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A simple and efficient method for the synthesis of Erlenmeyer azlactones

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ABSTRACT

We have recently developed a novel and efficient method for synthesising Erlenmeyer azlactones under mild and rapid conditions. The reaction is performed by reacting 2-phenyl-5-oxazolone with an aldehyde in dichloromethane using alumina as a catalyst. The materials react instantly at room temperature, negating the need for high temperatures and long reaction times. We have successfully used this method for both aliphatic, aromatic and heteroaromatic aldehydes, synthesising previously unmade Erlenmeyer azlactones in moderate to high yields.

1. Introduction

The Erlenmeyer reaction was first described in 1893 by Friedrich Gustav Carl Emil Erlenmeyer[1] who condensed benzaldehyde with *N*-acetylglycine in the presence of acetic anhydride and sodium acetate. The reaction goes via a Perkin condensation following the initial cyclisation of the *N*-acetylglycine[2] yielding the so-called Erlenmeyer azlactones. Erlenmeyer azlactones have been used in a wide variety of reactions as precursors for biologically active peptides,[3] herbicides and fungicides,[4] and as drugs, pesticides and agrochemical intermediates.[5] They have been used in active site titrations of enzymes,[6] as antihypertensives[7] and in the asymmetric synthesis of amino acids.[8]

The classical reaction has remained the same over the last century with certain modernisations over the past decade. C. Yu et al. described the use of an ytterbium(III) triflate catalysed reaction under solvent-free conditions,[9] while microwaves have also been employed successfully in the synthesis of these azlactones.[10,11]

A major drawback to both the classical and more modern procedures is the inability to synthesise aliphatic azlactones as the aliphatic aldehydes are unstable under the required reaction conditions. Chandrasekhar et al. have explored this problem and given reason for the possible failure of this reaction.[10] To overcome this limitation, they report a modified procedure, which involves the use of a commercial microwave and alumina (solid phase) as the basic catalyst. This prevented the self-condensation of the aldehydes, which is usually observed where stronger bases such as sodium acetate are employed. Finally, microwave irradiation provided high temperatures that possibly facilitate diffusion of the reactants on the surface of alumina, promoting the condensation step in which water is eliminated from the intermediate. The yields reported for the aliphatic aldehydes are, nonetheless, rather low.

Here we report a modified version of the above procedure, which leads to the synthesis of novel Erlenmeyer azlactones in moderate to high yields. Even with the most modern methods, the self-condensation of *N*-acetylglycine yields a very unstable intermediate, which cannot be isolated. This implies that the second step of the condensation must take place in the same reaction vessel without the possibility of fine-tuning the conditions, which would optimise the yield of the product. While aromatic aldehydes generally are fast reacting and yields achieved are good, where aliphatic aldehydes have been employed, the final yield is less than 30% (see table below). Our strategy involved first the optimised synthesis of a more stable intermediate by self-condensing hippuric acid. Although this reaction has been previously reported in the literature, the yields were always quite moderate (56%)[12] while we were able to reach 88%. Secondly, the condensations of a broad range of aldehydes were successfully achieved under solvent-free condition and at room temperature.

2. Results and discussions

The condensation of hippuric acid (**1**) was achieved as previously reported[12] (Scheme 1), however the work-up conditions were slightly altered to accommodate for the compound's instability. The reaction was heated to 90 °C and allowed to stir until all the hippuric acid had gone into solution. It was then quenched

