), 181 (PhPhCO, 100), 167 (64), 152 (83), 149 (28), 135 (17), 111 (M-PhPhCO, 35), 83 (23), 81 (26), 69 (59), 60 (24), 57 (50), 55 (59); ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 1.92 (s, 3H, CH$_3$), 2.42 (bs, 1H, exchanged with deuterium oxide, NH), 5.09 (s, 2H, CH$_2$CO), 6.55 (s, 1H, H-5), 7.29-7.51 (m, 3H, aromatic H), 7.62 (d, J = 7.58 Hz, 2H, aromatic H), 7.73 (d, J = 8.31 Hz, 2H, aromatic H), 8.07 (d, J = 8.31 Hz, 2H, aromatic H); ^{13}C nmr (dimethyl sulfoxide-d$_6$): δ 7.5 (CH$_3$), 49.6 (CH$_2$), 127.2, 127.3, 127.4, 128.4, 128.9, 129.4, 132.8, 138.8, 145.9, 158.4, 192.0.

2-Imino-4-methyl-3-(4'-chlorophenacyl)-2,3-dihydrooxazole (**10d**).

This was prepared in a similar manner from 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) and 4-chlorophenacyl bromide (2.38 g, 0.01 mole) as yellowish crystals (1.70 g, 67%) mp 125-126°; ir (potassium bromide): 1650, 1675, 3090, 3325 cm^{-1}; ms: m/z (%) 252 (M+2, 5), 250 (M$^+$, 13), 222 (M-28, 14), 139 (ClPhCO, 63), 125 (46), 111 (M-ClPhCO, 100), 89 (12), 75 (27), 55 (17); ^{1}H nmr (deuteriochloroform): δ 1.88 (d, J = 1.53 Hz, 3H, CH$_3$), 4.10 (bs, 1H, exchanged with deuterium oxide, NH), 5.01 (s, 2H, CH$_2$), 6.52 (d, J = 1.57 Hz, 1H, H-5), 7.48 (d, J = 8.53 Hz, 2H, aromatic H), 7.95 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.4 (CH$_3$), 48.0 (CH$_2$), 123.7 (C-5), 124.7 (C-1', aromatic C), 129.2 (C-3', aromatic C), 129.5 (C-2', aromatic C), 132.7 (C-4', aromatic C), 140.5 (C-4), 159.2 (C-2), 193.0 (CO).

2-Imino-4-methyl-3-(4'-methoxyphenacyl)-2,3-dihydrooxazole (**10e**).

This was prepared in a similar manner from 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) and 4-methoxyphenacyl bromide (2.34 g, 0.01 mole) as white crystals (1.30 g, 52%) mp 118-119°; ir (potassium bromide): 1640, 1670, 3325 cm^{-1}; ms: m/z (%) 246 (M$^+$, 12), 218 (M-28, 4), 135 (CH$_3$OPhCO, 100), 121 (59), 111 (M-CH$_3$OPhCO, 30), 107 (24), 92 (40), 77 (48), 63 (19), 55 (15); ^{1}H nmr (deuteriochloroform): δ 1.86 (d, J = 1.63 Hz, 3H, CH$_3$), 3.87 (s, 3H, OCH$_3$), 4.10 (bs, 1H, exchanged with deuterium oxide, NH), 4.97 (s, 2H, CH$_2$), 6.49 (d, J = 1.63 Hz, 1H, H-5), 6.96 (d, J = 8.90 Hz, 2H, aromatic H), 7.98 (d, J = 8.90 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.3 (CH$_3$), 47.6 (CH$_2$), 55.5 (CH$_3$O), 114.0 (C-3', aromatic C), 123.4 (C-5), 124.8 (C-1', aromatic C), 127.5 (C-4), 130.4 (C-2', aromatic C), 159.4 (C-2), 164.1 (C-4', aromatic C), 191.0 (CO).

2-Imino-4-methyl-3-(2'-naphthacyl)-2,3-dihydrooxazole (**10f**).

This was prepared in a similar manner from 2-amino-4-methyloxazole (**9a**) (1.0 g, 0.01 mole) and 2-bromoacetylnaphthalene (2.54 g, 0.01 mole) as a light pink solid (1.70 g, 62%) mp 128-130°; ir (potassium bromide): 1660, 1690, 3100, 3330 cm^{-1}; ms: m/z (%) 266 (M$^+$, 15), 248 (M-H$_2$O, 6), 238 (M-28, 13), 155 (naphthoyl, 100), 141 (54), 127 (94), 111 (M-naphthoyl, 43), 83 (35), 69 (72), 57 (65), 55 (79); ^{1}H nmr (deuteriochloroform): δ 1.89 (d, J = 1.68 Hz, 3H, CH$_3$), 4.13 (bs, 1H, exchanged with deuterium oxide, NH), 5.18 (s, 2H, CH$_2$), 6.53 (d, J = 1.68 Hz, 1H, H-5), 7.55-7.66 (m, 2H, naphthalene H), 7.90 (t, J = 8.81 Hz, 2h, naphthalene H), 7.98-8.06 (m, 2H, naphthalene H), 8.61 (s, 1H, naphthalene H); ^{13}C nmr (deuteriochloroform): δ 8.4 (CH$_3$), 48.1 (CH$_2$), 123.4, 123.7, 124.8, 127.0, 127.8, 128.8, 128.9, 129.7, 130.1, 131.8, 132.3, 135.9, 159.4 (C-2), 192.1 (CO).

4,5-Dimethyl-2-imino-3-phenacyl-2,3-dihydrooxazole (**10g**).

This was prepared in the same way from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and phenacyl bromide (1.78 g, 8.92 mmoles) as yellow crystals (1.34 g, 65%) mp 58-60°; ir (potassium bromide): 1640, 1680, 3335 cm^{-1}; ms: m/z (%) 230 (M$^+$, 30), 212 (16), 202 (M-CO, 15), 125 (M-PhCO, 100), 105 (PhCO, 36), 91 (13), 82 (71), 77 (28), 55 (36), 43 (15), 32 (80), 38 (100); ^{1}H nmr (deuteriochloroform): δ 1.81 (s, 3H, CH$_3$-4), 2.03 (s, 3H, CH$_3$-5), 4.82 (bs, 1H, exchanged with deuterium oxide, NH), 5.12 (s, 2H, CH$_2$), 7.48 (dd, J = 7.80 Hz, 2H, aromatic H), 7.63 (t, J = 7.40 Hz, 1H, aromatic H), 8.03 (d, J = 7.40 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.7 (CH$_3$-4), 9.8 (CH$_3$-5), 48.5 (CH$_2$), 118.2 (C-5), 128.2 (C-3', aromatic C), 128.9 (C-2', aromatic C), 132.1 (C-1', aromatic C), 134.0 (C-4', aromatic C), 134.3 (C-4), 158.8 (C-2), 191.06 (CO).

