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Synthesis of 1-(substituted phenyl)-2-phenyl-4-(2′-hydroxy-3′-iodo-5′-chloro-benzylidene)imidazol-5-ones

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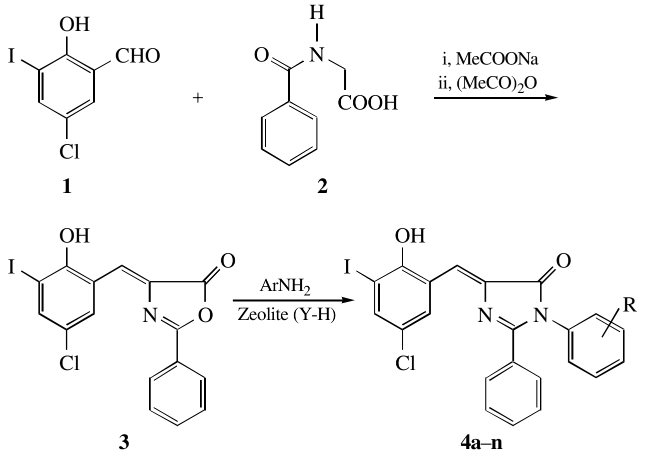
The title compounds were prepared by treating a mixture of 5-oxazolone derivatives with substituted aromatic amines in the presence of a zeolite (Y-H) catalyst.

Imidazolones exhibit several pharmacological activities.[1–4] Imidazolidinones have been reported to possess a potent CNS depressant activity. Some imidazoles and substituted imidazolones have been reported to possess monoamine oxidase (MAO) inhibitory and anticonvulsant activities.[5,6] This observation prompted us to synthesise new 1-(substituted phenyl)-2-phenyl-4-(2′-hydroxy-3′-iodo-5′-chlorobenzylidene)imidazol-5-one by a new method.

Earlier, imidazolones **4** have been prepared by heating a mixture of 5-oxazolone derivative **3**[†] with aromatic amines in the presence of pyridine for 10–15 h. The yield of imidazolones **4** was very low, and the reaction took a long time.[7–9]



a R = H
b R = 3-NO$_2$
c R = 4-NO$_2$
d R = 4-Br
e R = 4-I
f R = 2-OMe
g R = 3-OMe
h R = 4-OMe
i R = 2-Cl
j R = 4-Cl
k R = 3-Me
l R = 4-Me
m R = 2-COOH
n R = 4-COOH

Scheme 1

We synthesised new imidazolones **4**[‡] by the condensation of aromatic amines with compound **3** in the presence of zeolite (Y-H) (Scheme 1). The reaction took place in 3–5 h with excellent yields. The 5-oxazolone derivative (ozalactone) was prepared by the condensation of hippuric acid with 2-hydroxy-3-iodo-5-chlorobenzaldehyde in the presence of sodium acetate and acetic anhydride. The compounds were crystallised from ethanol and identified by elemental analysis and spectroscopic data.

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[†] Melting points (uncorrected) were determined in open capillary tubes. The purity of compounds was checked by TLC using silica gel G. The IR spectra in Nujol were recorded on a Perkin–Elmer 237 spectrophotometer. The ^{1}H NMR spectra in CDCl$_3$ were recorded on a Perkin–Elmer R-32 spectrometer using TMS as an internal standard.

General procedure for the preparation of 2-phenyl-4-(2'-hydroxy-3'-iodo-5-chlorobenzylidene)oxazol-5-one **3**: 2-hydroxy-3-iodo-5-chlorobenzaldehyde (10 mmol), hippuric acid (10 mmol), acetic anhydride (30 mmol) and sodium acetate (10 mmol) were heated on an electric hot plate with continuously shaking in a conical flask. As soon as the mixture was liquified completely, the flask was heated in a water bath for 2 h. Ethanol (5 ml) was added slowly to the contents of the flask, and the mixture was allowed to stand overnight. The separated crystalline solid was filtered off and successively washed with ice-cold ethanol and hot water to obtain **3**; yield 347 mg (82%), mp 127 °C. ^{1}H NMR, δ: 6.8 (s, 1H, Ph–C*H*), 7.2–7.8 (m, 7H, Ar–*H*), 9.9 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1605, 1610–1580, 1660–1650, 3720. Found (%): C, 48.45; H, 2.84; N, 3.32. Calc. for $C_{16}H_9NO_3ICl$ (%): C, 48.48; H, 2.87; N, 3.33.