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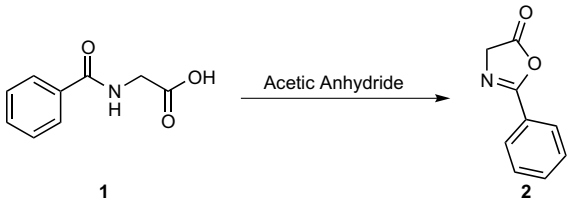
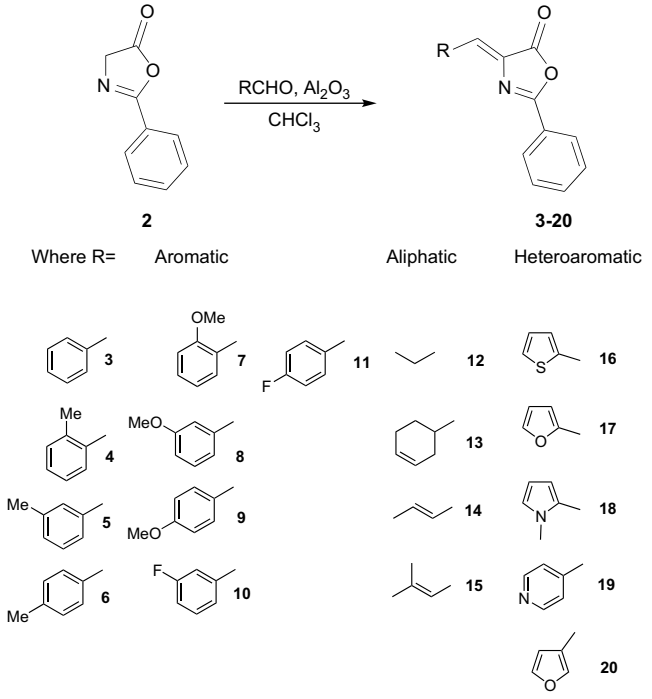
using iced water and diethyl ether at 0 °C, and the organic layer was washed using 10% sodium bicarbonate and dried over $MgSO_4$. The solvent was removed on a rotary evaporator, with particular attention to the temperature (kept below 40 °C). The yellow powder was then recrystallised from ethanol to yield pale yellow needles of 2-phenyloxazol-5-one (88%).



Scheme 1. The condensation of hippuric acid (**1**) to 2-phenyloxazol-5-one (**2**).

The aldehydes and compound **2** were dissolved in a minimal amount of dichloromethane and the mixture adsorbed onto 10 equiv of alumina. Despite what Chandrasekhar et al. reported, the use of the microwave is superfluous and in many cases detrimental to the overall yield. The reaction progresses quickly upon adsorption onto alumina and can be monitored by TLC (diethyl ether/pentane 55:45) (Scheme 2).



Scheme 2. Synthesis of 2-phenyl-Erlenmeyer azlactones: Perkin condensation of 2-phenyloxazol-5-one (**2**) and aldehydes (**3**–**20**) with alumina acting as a mild base.

We have successfully used this method for both aromatic (**3**–**11**), aliphatic (**12**–**15**) and heteroaromatic (**16**–**20**) aldehydes, synthesising previously unmade Erlenmeyer azlactones in moderate to high yields (Table 1).

We were able to condense aliphatic aldehydes in good yields and in any case with a dramatic improvement when we tested aldehydes previously reported and compared results. Compound (**13**) was synthesised with a threefold increase when the procedure was performed without the microwave step. With this methodology, even yields of aromatic and heteroaromatic products were noticeably improved: the oxazolone (**17**), for example, gave an overall yield of 71% with again over threefold increase on what had been achieved via the classical method.

Table 1
Comparison of yields (%) of the novel method with the microwave[10] and the classical[13,14] Erlenmeyer procedures[a]

	Yield %		
	Novel	Microwave	Classical
Aromatic aldehydes			
C_6H_5CHO (**3**)	88	45	63
2-MeC_6H_5CHO (**4**)	52	—	—
3-MeC_6H_5CHO (**5**)	76	—	—
4-MeC_6H_5CHO (**6**)	87	41	80
2-$MeOC_6H_5CHO$ (**7**)	89	43	—
3-$MeOC_6H_5CHO$ (**8**)	73	43	67
4-$MeOC_6H_5CHO$ (**9**)	88	60	64
3-FC_6H_5CHO (**10**)	87	—	74
4-FC_6H_5CHO (**11**)	96	30	—
Aliphatic aldehydes			
n-PrCHO (**12**)	74	65[10]	46
3-CyclohexeneCHO (**13**)	33	13	—
$CH_3CH{=}CHCHO$ (**14**)	49	—	—
$(CH_3)_2C{=}CHCHO$ (**15**)	61	—	—
Heteroaromatic aldehydes			
2-ThiopheneCHO (**16**)	70	—	56
2-FuranCHO (**17**)	71	—	23
2-*N*-Methylpyrrole (**18**)	45	—	11
4-PyridineCHO (**19**)	45	—	—
3-FuranCHO (**20**)	66	—	—