4,5-Dimethyl-2-imino-3-(4'-bromophenacyl)-2,3-dihydrooxazole (**10h**).

This was prepared in a similar manner from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and 4-bromophenacyl bromide (2.48 g, 8.92 mmoles) as a colorless solid (2.13 g, 77%) mp 133-134°; ir (potassium bromide): 1670, 1710, 3325 cm^{-1}; ms: m/z (%) 311 (M+2, 2), 309 (M$^+$, 3), 308 (M-1, 14), 292 (17), 290 (17), 282 (9), 280 (10), 125 (M-*p*-BrPhCO, 100), 111 (10), 82 (54), 55 (29), 32 (35), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.82 (s, 3H, CH$_3$-4), 2.04 (s, 3H, CH$_3$-5), 4.25 (bs, 1H, exchanged with deuterium oxide, NH), 5.16 (s, 2H, CH$_2$), 7.62 (d, J = 8.58 Hz, 2H, aromatic H), 7.91 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.7 (CH$_3$-4), 9.8 (CH$_3$-5), 48.7 (CH$_2$), 118.4 (C-5), 129.4 (C-4', aromatic C), 129.7 (C-3', aromatic C), 132.2 (C-2', aromatic C), 132.9 (C-1', aromatic C), 133.1 (C-4), 158.6 (C-2), 192.0 (CO).

4,5-Dimethyl-2-imino-3-(4'-phenylphenacyl)-2,3-dihydrooxazole (**10i**).

This was prepared in a similar manner from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and 4-phenylphenacyl bromide (2.45 g, 8.92 mmoles) as a colorless solid (1.72 g, 63%) mp 138-140°; ir (potassium bromide): 1675, 3345 cm^{-1}; ms: m/z (%) 306 (M$^+$, 68), 288 (M-H$_2$O, 100), 278 (M-CO, 15), 264 (39), 220 (30), 181 (66), 167 (44), 152 (35), 125 (M-(4-PhPhCO), 72), 82 (36), 55 (21), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.83 (d, J = 1.00 Hz, CH$_3$-4), 2.05 (d, J = 1.00 Hz, CH$_3$-5), 3.98 (bs, 1H, exchanged with deuterium oxide, NH), 5.16 (s, 2H, CH$_2$), 7.42-7.51 (m, 3H, aromatic H), 7.62 (d, J = 7.96 Hz, 2H, aromatic H), 7.73 (d, J = 8.43 Hz, 2H, aromatic H), 8.12 (d, J = 8.43 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.8 (CH_3-4), 9.8 (CH_3-5), 48.5 (CH_2), 118.2 (C-5), 127.2, 127.4, 128.4, 128.7, 128.9, 132.3, 133.1, 139.5, 146.6, 158.8 (C-2), 191.0 (CO).

4,5-Dimethyl-2-imino-3-(4'-chlorophenacyl)-2,3-dihydrooxazole (**10j**).

This was prepared in the same way from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and 4-chlorophenacyl bromide (2.08 g, 8.92 mmoles) as pale white crystals (1.84 g, 78%) mp 133-134°; ir (potassium bromide): 1690, 3350 cm^{-1}; ms: m/z (%) 266 (M+2, 5), 264 (M^+, 13), 236 (M-28, 7), 141 (17), 139 (ClPhCO, 49), 125 (M-ClPhCO, 100), 111 (52), 82 (59), 75 (36), 55 (58), 43 (33); ^{1}H nmr (deuteriochloroform): δ 1.84 (s, 3H, CH_3-4), 2.08 (s, 3H, CH_3-5), 4.88 (bs, 1H, exchanged with deuterium oxide, NH), 5.36 (s, 2H, CH_2), 7.47 (d, J = 8.54 Hz, 2H, aromatic H), 8.05 (d, J = 8.54 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.7 (CH_3-4), 9.8 (CH_3-5), 49.4 (CH_2), 118.9 (C-5), 129.2 (C-3', aromatic C), 129.9 (C-2', aromatic C), 132.4 (C-1', aromatic C), 134.1 (C-4', aromatic C), 140.7 (C-4), 158.4 (C-2), 191.5 (CO).

4,5-Dimethyl-2-imino-3-(4'-methoxyphenacyl)-2,3-dihydrooxazole (**10k**).

This was prepared in a similar procedure from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and 4-methoxyphenacyl bromide (2.04 g, 8.92 mmoles) as pale white crystals (1.85 g, 68%) mp 123-125°; ir (potassium bromide): 1690, 3325 cm^{-1}; ms: m/z (%) 260 (M^+, 7), 152 (13), 135 (CH_3OPhCO, 100), 125 (30), 121 (27), 107 (15), 92 (24), 77 (31), 60 (24), 55 (19), 45 (44); ^{1}H nmr (deuteriochloroform): δ 1.85 (s, 3H, CH_3-4), 2.10 (s, 3H, CH_3-5), 3.86 (s, 3H, OCH_3), 5.57 (s, 2H, CH_2), 5.97 (bs, 1H, exchanged with deuterium oxide, NH), 6.96 (d, J = 8.84 Hz, 2H, aromatic H), 8.07 (d, J = 8.84 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.5 (CH_3-4), 9.8 (CH_3-5), 49.7 (CH_2), 55.5 (OCH_3), 114.1 (C-3', aromatic C), 120.1 (C-5), 126.8 (C-1', aromatic C), 131.0 (C-2', aromatic C), 135.6 (C-4), 157.9 (C-2), 164.4 (C-4', aromatic C), 189.9 (CO).

4,5-Dimethyl-2-imino-3-(2'-naphthacyl)-2,3-dihydrooxazole (**10l**).

This was prepared by a similar procedure from 2-amino-4,5-dimethyloxazole (**9b**) (1.0 g, 8.92 mmoles) and 2-bromoacetylnaphthalene (2.22 g, 8.92 mmoles) as a yellow solid (1.85 g, 74%) mp 120-121°; ir (potassium bromide): 1675, 3125, 3335 cm^{-1}; ms: m/z (%) 280 (M^+, 17), 252 (M-28, 8), 155 (68), 141 (75), 127 (M-naphthoyl, 100), 115 (16), 82 (12), 55 (7), 43 (8); ^{1}H nmr (deuteriochloroform): δ 1.79 (s, 3H, CH_3-4), 2.01 (s, 3H, CH_3-5), 4.58 (bs, 1H, exchanged with deuterium oxide, NH), 5.23 (s, 2H, CH_2), 7.54-7.65 (m, 2H, naphthalene H), 7.86-8.07 (m, 4H, naphthalene H), 8.68 (s, 1H, naphthalene H); ^{13}C nmr (deuteriochloroform): δ 7.8 (CH_3-4), 9.8 (CH_3-5), 48.7 (CH_2), 118.2 (C-5), 123.4, 126.9, 127.7, 128.7, 128.9, 129.8, 130.4, 131.6, 132.2, 132.4, 135.9, 158.8 (C-2), 192.1 (CO).

