Novel and Efficient Synthesis of 2-Aminooxazoles from Pyrimidin-2(1H)-one

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Abstract: Stepwise conversion of pyrimidine-2(1H)-one to 2-amino-5-arylloxazoles via oxazolo[3,2-a]pyrimidinum salts is reported. The sequence involves, (i) regioselective N-alkylation of pyrimidone by phenacyl bromides, (ii) cyclization of obtained 1-(2-aryl-2-oxoethyl)pyrimidin-2(1H)-ones into oxazolo[3,2-a]pyrimidinium salts under the action of fuming sulfuric (or triflic) acid, and (iii) reaction of the obtained salts with hydrazine leading to 2-amino-5-arylloxazoles.

Key words: fused ring systems, ring closure, ring opening, oxazoles, protecting groups

In our previous investigation1 we described a simple route to 5-arylloxazoles IVa bearing a α-aminodiényl residue by ring opening of bicyclic oxazolo[3,2-a]pyrimidinum salts IIIa (Scheme 1), which in turn can easily be obtained from 2-pyrimidone Ia via N-phenacyl-2-pyridones IIA. The overall simplicity of this methodology to obtain a substituted five-membered azole (like IVa) from a six-membered azine Ia via bridgehead azolo-azine IIIa (rarely used in heterocyclic synthesis) stimulated our interest to expand this strategy to the related family of pyrimidine derivatives. The retrosynthetic sequence of the suggested conversions is shown on Scheme 2.

One would expect that similar transformations starting from pyrimidin-2(1H)-one (1, 2-pyrimidone) and involving N-phenacyl derivatives IIb and oxazolo[3,2-a]pyrimidinum salts IIIb may lead to unstable oxazoly-substituted aza-dienes IVb, which, therefore, could be precursors of 2-aminooxazoles V. In this communication we confirm this idea and report our first successful preparation of 5-aryl-2-aminooxazoles V starting from pyrimidone I. The overall sequence shown in Scheme 2 has never been realized, although some related reactions have been briefly discussed in the literature.

N-Phenacylation of Pyrimidin-2(1H)-one (1)
The reaction of 2-pyrimidone I and its derivatives with α-halogenocarbonyl compounds is poorly investigated in the literature. There are only two examples of phenacylation in the 2-pyrimidone series, namely for 5-chloro-4-phenyl-2-pyrimidone2 and the sterically hindered 4,6-dimethyl-2-pyrimidone.3 Regarding the parent pyrimidine I only reactions with diethylalactam of bromoacetaldehyde4 and chloroacetic acid derivatives5 have been studied. In all these cases exclusive formation of the N-alkyl isomer was observed. Several 4-aryl-N-phenacyl-2-pyrimidones were prepared from α-aminoketones by an alternative strategy, not involving the alkylation step.6

Earlier examined alkylation reactions were carried out in bipolar aprotic solvents with pyrimidone alkali salts. We studied phenacylation of I in two different ways: using K2CO3 as the base (Method A) and starting from the initially prepared sodium salt of I (Method B). Various phenacyl bromides have been used (Scheme 3, Table 1), and in all cases the N-phenacyl derivatives 2a–h were the only products obtained in high yields.

In the IR spectra of 2a–h two types of bands for CO group were observed, one for N–C=O fragment of pyrimidone (~1660 cm⁻¹) and another one for carbonyl group (~1700 cm⁻¹), thus clearly confirming selective N-alkylation. (Evidently, in the case of O-phenacylation one would ex-
pect no amide frequencies.) The structure of compound 2a (and the regioselectivity of alkylation) was confirmed by single crystal X-ray analysis (Figure 1).

![Figure 1 X-ray crystal structure of the compound 2a](image)

Cyclization of N-Phenacyl-2-pyrimidones 2 to Oxazolo[3,2-a]pyrimidinium Salts 3

Aromatic oxazolo[3,2-a]pyrimidinium cation with bridgehead nitrogen atom could be prepared by two different ways, either from oxazole or from pyrimidine, and both strategies have been realized. The first approach is illustrated by condensation of 4,5-disubstituted 2-aminooxazoles with acetylacetone7 leading to 5,7-dimethyloxazolo[3,2-a]pyrimidinium salts. The alternative way (Scheme 4) involved cyclization of hardly available N-phenacyl-2-pyrimidones VI (by using somewhat unsafe combination of Ac2O and HClO4) or their thione precursors VII, leading to 2,7-diaryl-substituted salts VIII.6,8

We have tried to perform the cyclization of N-phenacyl-2-pyrimidones 2 using the above protocol6 in a mixture of Ac2O and HClO4. The isolated crystalline substances, however, were not the desired bicyclic salts. In the 1H NMR spectra of the products the singlet of NCH2-group remained unchanged, and the general downfield shift of all peaks confirmed that the products were protonated starting materials 2 (Scheme 5). Bradsher had reported9 that sulfuric acid could be a suitable dehydration agent for analogous cyclization in the pyridone series (IIa to IIIa).