[a] The classical reactions were carried out as described by Kitazawa et al.;[14] heating a mixture of the aldehyde, hippuric acid and sodium acetate in acetic anhydride at 60 °C for approx. 3 h. The reaction was then left to cool, and poured over ice. The resulting precipitate was filtered and recrystallised from aqueous acetone. The microwave yields were obtained using Chandrasekhar et al.[10] general procedure, with differences in reaction timing and temperatures necessary for our microwave. The aldehydes and 2-phenyloxazol-5-one were adsorbed onto the alumina and irradiated in a CEM S-Class microwave oven at 300 W for 90 s, allowing a maximum temperature of 80 °C. The yield for compound (**12**) however was directly reported from the paper.

Compounds **5**, **15** and **20** have not been reported in the literature before hence we fully characterised them.

The products were generally purified by silica gel chromatography in diethyl ether/pentane (55:45). However, some of the compounds, e.g., 4-(3-methoxybenzylidene)-2-phenyloxazol-5-one (**8**), presented a very small R_f with their corresponding aldehydes, thus making column chromatography difficult. In these cases the azlactones could be recrystallised from aqueous acetone.

3. Conclusions

In conclusion, we have reported here an efficient procedure, which can be applied to the synthesis of aliphatic and (hetero)-aromatic azlactones in good yields. The solvent-free conditions and the efficiency of the solid catalyst at room temperature make this method also environmentally friendly. The high yields achieved with this procedure together with the versatility of the synthetic strategy have allowed for a broad range of new substrates to be synthesised and it should be applicable to many more.

4. Experimental

4.1. General

All chemicals and solvents were obtained from commercial sources and used without further purification. NMR solvents were purchased from Apollo Scientific Ltd. All ^1H and ^{13}C NMR spectra were obtained on Varian 300, 400 and 500 MHz spectrometers and referenced to internal tetramethylsilane (TMS) at 0.0 ppm. The spin multiplicities are indicated by the symbols s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet) and m (multiplet). Reactions were monitored by thin-layer chromatography (TLC)

using Merck TLC silica gel 60 F_{254} plates. Column chromatography was performed using Merck silica gel 60 (00040–0.063 mm) and eluted with the indicated solvent system. The alumina used in the reaction was Merck aluminium oxide 90 standardised. Microwave reactions were carried out on a CEM S-Class microwave.

4.2. Synthesis of 2-phenyloxazol-5-one (2)[12]

Hippuric acid (2 g, 11.16 mmol) and acetic anhydride (13 mL) were heated on a water bath for 30 min with constant stirring. The reaction mixture was then cooled and poured over iced water (20 mL) and diethyl ether (20 mL). This was then stirred for a further 15 min. The organic layer was separated and washed with sodium hydrogen carbonate (1%, 4×50 mL) until all traces of acetic anhydride were removed. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to leave the product, a bright yellow solid, which was recrystallised from ethanol yielding yellow needles (1.58 g, 88%), mp 84–86 °C (lit. mp 86).[12] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04–7.96 (m, 2H), 7.59 (t, J=7.4, 1H), 7.49 (t, J=7.4, 2H), 4.42 (s, 2H); MI^+ 161.9, MI^- 160.0; R_f in pentane/diethyl ether (50:50) 0.4.

4.3. General synthesis of 4-(2-phenyloxazol)-5-ones

The aldehydes (2.5 mmol, 2.5 equiv) and 2-phenyloxazol-5-one (0.161 g, 1 mmol, 1 equiv) were dissolved in chloroform and alumina (10 equiv) was added to the mixture and swirled. The chloro form was removed in vacuo. The product was isolated over SiO_2 in diethyl ether/pentane (55:45).