2-Imino-3-phenacyl-2,3,4,5,6,7-hexahydrobenzoxazole (**10m**).

This was prepared by a similar procedure from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and phenacyl bromide (1.44 g, 7.24 mmoles) as a yellow solid (1.2 g, 65%) mp 139-141°; ir (potassium bromide): 1650, 1700, 1740 cm^{-1}; ms: m/z (%) 256 (M^+, 72), 238 (M-H_2O, 8), 228 (M-CO, 17), 151 (M-PhCO, 100), 137 (24), 108 (42), 105 (PhCO, 20), 91 (14), 81 (31), 77 (26), 67 (18), 41 (19); ^{1}H nmr (deuteriochloroform): δ 1.71-1.83 (m, 4H, H-5 and H-6), 2.12-2.34 (m, 4H, H-4 and H-7), 4.37 (bs, 1H, exchanged with deuterium oxide, NH), 4.95 (s, 2H, CH_2CO), 7.43-7.47 (m, 2H, aromatic H), 7.60 (t, J = 7.60 Hz, 1H, aromatic H), 7.98 (d, J = 7.50 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.3, 20.9, 21.6, 22.2, 48.4 (CH_2), 121.6 (C-7a), 122.5 (C-3a), 128.14 (C-3', aromatic C), 128.8 (C-2', aromatic C), 129.4 (C-1', aromatic C), 133.9 (C-4', aromatic C), 159.1 (C-2), 193.1 (CO).

2-Imino-3-(4'-bromophenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10n**).

This was prepared by a similar manner from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and 4-bromophenacyl bromide (2.01 g, 7.24 mmoles) as a yellowish-red solid (1.70 g, 70%) mp 108-110°; ir (potassium bromide): 1655, 1680, 1720, 3325 cm^{-1}; ms: m/z (%) 336 (M+2, 10), 334 (M^+, 11), 238 (14), 183 (24), 155 (27), 151 (M-BrPhCO, 100), 149 (25), 108 (34), 81 (61), 67 (65), 55 (51); ^{1}H nmr (deuteriochloroform): δ 1.74-1.87 (m, 4H, H-5 and H-6), 2.15-2.41 (m, 4H, H-4 and H-7), 3.91 (bs, 1H, exchanged with deuterium oxide, NH), 5.02 (s, 2H, CH_2), 7.64 (d, J = 8.50 Hz, 2H, aromatic H), 7.91 (d, J = 8.50 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.3, 20.9, 21.8, 22.2, 48.4 (CH_2CO), 121.6 (C-7a), 129.3 (C-4', aromatic C), 129.7 (C-3', aromatic C), 132.2 (C-2', aromatic C), 133.2 (C-1', aromatic C), 135.4 (C-3a), 159.0 (C-2), 193.0 (CO).

2-Imino-3-(4'-phenylphenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10o**).

This was prepared by a similar manner from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and 4-phenylphenacyl bromide (1.99 g, 7.24 mmoles) as a light pinkish solid (1.50 g, 62%) mp 228-230°; ir (potassium bromide): 1665, 3325 cm^{-1}; ms: m/z (%) 332 (M^+, 22), 314 (M-H_2O, 21), 236 (25), 181 (PhPhCO, 7), 109 (12), 81 (38), 69 (100), 55 (11); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.72-1.81 (m, 4H, H-5 and H-6), 2.34-2.56 (m, 4H, H-4 and H-7), 3.36 (bs, 1H, exchanged with deuterium oxide, NH), 5.71 (s, 2H, CH_2CO), 7.43-7.56 (m, 3H, aromatic H), 7.81 (d, J = 7.10 Hz, aromatic H), 7.94 (d, J = 8.43 Hz, 2H, aromatic H), 8.13 (d, J = 8.43 Hz, 2H, aromatic H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 18.5, 20.3, 21.1, 21.7, 50.1 (CH_2CO), 124.5, 127.2, 127.3, 128.9, 129.42, 132.7, 138.8, 140.0, 145.9, 157.8 (C-2), 190.6 (CO).

2-Imino-3-(4'-chlorophenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10p**).

This was prepared by a similar manner from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and 4-chlorophenacyl bromide (1.69 g, 7.24 mmoles) as a yellowish-red solid (1.50 g, 71%) mp 110-112°; ir (potassium bromide): 1650, 1685, 1720, 3335 cm^{-1}; ms: m/z (%) 292 (M+2, 4), 290 (M^+, 14), 272 (M-H_2O, 6), 262 (M-28, 7), 151 (M-ClPhCO, 100), 139 (ClPhCO, 37), 111 (52), 108 (34), 81 (32), 67 (34), 55 (19); ^{1}H nmr (deuteriochloroform): δ 1.72-1.83 (m, 4H, H-5 and H-6), 2.13-2.38 (m, 4H, H-4 and H-7), 4.27 (bs, 1H, exchanged with deuterium oxide, NH), 4.99 (s, 2H, CH_2), 7.47 (d, J = 8.50 Hz, 2H, aromatic H), 7.98 (d, J = 8.50 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.3, 20.9, 21.8, 22.2, 48.4 (CH_2CO), 121.5 (C-7a), 129.1 (C-3', aromatic C), 129.6 (C-2', aromatic C), 132.8 (C-4', aromatic C), 135.2 (C-1', aromatic C), 140.4 (C-3), 159.0 (C-2), 193.1 (CO).

2-Imino-3-(4'-methoxyphenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10q**).

This was prepared by a similar procedure from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and 4-methoxyphenacyl bromide (1.66 g, 7.24 mmoles) as a yellowish-brown solid (1.40 g, 67%) mp 135-137°; ir (potassium bromide): 1685, 3335 cm^{-1}; ms: m/z (%) 286 (M$^+$, 16), 190 (8), 175 (9), 151 (M-CH_3OPhCO, 35), 135 (CH_3OPhCO, 100), 121 (25), 107 (16), 92 (40), 81 (32), 77 (53), 67 (21), 55 (19), 43 (20); ^{1}H nmr (deuteriochloroform): δ 1.74-1.82 (m, 4H, H-4 and H-6), 2.18-2.41 (m, 4H, H-4 and H-7), 3.86 (s, 3H, OCH_3), 5.05 (s, 2H, CH_2CO), 5.36 (bs, 1H, exchanged with deuterium oxide, NH), 6.96 (d, J = 8.60 Hz, 2H, aromatic H), 8.04 (d, J = 8.60 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.1, 20.8, 21.6, 22.0, 49.0 (CH_2CO), 55.5 (OCH_3), 114.1 (C-3', aromatic C), 122.9 (C-7a), 127.0 (C-1', aromatic C), 130.8 (C-2', aromatic C), 137.5 (C-3a), 158.7 (C-2), 164.3 (C-4', aromatic C), 190.3 (CO).