[‡] *General procedure for the preparation of 1-(substituted phenyl)-2-phenyl-4-(2'-hydroxy-3'-iodo-5'-chlorobenzylidene)imidazole-5-one* **4**: oxazolone **3** (10 mmol) was heated with an equimolar quantity of an aromatic amine in pyridine (10 mmol) with a zeolite (Y-H) catalyst in an oil bath at 150 °C for 3–5 h. The excess of pyridine was distilled off. The mixture was cooled and poured into crushed ice and HCl. The product was filtered off and crystallised from ethanol to give **4a**–**n**.

4a: yield 95%, mp 130 °C. ^{1}H NMR, δ: 6.9 (s, 1H, Ph–C*H*), 7.1–8.2 (m, 12H, Ar–*H*), 9.7 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1610, 1615–1580, 1655–1635, 3680. Found (%): C, 52.72; H, 2.77; N, 5.55. Calc. for $C_{22}H_{14}N_2O_2ICl$ (%): C, 52.77; H, 2.82; N, 5.59.

4b: yield 85%, mp 105 °C. ^{1}H NMR, δ: 6.7 (s, 1H, Ph–C*H*), 7.2–8.2 (m, 11H, Ar–*H*), 9.9 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1620–1610, 1615–1575, 1650–1635, 3680. Found (%): C, 48.38; H, 2.36; N, 7.65. Calc. for $C_{22}H_{13}N_3O_4ICl$ (%): C, 48.42; H, 2.40; N, 7.70.

4c: yield 92%, mp 160 °C. ^{1}H NMR, δ: 6.9 (s, 1H, Ph–C*H*), 7.3–8.4 (m, 11H, Ar–*H*), 9.8 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1620–1615, 1618–1585, 1650–1635, 3675. Found (%): C, 48.40; H, 2.35; N, 7.66. Calc. for $C_{22}H_{13}N_3O_4ICl$ (%): C, 48.42; H, 2.40; N, 7.70.

4d: yield 98%, mp 145 °C. ^{1}H NMR, δ: 7.0 (s, 1H, Ph–C*H*), 7.0–8.2 (m, 11H, Ar–*H*), 9.7 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1610, 1615–1585, 1650–1635, 3670. Found (%): C, 45.54; H, 2.22; N, 4.75. Calc. for $C_{22}H_{13}N_2O_2BrICl$ (%): C, 45.59; H, 2.26; N, 4.83.

4e: yield 93%, mp 111 °C. ^{1}H NMR, δ: 6.8 (s, 1H, Ph–C*H*), 7.1–8.3 (m, 11H, Ar–*H*), 9.6 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1620–1610, 1620–1585, 1655–1630, 3690. Found (%): C, 42.12; H, 2.02; N, 4.43. Calc. for $C_{22}H_{13}N_2O_2I_2Cl$ (%): C, 42.17; H, 2.09; N, 4.47.

4f: yield 90%, mp 118 °C. ^{1}H NMR, δ: 3.9 (s, 3H, OMe), 6.8 (s, 1H, Ph–C*H*), 7.2–8.4 (m, 11H, Ar–*H*), 9.9 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1630–1610, 1615–1580, 1665–1635, 3670. Found (%): C, 52.00; H, 2.98; N, 5.23. Calc. for $C_{23}H_{16}N_2O_3ICl$ (%): C, 52.05; H, 3.04; N, 5.28.