4.3.1. 4-Benzylidene-2-phenyloxazol-5-one (**3**)

Bright yellow needles, 88%, mp 167–168 °C (lit. mp 168–169).[15] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22–8.20 (m, 2H), 8.20–8.17 (m, 2H), 7.61 (t, J=7.4, 1H), 7.53 (t, J=7.7, 2H), 7.51–7.42 (m, 3H), 7.25 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 110.0, 125.6, 128.4, 128.8, 128.9, 131.2, 131.8, 132.4, 133.3, 133.5, 163.6, 167.6; IR (KBr) 1784.58, 1724.79, 1648.08, 1553.87, 1449.25, 1295.45, 984.00, 865.88, 767.05 cm^{-1}. Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 76.94; H, 4.53; N, 5.87.

4.3.2. 4-(2-Methylbenzylidene)-2-phenyloxazol-5-one (**4**)

Dark yellow solid, 52%, mp 140–142 °C (lit. mp 141).[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (dt, J=4.9, 2.8, 1H), 8.21–8.16 (m, 2H), 7.64–7.58 (m, 1H), 7.55 (dd, J=5.6, 4.2, 2H), 7.52 (dd, J=4.9, 3.3, 1H), 7.37–7.33 (m, 2H), 7.26 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.0, 125.6, 126.5, 128.4, 128.6, 128.9, 130.7, 131.1, 132.0, 132.2, 133.2, 133.3, 139.9, 163.7, 167.8; IR (KBr) 1797.07, 1647.40, 1596.78, 1552.90, 1448.28, 1325.82, 1296.20, 1168.17, 978.70, 862.51, 767.05 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.54; H, 4.86; N, 5.44.

4.3.3. 4-(3-Methylbenzylidene)-2-phenyloxazol-5-one (**5**)

Bright yellow solid, 76%, mp 125–127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (dt, J=4.9, 2.8, 1H), 8.21–8.16 (m, 2H), 7.64–7.58 (m, 1H), 7.55 (dd, J=5.6, 4.2, 2H), 7.52 (dd, J=4.9, 3.3, 1H), 7.37–7.33 (m, 2H), 7.26 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.4, 125.7, 128.3, 128.8, 128.9, 129.7, 132.1, 132.1, 133.1, 133.2, 133.3, 133.5, 138.5, 163.4, 167.7; IR (KBr) 1785.77, 1647.88, 1596.55, 1555.80, 1487.33, 1449.25, 1324.86, 1294.97, 1168.34, 975.60, 862.23, 764.89 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.56; H, 4.92; N, 5.38.

4.3.4. 4-(4-Methylbenzylidene)-2-phenyloxazol-5-one (**6**)

Bright yellow solid, 87%, mp 143–144 °C (lit. mp 141).[15] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19–8.16 (m, 2H), 8.10 (d, J=8.1, 2H), 7.62–7.58 (m, 1H), 7.52 (dd, J=10.5, 4.6, 2H), 7.28 (d, J=8.0, 2H), 7.23 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.3, 125.6, 128.0, 128.6, 128.9, 129.6, 132.1, 132.3, 133.1, 133.3, 133.4, 133.6, 139.0, 163.5, 167.7; IR (KBr) 1792.52, 1645.95, 1605.45, 1554.86, 1489.75, 1327.75, 1925.45, 1161.42, 1107.42, 983.52, 858.65, 815.74 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.49; H, 4.96; N, 5.34.

4.3.5. 4-(2-Methoxybenzylidene)-2-phenyloxazol-5-one (**7**)

Bright yellow solid, 89%, mp 156–157 °C (lit. mp 154).[16] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (dd, J=7.9, 1.5, 1H), 8.20–8.15 (m, 2H), 7.87 (s, 1H), 7.59 (t, J=7.4, 1H), 7.52 (t, J=7.6, 2H), 7.45–7.39 (m, 1H), 7.09 (t, J=7.6, 1H), 6.93 (d, J=8.3, 1H), 3.91 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.7, 110.0, 110.8, 121.0, 122.7, 125.8, 126.0, 128.2, 128.9, 132.5, 132.9, 133.0, 133.1, 159.3, 163.0, 167.8; IR (KBr) 1790.59, 1649.81, 1595.81, 1556.76, 1483.96, 1464.67, 1326.31, 1291.11, 1248.20, 1223.13, 1166.72, 1023.05, 983.52, 871.67, 754.99 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 72.98; H, 4.64; N, 4.98.