2-Imino-3-(2'-naphthacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10r**).

This was prepared in a similar manner from 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 7.24 mmoles) and 2-bromoacetylnaphthalene (1.80 g, 7.24 mmoles) as a pink solid (1.70 g, 77%) mp 226-227°; ir (potassium bromide): 1670, 3350 cm^{-1}; ms: m/z (%) 306 (M$^+$, 17), 288 (M-H_2O, 7), 210 (7), 155 (naphthoyl, 48), 151 (M-naphthoyl, 45), 141 (28), 127 (100), 108 (27), 81 (34), 69 (54), 54 (40); ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 1.71-1.81 (m, 4H, H-5 and H-6), 2.34-2.54 (m, 4H, H-4 and H-7), 2.98 (bs, 1H, exchanged with deuterium oxide, NH), 5.77 (s, 2H, CH_2CO), 7.66-7.76 (m, 2H, naphthalene H), 8.00-8.20 (m, 4H, naphthalene H), 8.83 (s, 1H, naphthalene H); ^{13}C nmr (dimethyl sulfoxide-d$_6$): δ 18.6, 20.3, 21.8, 52.0 (CH_2CO), 123.6, 124.3, 127.6, 128.1, 128.8, 129.5, 129.8, 131.0, 131.3, 139.4, 157.8 (C-2), 191.3 (CO).

1,4-Bis[3-(2',3',4',5',6',7',-hexahydrobenzoxazolyl)acetyl]benzene (**16**).

A solution of 1,4-bis(2-bromoacetyl)benzene (**15**) (1.16 g, 3.62 mmoles) in hot dry tetrahydrofuran (25 ml) was added during 15 minutes to a stirred solution of 2-amino-4,5,6,7-tetrahydrobenzoxazole (**14**) (1.0 g, 3.62 mmoles) in dry acetonitrile (20 ml) at room temperature under a nitrogen atmosphere, and the mixture was stirred for 24 hours. The precipitate was collected and washed with cold acetonitrile (20 ml). The solid product was slurried in ice-cold water (40 ml), and basified with 2 *M* ammonium hydroxide solution to *p*H 9-10. The separated crystals were filtered off, washed with a small amount of water, and dried *in vacuo* over phosphorus pentoxide. This gave the title compound **16** as yellow crystals (1.24 g, 78%) mp 213-215°. This was homogenous by thin layer chromatography (dichloromethane/methanol, 20:1, v/v) and used directly for cyclization without further purification; ir (potassium bromide): 1655, 1700, 3312 cm^{-1}; ms: m/z (%) 434 (M$^+$, 12), 406 (M-28, 9), 283 (64), 151 (100), 69 (21), 55 (42), 43 (19); ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 1.73-1.74 (m, 8H, H-5 and H-6), 2.18-2.37 (m, 8H, H-4 and H-7), 4.42 (bs, 2H, exchanged with deuterium oxide, NH), 4.98 (s, 4H, NCH_2CO), 7.46-7.48 (s, aromatic H); ^{13}C nmr (dimethyl sulfoxide-d$_6$): δ 19.1, 21.2, 21.7, 22.3, 48.7 (NCH_2CO), 121.7 (C-2', aromatic C), 128.6 (C-1', aromatic C), 132.9 (C-3a), 138.3 (C-7a), 157.4 (C-2), 205.6 (CO).

Synthesis of Imidazo[2,1-*b*]oxazoles **11a**-**11r**.

All imidazo[2,1-*b*]oxazoles were prepared following the general procedure illustrated by the preparation of 3-methyl-6-phenylimidazo[2,1-*b*]oxazole (**11a**), using the appropriate 2-imino-3-[4-(un)substitutedphenacyl]-2,3-dihydroxazole. Analogues are listed after this procedure with their physical characteristics, and variations are noted under the individual products.

3-Methyl-6-phenylimidazo[2,1-*b*]oxazole (**11a**).

2-Imino-4-methyl-3-phenacyl-2,3-dihydroxazole (**10a**) (1.0 g, 4.63 mmoles) was suspended in sodium dried toluene (30 ml) and cooled in an ice-salt mixture (-10°). To this, magnetically stirred heterogenous mixture, was added dry titanium(IV) chloride (2.20 g, 2.5 mole equivalent) under a nitrogen atmosphere, dropwise over 30 minutes. After the addition was complete the ice bath was removed and the reaction mixture was allowed to warm slowly to room temperature during 30 minutes, before heated under reflux for another two hours. This was then cooled to room temperature and poured onto crushed ice (~30 g). The organic layer was separated. The aqueous phase was further extracted with chloroform (3 x 30 ml). The combined organic phase was passed through a short column of potassium carbonate (this helps to overcome emulsion problems and to free the product from possible hydrochloric acid contamination from the Lewis acid), collected, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the brown oily residue was crystallized by trituration with diethyl ether. The solid product was filtered off, and recrystallized from aqueous methanol. This gave 3-methyl-6-phenylimidazo[2,1-*b*]oxazole (**11a**) as white crystals (0.60 g, 65%) mp 111-112°; ir (potassium bromide): 1605, 3155 cm^{-1}; ms: m/z (%) 198 (M$^+$, 100), 197 (M-1, 13), 170 (M-CO, 10), 126 (7), 103 (11), 99 (10), 77 (8), 67 (7), 32 (93), 28 (98); ^{1}H nmr (deuteriochloroform): δ 2.31 (d, J = 1.56 Hz, 3H, CH_3), 7.09 (q, J = 1.56 Hz, 1H, H-2), 7.11 (s, 1H, H-5), 7.28 (t, J = 8.60 Hz, 1H, aromatic H), 7.36 (dd, J = 7.86, 7.33 Hz, 2H, aromatic H), 7.82 (d, J = 8.95 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.4 (CH_3), 100.7 (C-5), 121.0 (C-1', aromatic C), 124.9 (C-3', aromatic C), 127.1 (C-4', aromatic C), 128.5 (C-2', aromatic C), 133.2 (C-2), 134.4 (C-6), 144.2 (C-3), 155.9 (C-7a).

Anal. Calcd. for $C_{12}H_{10}N_2O$: C, 72.72; H, 5.09; N, 14.13. Found: C, 72.59; H, 4.97; N, 14.05.

3-Methyl-6-(4'-bromophenyl)imidazo[2,1-*b*]oxazole (**11b**).