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4g: yield 89%, mp 95 °C. ^{1}H NMR, δ: 4.1 (s, 3H, OMe), 6.6 (s, 1H, Ph–C*H*), 7.0–8.5 (m, 11H, Ar–*H*), 9.5 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1620–1610, 1615–1575, 1655–1645, 3675. Found (%): C, 52.08; H, 2.95; N, 5.21. Calc. for $C_{23}H_{16}N_2O_3ICl$ (%): C, 52.05; H, 3.04; N, 5.28.

4h: yield 95%, mp 135 °C. ^{1}H NMR, δ: 4.0 (s, 3H, OMe), 7.0 (s, 1H, Ph–C*H*), 7.3–8.3 (m, 11H, Ar–*H*), 9.9 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1610, 1615–1580, 1655–1635, 3680. Found (%): C, 52.00; H, 3.01; N, 5.24. Calc. for $C_{23}H_{16}N_2O_3ICl$ (%): C, 52.05; H, 3.04; N, 5.28.

4i: yield 86%, mp 121 °C. ^{1}H NMR, δ: 7.0 (s, 1H, Ph–C*H*), 7.4–8.4 (m, 11H, Ar–*H*), 9.7 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1615, 1620–1580, 1645–1635, 3685. Found (%): C, 49.35; H, 2.40; N, 5.20. Calc. for $C_{22}H_{13}N_2O_2ICl_2$ (%): C, 49.38; H, 2.45; N, 5.23.

4j: yield 93%, mp 147 °C. ^{1}H NMR, δ: 6.9 (s, 1H, Ph–C*H*), 7.2–8.2 (m, 11H, Ar–*H*), 9.8 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1610, 1615–1580, 1655–1635, 3680. Found (%): C, 49.33; H, 2.42; N, 5.18. Calc. for $C_{22}H_{13}N_2O_2ICl_2$ (%): C, 49.38; H, 2.45; N, 5.23.

4k: yield 97%, mp 127 °C. ^{1}H NMR, δ: 2.4 (s, 3H, Me), 6.6 (s, 1H, Ph–C*H*), 7.2–8.2 (m, 11H, Ar–*H*), 9.6 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1615, 1620–1575, 1650–1635, 3690. Found (%): C, 53.64; H, 3.09; N, 5.88. Calc. for $C_{23}H_{16}N_2O_2ICl$ (%): C, 53.67; H, 3.13; N, 5.94.

4l: yield 90%, mp 155 °C. ^{1}H NMR, δ: 2.3 (s, 3H, Me), 6.7 (s, 1H, Ph–C*H*), 7.2–8.0 (m, 11H, Ar–*H*), 9.7 (s, 1H, Ar–O*H*). IR, ν/cm^{-1}: 1625–1610, 1620–1580, 1655–1635, 3685. Found (%): C, 53.61; H, 3.08; N, 5.89. Calc. for $C_{23}H_{16}N_2O_2ICl$ (%): C, 53.67; H, 3.13; N, 5.94.

4m: yield 85%, mp 170 °C. ^{1}H NMR, δ: 6.6 (s, 1H, Ph–C*H*), 7.2–8.3 (m, 11H, Ar–*H*), 9.8 (s, 1H, Ar–O*H*), 10.2 (s, 1H, COOH). IR, ν/cm^{-1}: 1625–1610, 1630–1580, 1655–1645, 2955–2670, 3685. Found (%): C, 50.66; H, 2.55; N, 5.10. Calc. for $C_{23}H_{14}N_2O_4ICl$ (%): C, 50.71; H, 2.59; N, 5.14.

4n: yield 91%, mp 165 °C. ^{1}H NMR, δ: 6.8 (s, 1H, Ph–C*H*), 7.2–8.2 (m, 11H, Ar–*H*), 9.8 (s, 1H, Ar–O*H*), 10.5 (s, 1H, COOH). IR, ν/cm^{-1}: 1625–1610, 1635–1580, 1650–1645, 2975–2575, 3675. Found (%): C, 50.65; H, 2.53; N, 5.11. Calc. for $C_{23}H_{14}N_2O_4ICl$ (%): C, 50.71; H, 2.59; N, 5.14.