4.3.6. 4-(3-Methoxybenzylidene)-2-phenyloxazol-5-one (**8**)

Yellow solid, 73%, mp 99–102 °C (lit. mp 102–104).[17] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J=7.6, 2H), 7.94 (s, 1H), 7.62 (t, J=7.4, 1H), 7.53 (t, J=7.6, 2H), 7.38 (t, J=8.0, 1H), 7.23 (s, 1H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.3, 116.6, 117.7, 125.4, 125.6, 128.3, 128.9, 129.8, 131.7, 133.4, 133.4, 134.7, 159.8, 163.6, 167.5; IR (KBr) 1798.78, 1665.11, 1602.08, 1576.04, 1489.75, 1430.44, 1329.20, 1280.51, 1199.03, 1167.21, 1040.41, 982.07, 879.35, 849.49, 768.98 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.08; H, 4.67; N, 5.04.

4.3.7. 4-(4-Methoxybenzylidene)-2-phenyloxazol-5-one (**9**)

Orange Solid, 88%, mp 157–158 °C (lit. mp 157).[15] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J=8.8, 2H), 8.16 (d, J=7.4, 2H), 7.59 (t, J=7.4, 1H), 7.52 (t, J=7.5, 2H), 7.21 (s, 1H), 7.00 (d, J=8.9, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.4, 114.5, 125.9, 126.6, 128.1, 128.9, 131.1, 131.9, 133.0, 134.6, 162.2, 162.5, 167.9; IR (KBr) 1789.14, 1770.82, 1654.15, 1596.78, 1512.40, 1448.76, 1309.91, 1266.52, 1162.39, 1031.25, 831.65 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.24; H, 4.72; N, 5.14.

4.3.8. 4-(3-Fluorobenzylidene)-2-phenyloxazol-5-one (**10**)

Pale yellow powder, 87%, mp 158–159 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J=7.7, 2H), 8.14 (d, J=10.1, 1H), 7.79 (d, J=7.7, 1H), 7.63 (t, J=7.4, 1H), 7.54 (t, J=7.7, 2H), 7.43 (td, J=8.0, 6.1, 1H), 7.19 (s, 1H), 7.15 (td, J=8.3, 2.4, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 118.0, 118.2, 118.3, 118.4, 125.3, 128.4, 128.5, 128.6, 128.7, 128.9, 129.0, 129.8, 129.9, 130.2, 130.3, 133.6, 134.3, 135.4, 135.5, 161.8, 163.8, 164.2, 167.2; IR (KBr) 1792.52, 1658.97, 1582.31, 1556.28, 1488.78, 1445.87, 1366.80, 1324.86, 1258.33, 1166.24, 1150.81, 952.66, 864.92 cm^{-1}. Anal. Calcd for $C_{16}H_{10}FNO_2$: C, 71.91; H, 3.77; F, 7.11; N, 5.24. Found: C, 71.86; H, 3.89; F, 7.25; N, 5.37.

4.3.9. 4-(4-Fluorobenzylidene)-2-phenyloxazol-5-one (**11**)

Pale yellow powder, 96%, mp 183–185 °C (lit. mp 181–182).[18] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26–8.21 (m, 2H), 8.18 (dd, J=5.3, 3.3, 2H), 7.62 (ddd, J=6.6, 3.9, 1.3, 1H), 7.57–7.50 (m, 2H), 7.21 (d, J=4.1, 1H), 7.20–7.13 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 110.0, 116.1, 116.3, 128.4, 128.9, 130.3, 130.4, 133.4, 134.6, 134.7, 163.0, 163.7, 167.5; IR (KBr) 1796.86, 1770.34, 1660.90, 1596.78, 1556.76, 1505.66, 1325.34, 1294.97, 1235.19, 1157.08, 1094.89, 984.97, 834.06 cm^{-1}. Anal. Calcd for $C_{16}H_{10}FNO_2$: C, 71.91; H, 3.77; F, 7.11; N, 5.24. Found: C, 72.05; H, 3.92; F, 7.36; N, 5.34.