This was prepared in a similar manner from 2-imino-4-methyl-3-(4'-bromophenacyl)-2,3-dihydrooxazole (**10b**) (1.0 g, 3.39 mmoles) and recrystallized from aqueous ethanol. It formed shiny white crystals (0.70 g, 76%), mp 161-162°; ir (potassium bromide): 1605, 1640, 3155 cm^{-1}; ms: m/z (%) 279 (M+2, 16), 277 (M$^+$, 18), 276 (M-1, 100), 250 (M-CO, 10), 248 (6), 183 (9), 181 (10), 102 (15), 67 (12), 32 (19), 28 (76); ^{1}H nmr (deuteriochloroform): δ 2.28 (d, J = 1.56 Hz, 3H, CH_3), 7.09 (q, J = 1.56 Hz, 1H, H-2), 7.18 (s, 1H, H-5), 7.47 (d, J = 8.58 Hz, 2H, aromatic H), 7.63 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.4 (CH_3), 101.1 (C-5), 120.6 (C-4', aromatic C), 121.0 (C-1', aromatic C), 126.4 (C-3', aromatic C), 131.6 (C-2', aromatic C), 133.4 (C-2), 142.9 (C-3), 155.8 (C-7a).

Anal. Calcd. for $C_{12}H_9N_2OBr$: C, 52.01; H, 3.27; N, 10.10. Found: C, 51.69; H, 3.13; N, 9.84.

3-Methyl-6-(4'-phenylphenyl)imidazo[2,1-*b*]oxazole (**11c**).

This was prepared by a similar manner from 2-imino-4-methyl-3-(4'-phenylphenacyl)-2,3-dihydroxazole (**10c**) (1.0 g, 3.42 mmoles) and recrystallized from ethanol. It formed white needle crystals (0.70 g, 75%) mp 203-204°; ir (potassium bromide): 1610, 3150 cm^{-1}; ms: m/z (%) 274 (M$^+$, 100), 179 (5), 137 (5), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.29 (d, J = 1.41 Hz, 3H, CH_3), 7.09 (q, J = 1.41 Hz, 1H, H-2), 7.25 (s, 1H, H-5), 7.36 (t, J = 7.25 Hz, 1H, aromatic H), 7.46 (dd, J = 7.23, 7.81 Hz, 2H, aromatic H), 7.54 (d, J = 8.34 Hz, 2H, aromatic H), 7.67 (d, J = 7.31 Hz, 2H, aromatic H), 7.91 (d, J = 8.34 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.3 (CH_3), 100.8 (C-5), 121.0 (C-4', aromatic C), 125.2, 126.8, 127.2, 128.7, 133.2 (C-2), 133.5 (C-6), 139.6, 140.7, 143.7 (C-3), 155.8 (C-7a).

Anal. Calcd. for $C_{18}H_{14}N_2O$: C, 78.82; H, 5.14; N, 10.21. Found: C, 78.57; H, 4.84; N, 9.98.

3-Methyl-6-(4'-chlorophenyl)imidazo[2,1-*b*]oxazole (**11d**).

This was prepared by a similar manner from 2-imino-4-methyl-3-(4'-chlorophenacyl)-2,3-dihydroxazole (**10d**) (1.0 g, 3.99 mmoles) and recrystallized from aqueous ethanol. It formed shiny brown crystals (0.60 g, 65%) mp 139-140°; ir (potassium bromide): 1640, 3155 cm^{-1}; ms: m/z (%) 234 (M+2, 31), 232 (M$^+$, 100), 206 (6), 204 (M-CO, 8), 138 (10), 108 (9), 67 (8), 40 (30), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.25 (d, J = 1.51 Hz, 3H, CH_3), 7.05 (q, J = 1.51 Hz, 1H, H-2), 7.13 (s, 1H, H-5), 7.29 (d, J = 8.58 Hz, 2H, aromatic H), 7.68 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.3 (CH_3), 101.0 (C-5), 121.0 (C-1', aromatic C), 125.9 (C-2', aromatic C), 128.5 (C-3', aromatic C), 132.4 (C-4', aromatic C), 132.9 (C-6), 133.2 (C-2), 142.8 (C-3), 155.7 (C-7a).

Anal. Calcd. for $C_{12}H_9N_2OCl$: C, 61.95; H, 3.90; N, 12.04. Found: C, 61.69; H, 3.78; N, 11.81.

3-Methyl-6-(4'-methoxyphenyl)imidazo[2,1-*b*]oxazole (**11e**).

This was prepared in a similar manner from 2-imino-4-methyl-3-(4'-methoxyphenacyl)-2,3-dihydrooxazole (**10e**) (0.80 g, 3.25 mmoles) and recrystallized from aqueous ethanol. It formed off-white crystals (0.52 g, 70%) mp 127-128°; ir (potassium bromide): 1640, 3155 cm^{-1}; ms: m/z (%) 228 (M$^+$, 100), 213 (M-CH_3, 66), 183 (19), 114 (11), 32 (8), 28 (22); ^{1}H nmr (deuteriochloroform): δ 2.26 (d, J = 1.34 Hz, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.91 (d, J = 8.77 Hz, 2H, aromatic H), 7.05 (q, J = 1.34 Hz, 1H, H-2), 7.09 (s, 1H, H-2), 7.71 (d, J = 8.77 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.3 (CH_3), 55.2 (OCH_3), 99.6 (C-5), 113.9 (C-3', aromatic C), 121.0 (C-1', aromatic C), 126.0 (C-2', aromatic C), 127.2 (C-6), 132.9 (C-2), 143.9 (C-3), 155.7 (C-7a), 158.8 (C-4', aromatic C).

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found : C, 68.80; H, 5.05; N, 12.24.

3-Methyl-6-(2'-naphthyl)imidazo[2,1-*b*]oxazole (**11f**).

This was prepared in the same way from 2-imino-4-methyl-3-(2'-naphthacyl)-2,3-dihydrooxazole (**10f**) (1.0 g, 3.76 mmoles) and recrystallized from ethanol. It formed brownish yellow crystals (0.53 g, 57%) mp 155-156°; ir (potassium bromide): 1600, 1620, 3155 cm^{-1}; ms: m/z (%) 248 (M$^+$, 100), 220 (M-CO, 10), 153 (12), 124 (13), 40 (7), 32 (94), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.18 (d, J = 1.40 Hz, 3H, CH_3), 7.01 (q, J = 1.40 Hz, 1H, H-2), 7.23 (s, 1H, H-5), 7.41-7.50 (m, 2H, naphthalene H), 7.79-7.89 (m, 4H, naphthalene H), 8.33 (s, 1H, naphthalene H); ^{13}C nmr (deuteriochloroform): δ 8.2 (CH_3), 101.3 (C-5), 120.9 (C-2', naphthalene C), 123.1, 123.2, 125.4, 126.1, 127.5, 127.9, 131.8, 132.6, 133.1 (C-2), 133.6, 143.9 (C-3), 155.8 (C-7a).