4.3.10. 2-Phenyl-4-propylideneoxazol-5-one (**12**)

Beige needles, 62%, mp 86–87 °C (lit. mp 85–86).[19] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J=7.6, 2H), 7.58 (t, J=7.4, 1H), 7.50

(t, *J*=7.7, 2H), 6.68 (t, *J*=7.9, 1H), 2.70 (m, 2H), 1.20 (t, *J*=7.6, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 12.9, 22.2, 125.7, 128.1, 128.8, 133.0, 135.7, 141.0, 162.6, 166.2; IR (KBr) 3069.65, 2964.07, 2837.48, 1798.78, 1748.64, 1673.91, 1559.19, 876.49, 849.97, 779.10 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.85; H, 5.65; N, 6.74.

*4.3.11. 4-Cyclohex-3-enylmethylene-2-phenyloxazol-5-one (**13**)*

White powder, 33%, mp 109–110 °C (lit. mp 109–110).[20] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J*=8.0, 2H), 7.58 (t, *J*=7.4, 1H), 7.49 (t, *J*=7.7, 2H), 6.64 (d, *J*=9.9, 1H), 5.82–5.67 (m, 2H), 3.38–3.27 (m, 1H), 2.26 (t, *J*=14.8, 1H), 2.22–2.13 (m, 2H), 2.09–1.99 (m, 1H), 1.94–1.85 (m, 1H), 1.72–1.60 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.1, 27.9, 30.5, 34.0, 125.2, 125.9, 127.3, 128.4, 129.1, 133.3, 135.4, 143.7, 162.9, 166.7; IR (KBr) 3025.78, 2976.52, 2913.93, 2845.26, 2834.86, 1805.53, 1671.02, 1605.44, 1568.33, 1491.67, 1453.10, 878.42, 861.00, 842.74, 781.03 cm^{-1}. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.02; H, 5.84; N, 5.72.

*4.3.12. 4-(But-2-enylidene)-2-phenyloxazol-5-one (**14**)*

White powder, 49%, mp 154–156 °C (lit. mp 154).[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14–8.06 (m, 2H), 7.61–7.55 (m, 1H), 7.49 (dd, *J*=9.7, 5.3, 2H), 6.97 (d, 1H), 6.52–6.37 (m, 1H), 2.02 (d, *J*=7.1, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.4, 127.3, 128.0, 128.8, 132.5, 132.9, 133.2, 144.2, 145.5, 161.9, 167.0; IR (KBr) 3034.94, 2962.14, 2938.03, 2913.44, 1789.14, 1762.14, 1654.63, 1556.76, 1449.73, 977.25, 882.27, 860.58, 780.37 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_2$ requires: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.31; H, 5.27; N, 6.48.

*4.3.13. 4-(3-Methylbut-2-enylidene)-2-phenyloxazol-5-one (**15**)*

Bright yellow solid, 61%, mp 113–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J*=7.2, 2H), 7.56 (dd, *J*=10.4, 4.3, 1H), 7.49 (t, *J*=7.4, 2H), 7.26 (d, *J*=3.6, 1H), 6.84 (d, *J*=12.2, 1H), 2.04 (d, *J*=10.9, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.5, 27.3, 121.6, 125.9, 127.9, 128.8, 129.4, 132.0, 132.8, 152.7, 161.5, 167.4; IR (KBr) 3056.15, 2970.33, 2910.55, 2850.77, 1783.36, 1664.99, 1589.28, 1448.76, 871.67, 774.28 cm^{-1}. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.18; H, 5.82; N, 6.08.