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.41; H, 4.87; N, 11.28. Found: C, 77.11; H, 4.80; N, 10.88.

2,3-Dimethyl-6-phenylimidazo[2,1-*b*]oxazole (**11g**).

This was prepared in a similar manner from 4,5-dimethyl-2-imino-3-phenacyl-2,3-dihydrooxazole (**10g**) (0.72 g, 3.13 mmoles) and recrystallized from aqueous methanol as shiny brown crystals (0.55 g, 82%) mp 133-134°; ir (potassium bromide): 1610 cm^{-1}; ms: m/z (%) 212 (M$^+$, 100), 211 (9), 184 (M-CO, 8), 116 (7), 106 (6), 32 (68), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.22 (s, 3H, CH_3-3), 2.28 (s, 3H, CH_3-2), 7.13 (s, 1H, H-5), 7.24 (t, J = 7.40 Hz, 1H, aromatic H), 7.37 (m, 2H, aromatic H), 7.78 (d, J = 7.49 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.1 (CH_3-3), 10.8 (CH_3-2), 100.7 (C-5), 115.0 (C-1', aromatic C), 124.7 (C-3', aromatic C), 126.7 (C-4', aromatic C), 128.4 (C-2', aromatic C), 134.7 (C-6), 142.3 (C-2), 142.8 (C-3), 154.7 (C-7a).

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.19. Found: C, 73.71; H, 5.65; N, 12.58.

2,3-Dimethyl-6-(4'-bromophenyl)imidazo[2,1-*b*]oxazole (**11h**).

This was prepared in the same way from 4,5-dimethyl-2-imino-3-(4'-bromophenacyl)-2,3-dihydrooxazole (**10h**) (0.80 g, 2.59 mmoles) and recrystallized from aqueous ethanol. It formed off-white needle crystals (0.60 g, 80%) mp 194-195°; ir (potassium bromide): 1600 cm^{-1}; ms: m/z (%) 293 (M+2, 18), 292 (100), 291 (M$^+$, 19), 290 (100), 264 (9), 262 (10), 102 (9), 32 (10), 28 (31); ^{1}H nmr (deuteriochloroform): δ 2.20 (s, 3H, CH_3-3), 2.28 (s, 3H, CH_3-2), 7.09 (s, 1H, H-5), 7.45 (d, J = 8.55 Hz, 2H, aromatic H), 7.62 (d, J = 8.55 Hz, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.1 (CH_3-3), 10.8 (CH_3-2), 100.9 (C-5), 115.1 (C-4', aromatic C), 120.3 (C-1', aromatic C), 126.3 (C-3', aromatic C), 131.5 (C-2', aromatic C), 133.8 (C-6), 141.8 (C-2), 142.6 (C-3), 154.7 (C-7a).

Anal. Calcd. for $C_{13}H_{11}N_2OBr$: C, 53.63; H, 3.81; N, 9.62. Found: C, 53.62; H, 3.58; N, 9.49.

2,3-Dimethyl-6-(4'-phenylphenyl)imidazo[2,1-*b*]oxazole (**11i**).

This was prepared in a similar manner from 4,5-dimethyl-2-imino-3-(4'-phenylphenacyl)-2,3-dihydrooxazole (**10i**) (0.80 g, 2.61 mmoles) and recrystallized from methanol. It formed white crystals (0.56 g, 74%) mp 192-193°; ir (potassium bromide): 1620 cm^{-1}; ms: m/z (%) 288 (M$^+$, 100), 260 (M-CO, 10), 179 (8), 144 (12), 32 (19), 28 (78); ^{1}H nmr (deuteriochloroform): δ 2.21 (s, 3H, CH_3-3), 2.28 (s, 3H, CH_3-2), 7.16 (s, 1H, H-5), 7.36 (t, J = 7.31 Hz, aromatic H), 7.45 (dd, J = 7.31, 7.8 Hz, 2H, aromatic H), 7.62-7.69 (m, 4H, aromatic H), 7.86 (d, J = 8.31 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.1 (CH_3-3), 10.8 (CH_3-2), 100.8 (C-5), 115.0, 125.1, 126.8, 127.1, 127.2, 128.7, 133.1, 139.3, 140.8, 142.3, 142.4, 154.7.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.15; H, 5.59; N, 9.71. Found: C, 78.88; H, 5.45; N, 9.60.

2,3-Dimethyl-6-(4'-chlorophenyl)imidazo[2,1-*b*]oxazole (**11j**).

This was prepared in a similar manner from 4,5-dimethyl-2-imino-3-(4'-chlorophenacyl)-2,3-dihydrooxazole (**10j**) (1.0 g, 3.78 mmoles) and recrystallized from aqueous ethanol. It formed white, shiny crystals (0.75 g, 81%) mp 189-190°; ir (potassium bromide): 1600 cm^{-1}; ms: m/z (%) 248 (M+2, 36), 246 (M$^+$, 100), 220 (7), 218 (M-CO, 22), 123 (8), 32 (40), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.19 (s, 3H, CH_3-3), 2.26 (s, 3H, CH_3-2), 7.07 (s, 1H, H-5), 7.31 (d, J = 8.58 Hz, 2H, aromatic H), 7.68 (d, J = 8.58 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 7.9 (CH_3-3), 10.7 (CH_3-2), 100.9 (C-5), 115.0 (C-1', aromatic C), 125.8 (C-3', aromatic C), 128.5 (C-2', aromatic C), 132.1 (C-4', aromatic C), 133.3 (C-6), 141.7 (C-2), 142.5 (C-3), 154.6 (C-7a).

Anal. Calcd. for $C_{13}H_{11}N_2OCl$: C, 63.30; H, 4.49; N, 11.35. Found: C, 63.13; H, 4.26; N, 11.18.

2,3-Dimethyl-6-(4'-methoxyphenyl)imidazo[2,1-*b*]oxazole (**11k**).

This was prepared in a similar manner from 4,5-dimethyl-2-imino-3-(4'-methoxyphenacyl)-2,3-dihydrooxazole (**10k**) (1.20 g, 4.61 mmoles) and was recrystallized from aqueous methanol. It formed light-brown crystals (0.73 g, 65%) mp 183-184°; ir (potassium bromide): 1590 cm^{-1}; ms: m/z (%) 242 (M^+, 33), 227 (M-CH_3, 18), 199 ((M-CH_3)-CO, 8), 111 (11), 97 (17), 83 (16), 71 (17), 69 (19), 57 (21), 44 (100), 40 (100), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.19 (s, 3H, CH_3-3), 2.26 (s, 3H, CH_3-2), 3.82 (s, 3H, OCH_3), 6.92 (d, J = 8.76 Hz, 2H, aromatic H), 7.02 (s, 1H, H-5), 7.71 (d, J = 8.76 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 8.0 (CH_3-3), 10.7 (CH_3-2), 55.2 (OCH_3), 99.6 (C-5), 113.9 (C-3', aromatic C), 115.0 (C-1', aromatic C), 125.9 (C-2', aromatic C), 127.6 (C-6), 142.0 (C-2), 142.7 (C-3), 154.6 (C-7a), 158.6 (C-4', aromatic C).

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.43; H, 5.66; N, 11.49.

2,3-Dimethyl-6-(2'-naphthyl)imidazo[2,1-*b*]oxazole (**11l**).

This was prepared in a similar manner from 4,5-dimethyl-2-imino-3-(4'-naphthacyl)-2,3-dihydrooxazole (**10l**) (1.20 g, 4.28 mmoles) and recrystallized from methanol. It formed brown crystals (0.81 g, 74%) mp 217-218°; ir (potassium bromide): 1610, 1640 cm^{-1}; ms: m/z (%) 262 (M^+, 100), 234 (M-CO, 8), 153 (10), 131 (11), 40 (12), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 2.17 (s, 3H, CH_3-3), 2.26 (s, 3H, CH_3-2), 7.21 (s, 1H, H-5), 7.41-7.47 (m, 2H, naphthalene H), 8.31 (s, 1H, naphthalene H); ^{13}C nmr (deuteriochloroform): δ 7.9 (CH_3-3), 10.7 (CH_3-2), 101.2 (C-5), 115.0 (C-2', naphthalene C), 122.8, 123.3, 126.0, 127.5, 127.9, 128.0, 132.0, 132.5, 133.7, 142.3 (C-2), 142.8 (C-3), 154.8 (C-7a).

Anal. Calcd. for $C_{17}H_{14}N_2O$: C, 77.85; H, 5.38; N, 10.68. Found: C, 77.90; H, 5.43; N, 10.53.

2-Phenyl-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11m**).

This was prepared in a similar manner from 2-imino-3-phenacyl-2,3,4,5,6,7-hexahydrobenzoxazole (**10m**) (1.0 g, 3.91 mmoles) and recrystallized from aqueous ethanol. It formed shiny, white crystals (0.65 g, 70%) mp 161-162°; ir (potassium bromide): 1605 cm^{-1}; ms: m/z (%) 238 (M^+, 100), 210 (M-CO, 22), 195 (7), 182 (9), 120 (14), 105 (23), 77 (15), 57 (13), 40 (38), 32 (100), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.91-1.94 (m, 4H, H-6 and H-7), 2.61-2.69 (m, 4H, H-5 and H-8), 7.17 (s, 1H, H-3), 7.27 (t, J = 7.50 Hz, 1H, aromatic H), 7.38 (dd, J = 7.53, 7.70 Hz, 2H, aromatic H), 7.81 (d, J = 7.70 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.9, 21.8, 22.1, 22.2, 100.8, 118.2, 124.7, 126.7, 128.5, 134.8, 142.6, 145.4, 155.3.

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.75. Found: C, 75.63; H, 5.95; N, 11.73.

2-(4'-Bromophenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11n**).

This was prepared in the same way from 2-imino-3-(4'-bromophenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10n**) (1.0 g, 2.98 mmoles) and recrystallized from ethanol. It formed white needles (0.80 g, 85%) mp 236-237°; ir (potassium bromide): 1600 cm^{-1}; ms: m/z (%) 319 (M+2, 18), 317 (M^+, 20), 316 (M-1, 100), 290 (15), 288 (17), 196 (6), 194 (7), 32 (29), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.82-1.93 (m, 4H, H-6 and H-7), 2.61-2.69 (m, 4H, H-5 and H-8), 7.15 (s, 2H, H-3), 7.48 (d, J = 8.55 Hz, 2H, aromatic H), 7.65 (d, J = 8.55 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.9, 21.8, 22.1, 22.2, 101.1 (C-3), 118.2 (C-1', aromatic C), 120.3 (C-4', aromatic C), 126.3 (C-3', aromatic C), 131.5 (C-2', aromatic C), 133.8 (C-2), 141.5 (C-8a), 145.7 (C-4a), 155.3 (C-9a).

Anal. Calcd. for $C_{15}H_{13}N_2OBr$: C, 56.80; H, 4.13; N, 8.83. Found: C, 57.03; H, 3.90; N, 8.68.

2-(4'-Phenylphenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11o**).

This was prepared in a similar manner from 2-imino-3-(4'-phenylphenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10o**) (1.0 g, 3.01 mmoles) and recrystallized from methanol. It formed white crystals (0.72 g, 76%) mp 210-211°; ir (potassium bromide): 1610 cm^{-1}; ms: m/z (%) 314 (M^+, 100), 286 (M-CO, 12), 163 (8), 32 (7), 28 (21); ^{1}H nmr (deuteriochloroform): δ 1.81-1.92 (m, 4H, H-6 and H-7), 2.63-2.68 (m , 4H, H-5 and H-8), 7.18 (s, 1H, H-3), 7.35 (t, J = 7.30 Hz, 1H, aromatic H), 7.45 (dd, J = 7.2, 7.71 Hz, 2H, aromatic H), 7.62 (d, J = 8.48 Hz, aromatic H), 7.67 (d, J = 7.2 Hz, 2H, aromatic H), 7.88 (d, J = 8.48 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.9, 21.7, 22.1, 22.2, 101.0 (C-3), 118.2 (C-1', aromatic C), 125.0, 126.8, 127.0, 127.1, 128.7, 133.8 (C-2), 139.3, 140.8, 142.2 (C-8a), 145.4 (C-4a), 155.3 (C-9a).

Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 79.90; H, 5.78; N, 8.76.

2-(4'-Chlorophenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11p**).

This was prepared in a similar manner from 2-imino-3-(4'-chlorophenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10p**) (1.0 g, 3.44 mmoles) and recrystallized from ethanol. It formed brown crystals (0.75 g, 80%) mp 209-210°; ir (potassium bromide): 1605 cm^{-1}; ms: m/z (%) 274 (M+2, 32), 272 (M^+, 100), 246 (6), 244 (M-CO, 19), 216 (10), 40 (11), 32 (72), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.82-1.91 (m, 4H, H-6 and H-7), 2.58-2.66 (m ,4H, H-5 and H-8), 7.11 (s, 1H, H-3), 7.31 (d, J = 8.55 Hz, 2H, aromatic H), 7.69 (d, J = 8.55 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.9, 21.7, 22.1, 22.2, 101.1 (C-3), 118.2 (C-1', aromatic C), 125.9 (C-3', aromatic C), 128.5 (C-2', aromatic C), 132.1 (C-4', aromatic C), 133.3 (C-2), 141.4 (C-8a), 145.6 (C-4a), 155.3 (C-9a).