*4.3.14. 2-Phenyl-4-(2-thiophenyl)-5-oxazolone (**16**)*

Bright yellow solid, 70%, mp 174–175 °C (lit. mp 175).[21] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20–8.14 (m, 2H), 7.72 (d, *J*=5.1, 1H), 7.63 (d, *J*=3.7, 1H), 7.62–7.58 (m, 1H), 7.52 (t, *J*=7.6, 2H), 7.48 (s, 1H), 7.16 (dd, *J*=5.0, 3.8, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 124.8, 125.6, 127.9, 128.3, 128.9, 130.9, 133.1, 134.9, 135.3, 137.6, 162.5, 166.9; IR (KBr) 3445.71, 3424.01, 1791.55, 1770.82, 1643.54, 1554.35, 1415.02, 855.76, 783.56 cm^{-1}. Anal. Calcd for $C_{14}H_9NO_2S$: C, 65.87, H, 3.55, N, 5.49, S, 12.56. Found: C, 65.64, H, 3.66, N, 5.40, S, 12.40.

*4.3.15. 2-Phenyl-4-(2-furanyl)-5-oxazolone (**17**)*

Bright yellow powder, 71%, mp 175–176 °C (lit. mp 175).[22] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19–8.14 (m, 1H), 7.69 (d, *J*=1.2, 1H), 7.60 (dd, *J*=14.1, 5.5, 2H), 7.51 (dd, *J*=18.0, 11.0, 2H), 7.26 (s, 1H), 7.19 (s, 1H), 6.66 (dd, *J*=3.3, 1.5, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 113.7, 118.3, 120.1, 125.6, 127.7, 128.3, 128.9, 130.4, 133.2, 146.6, 150.5, 167.1; IR (KBr) 3482.35, 3410.99, 1789.62, 1654.15, 1559.19, 1557.24, 1492.16, 1465.16, 883.56, 861.06, 757.41 cm^{-1}. Anal. Calcd for $C_{14}H_9NO_3$: C, 70.29; H, 3.79; N, 5.86. Found: C, 70.46; H, 3.82; N, 5.62.

*4.3.16. 2-Phenyl-4-(N-methylpyrrolo)-5-oxazolone (**18**)*

Dark yellow powder, 45%, mp 185–186 °C (lit. mp 185–186).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.11 (m, 6H), 7.74 (dd, *J*=4.1, 1.2, 3H), 7.56–7.53 (m, 1H), 7.51 (dd, *J*=6.2, 1.4, 2H), 7.18 (s, 3H), 6.94–6.90 (m, 3H), 6.41–6.34 (m, 4H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 34.2, 111.1, 111.6, 118.8, 121.1, 121.2, 124.6, 126.2, 127.2, 127.5, 127.8, 128.8, 128.9, 129.0, 129.7, 132.0, 132.4, 161.0, 168.2; IR (KBr) 3481.38, 3429.31, 3379.64, 1759.73, 1643.06, 1556.28, 1486.37, 1416.95, 1383.68, 866.85, 729.92 cm^{-1}. Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.65; H, 4.82; N, 11.25.

*4.3.17. 2-Phenyl-4-(4-pyridinyl)-5-oxazolone (**19**)*

Beige powder, 45%, mp 168–169 °C (lit. mp 168).[24] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J*=5.5, 2H), 8.21 (d, *J*=7.3, 2H), 8.01 (d, *J*=5.8, 2H), 7.67 (t, *J*=7.4, 1H), 7.57 (t, *J*=7.6, 2H), 7.13 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 125.0, 125.1, 127.7, 128.8, 129.1, 134.2, 137.1, 140.1, 150.5, 165.5, 166.5; IR (KBr) 3440.88, 3385.44, 1797.82, 1768.89, 1657.04, 1591.95, 1559.17, 868.29, 814.78 cm^{-1}. Anal. Calcd for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 72.14; H, 4.21; N, 11.04.

*4.3.18. 4-(Furan-3-ylmethylene)-2-phenyloxazol-5(4H)-one (**20**)*

Pale yellow powder, 66%, mp 195–197 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J*=7.6, 2H), 8.11 (s, 1H), 7.60 (t, *J*=7.3, 1H), 7.52 (t, *J*=7.5, 3H), 7.20 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 110.0, 111.1, 117.9, 121.4, 122.8, 125.7, 128.2, 128.9, 132.8, 133.1, 144.3, 147.8; IR (KBr) 3447.63, 3422.56, 1793.00, 1655.11, 1554.83, 1490.23, 858.17, 803.21, 754.28 cm^{-1}. Anal. Calcd for $C_{14}H_9NO_3$: C, 70.29; H, 3.79; N, 5.86. Found: C, 70.37; H, 3.65; N, 5.87.