Anal. Calcd. for $C_{15}H_{13}N_2OCl$: C, 66.06; H, 4.80; N, 10.27. Found: C, 66.34; H, 4.86; N, 10.10.

2-(4'-Methoxyphenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11q**).

This was prepared in a similar manner from 2-imino-3-(4'-methoxyphenacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10q**) (1.0 g, 3.49 mmoles) and recrystallized from aqueous methanol. It formed brown crystals (0.70 g, 75%) mp 184-185°; ir (potassium bromide): 1590 cm^{-1}; ms: m/z (%) 268 (M^+, 100), 253

($M-CH_3$, 48), 240 (M-CO, 12), 223 (14), 152 (22), 135 (81), 107 (28), 92 (36), 91 (89), 77 (33), 57 (81), 43 (43), 32 (96), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.82-1.91 (m, 4H, H-6 and H-7), 2.54-2.63 (m, 4H, H-5 and H-8), 3.81 (s, 3H, OCH_3), 6.90 (d, J = 8.74 Hz, aromatic H), 7.02 (s, 1H, H-3), 7.69 (d, J = 8.74 Hz, 2H, aromatic H); ^{13}C nmr (deuteriochloroform): δ 19.8, 21.7, 22.0, 22.1, 55.2 (OCH_3), 99.8 (C-3), 113.8 (C-3', aromatic C), 118.2 (C-1', aromatic C), 125.8 (C-2', aromatic C), 127.6 (C-2), 142.3 (C-8a), 145.0 (C-4a), 155.1 (C-9a), 158.5 (C-4', aromatic C).

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.63; H, 6.01; N, 10.44. Found: C, 71.93; H, 6.22; N, 10.50.

2-(2'-Naphthyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzoxazole (**11r**).

This was prepared in a similar procedure from 2-imino-3-(2'-naphthacyl)-2,3,4,5,6,7-hexahydrobenzoxazole (**10r**) (1.0 g, 3.27 mmoles) and recrystallized from ethanol. It formed brown crystals (0.80 g, 85%) mp 187-189°; ir (potassium bromide): 1620 cm^{-1}; ms: m/z (%) 288 (M^+, 29), 260 (M-CO, 14), 127 (10), 90 (29), 89 (41), 84 (27), 82 (41), 51 (17), 49 (13), 32 (55), 28 (100); ^{1}H nmr (deuteriochloroform): δ 1.84-1.93 (m, 4H, H-6 and H-7), 2.55-2.63 (m, 4H, H-5 and H-8), 7.22 (s, 1H, H-3), 7.44 (d, J = 9.0 Hz, 1H, naphthalene H), 7.79-7.89 (m, 4H, naphthalene H), 8.31 (s, 1H, naphthalene H); ^{13}C nmr (deuteriochloroform): δ 19.8, 21.7, 22.1, 22.1, 101.4 (C-3), 118.2, 122.8, 123.3, 125.2, 126.1, 127.6, 127.9, 128.1, 132.2, 132.6, 133.8, 142.5 (C-8a), 145.5 (C-4a), 155.4 (C-9a).

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.15; H, 5.59; N, 9.71. Found: C, 79.28; H, 5.62; N, 9.92.

1,4-Bis[2-(5',6',7',8'-tetrahydroimidazo[2,1-*b*]benzoxazolyl)]-benzene (**17**).

The imine compound **16** (1.0 g, 2.3 mmoles) was suspended in sodium dried toluene (30 ml) and cooled in a bath of ice-salt (-10°). To this magnetically stirred heterogenous mixture, was added dry titanium(IV) chloride (2.18 g, 11.5 mmoles) under a nitrogen atmosphere, dropwise over 45 minutes. After the addition was complete the ice bath was removed and the reaction mixture was allowed to warm to room temperature during 30 minutes, followed by reflux for an additional two hours. It was then cooled to room temperature and poured into crushed ice (~30 g), and neutralised with aqueous sodium carbonate solution. The organic layer was separated. The aqueous phase was further extracted with dichloromethane (3 x 40 ml). The combined organic phase was passed through a short column of potassium carbonate, collected and dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue was triturated with diethyl ether/petroleum ether (60-80°). The brown solid was filtered off, and formed a brown solid (0.44 g, 46%) mp 234-238°; ir (potassium bromide): 1615 cm^{-1}; ms: m/z (%) 398 (M^+, 23), 265 (32), 202 (8), 139 (10), 105 (13), 91 (18), 78 (35), 57 (22), 44 (100); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.93-1.97 (m, 8H, H-6 and H-7), 2.59-2.68 (m, 8H, H-5 and H-8), 7.19 (s, 2H, H-3), 7.83 (s, 4H, aromatic H).

Anal. Calcd. for $C_{24}H_{22}N_4O_2$: C, 72.35; H, 5.57; N, 14.06. Found: C, 72.04; H, 5.89; N, 13.68.

Crystal Data and Structure Determination.

Reflexion data were measured with an Enraf-Nonius CAD-4 diffractometer in θ/2θ scan mode using nickel filtered copper radiation (λ 1.5418Å). Data were corrected for absorption using the analytical method of de Meulenaer and Tompa [22]. Reflexions with $I > 3\sigma(I)$ were considered observed. The structure was determined by direct phasing and Fourier methods. Hydrogen atoms were included in calculated positions, and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full matrix least squares. Reflexion weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual is defined as $R_w=(\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray Crystallography [23]. Structure solution was by MULTAN80 [24] and refinement used BLOCKLS, a local version of ORFLS [25]. ORTEP-II [26] running on a Macintosh IIcx was used for the structural diagram, and a DEC Alpha-AXP workstation was used for calculations.

Compound **11n** with formula $C_{15}H_{13}BrN_2O$ has molecular weight 317.2, triclinic, space group $P^-{}_1$, a 7.078(1), b 7.574(1), c 13.511(1)Å, α 74.71(1), β 88.42(1), γ 70.46(1)°, V 657.0(2)Å^3, D_c 1.60 g cm^{-3}, Z 2, μ_{Cu} 42.23 cm^{-1}, $2\theta_{max}$ 140°. The number of reflexions was 2124 considered observed out of 2493 unique data. Final residuals R, R_w were 0.032, 0.048.

The structure and atom numbering scheme is shown in Figure 1. Bond lengths, bond angles, and selected atomic parameters are given in Tables 2-4 respectively. Supplementary material comprises all atom and thermal parameters, inter atomic distances, angles and torsional angles, and observed and calculated structure factors.

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