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References and notes

1. Erlenmeyer, E. *Annalen.* **1893**, *275*, 1–12.
2. Baltazzi, E. *Q. Rev., Chem. Soc.* **1955**, *9*, 150–173.
3. (a) Etschenberg, E.; Opitz, W.; Raddatz, S. Brit. 1570140, 1980, 25; (b) Reed, J. W.; Kingston, G. I. D. *J. Nat. Prod.* **1986**, *49*, 626–630.
4. (a) Bakos, J.; Neil, B.; Toros, S.; Eifert, G.; Bihari, F.; Nagy, M.; Saros, L.; Durko, A.; Kuronya, I.; Bohus. P. Ger. Offen. DE 3641046, 1987, 11; (b) Jeschkeit, H.; Breaemer, B.; Lehmann, H.; Seewald, I.; Kleppel, M. Ger. (East) DD 266021, 1989, 22.
5. (a) Augustin, M.; Thondorf, I.; Strube, M. Ger. (East) DD 260063, 1988, 14; (b) Augustin, M.; Strube, M.; Thondorf, I. Ger. (East) DD 259862, 1988, 7.
6. Bacse, H. J.; Havsteen, B. *Anal. Biochem.* **1989**, *181*, 321–330.
7. Urano, K.; Tornioka, Y.; Okubo, K.; Yarnazaki, K.; Nagamatsu, A. Jpn. Kokai Tokkyo Koho JP 01 29369 189 29, 3691, 1989.
8. (a) Gillespie, H. B.; Snyder, H. R. *Org. Synth., Coll. Vol.* **1943**, *2*, 489; *Org. Synth., Coll. Vol.* **1939**, *19*, 67; (b) Chandrasekhar, S.; Karri, P. *Tetrahedron Lett.* **2006**, *47*, 5763–5766.
9. Chuanming, Y.; Baocheng, Z.; Weike, S.; Zhenyuan, X. *Synth. Commun.* **2006**, *36*, 3447–3453.
10. Chandrasekhar, S.; Phaneendrasai, K. *Tetrahedron Lett.* **2007**, *48*, 785–786.
11. Mogilaiah, K.; Prashanthi, M.; Reddy, S. C. *Indian J. Chem.* **2003**, *42B*, 2126–2128.
12. Crawford, M.; Little, W. T. *J. Chem. Soc.* **1959**, 729–731.
13. Rosen, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Peragmon: Oxford, 1991; Vol. 2, pp 402–407, and references cited therein.
14. Kitazawa, M.; Higuchi, R.; Takahashi, M.; Wada, T.; Sasabe, H. *J. Phys. Chem.* **1995**, *99*, 14784–14792.
15. Bautista, F. M.; Campelo, J. M.; Garcia, A.; Luna, D.; Marinas, J. M.; Romero, A. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 227–234.
16. Rao, Y. S. *J. Org. Chem.* **1976**, *41*, 722–725.
17. Arenal, I. *An. Quim., Ser. C* **1981**, *77*, 56–62.
18. Bennett, E. L. *J. Am. Chem. Soc.* **1950**, *72*, 1803–1805.
19. Hamidian, H. *Asian J. Chem.* **2007**, *19*, 970–974.
20. Fissekis, J. D.; Skinner, C. G.; Shive, W. *J. Org. Chem.* **1959**, *24*, 1722–1725.
21. Khan, K. M. *Lett. Drug Des. Discov.* **2008**, *5*, 52–56.
22. Icli, S.; Icil, H.; Alp, S.; Koc, H.; McKillop, A. *Spectrosc. Lett.* **1994**, *27*, 1115–1128.
23. Cativiela, C. *An. Quim., Ser. C* **1985**, *81*, 56–61.
24. Slater, G. *Tetrahedron* **1966**, *22*, 35–42.