Nevertheless, fuming sulfuric acid (20–30 mass% of SO3) turned out to be the reagent of choice, and its use resulted in the formation of the desired salts 3a–e (Scheme 5) in excellent yields (Table 2, Method A).

### Table 1 N-Phenacyl-2-pyrimidones 2a–h Prepared

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar Method Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>4-ClC6H4 A 90</td>
</tr>
<tr>
<td>2b</td>
<td>4-BrC6H4 A 95</td>
</tr>
<tr>
<td>2c</td>
<td>2,4-Cl2C6H3 B 60</td>
</tr>
<tr>
<td>2d</td>
<td>4-NO2C6H4 B 65</td>
</tr>
<tr>
<td>2e</td>
<td>3-NO2C6H4 B 63</td>
</tr>
<tr>
<td>2f</td>
<td>Ph A 79</td>
</tr>
<tr>
<td>2g</td>
<td>4-MeC6H4 A 81</td>
</tr>
<tr>
<td>2h</td>
<td>4-MeOC6H4 A 70</td>
</tr>
</tbody>
</table>

![Scheme 3](image)

![Scheme 4](image)

![Scheme 5](image)

### Table 2 2-Aryloxazolo[3,2-a]pyrimidinium Perchlorates 3a–g Prepared

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar Method Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>4-ClC6H4 A 90</td>
</tr>
<tr>
<td>3b</td>
<td>4-BrC6H4 A 85</td>
</tr>
<tr>
<td>3c</td>
<td>2,4-Cl2C6H3 A 83</td>
</tr>
<tr>
<td>3d</td>
<td>4-NO2C6H4 A 80</td>
</tr>
<tr>
<td>3e</td>
<td>3-NO2C6H4 A 87</td>
</tr>
<tr>
<td>3f</td>
<td>Ph A 55</td>
</tr>
<tr>
<td>3g</td>
<td>4-MeC6H4 B 75</td>
</tr>
</tbody>
</table>
The salts 3 could be easily isolated as perchlorates. The singlet of CH₂ group at 5.4 ppm (initially observed in parent N-phenacyl-2-pyrimidones) disappeared in the ¹H NMR spectra of the salts 3, and new downfield singlet of formed oxazole ring appeared at 9.24–9.59 ppm. Respectively, in the ¹³C spectra the signal for the methylene group observed for phenacyl derivatives 2 (at ~55 ppm) is changed to aromatic oxazole signal (at 110–115 ppm) for 3. Final confirmation of the structural change followed from X-ray structure analysis of the crystal of compound 3b (Figure 2).

![Figure 2 X-ray crystal structure of the compound 3b](image)

In the case of N-phenacyl-2-pyrimidones 2g,h with donor groups (4-Me or 4-MeO) in the benzene ring, the obtained products were insoluble in most solvents and had high melting points, so it was difficult to prove their structures. We suppose that in these cases SO₃ caused sulfonation of the benzene ring. (Analogous sulfonation was observed during the attempts to prepare oxazolopyridinium salts from electron rich phenacyl pyridones in sulfuric acid,⁹ during the attempts to prepare oxazolopyridinium salts the benzene ring. (Analogous sulfonation was observed (Table 2, Method B), whereas the compound 3a underwent selective cleavage of the pyrimidine fragment leading with excellent yields to 2-amino-5-aryloxazoles 4a–g (Scheme 7, Table 3). Although hydrazinolysis of structurally related oxazolopyridinium salt IIIa led to the cleavage and transformation of oxazole part,¹¹ in the case of the salts 3 there is no evidence for amibdent properties of the bicycle. Melting points and ¹H NMR spectral data of the aminooxazoles 4a,b,d,f,g correspond to literature data, and for previously unknown compound 4c,e we obtained satisfactory data of elementary analysis. Structure of most oxazoles 4 was confirmed by ¹³C NMR spectra and mass spectra (which are absent in the literature), and the structure 4b was proved by X-ray analysis (Figure 3).

Derivatives of 2-aminooxazole possess various types of biological activities; the parent scaffold is present in some
class of VEGFR2 kinase inhibitors. Therefore, development of starting materials would be poorly available.

Another old strategy – is difficult to apply for the synthesis of 2-aminooxazoles – reaction of cyanamide with carbonyl compounds is difficult to apply for the synthesis of 2-aminooxazoles, which is frequently multistep reactions accompanied by side reactions. The ‘handbook’ strategy to obtain 2-aminooxazoles is also complex, requiring complicated reagents or processes are accompanied by side reactions.

Closer inspection of the suggested strategy may clarify, that actual use of 2-pyrimidone as the source of NCO fragment of 2-aminooxazoles is nothing else but applying the idea of protecting group. Indeed, reaction of urea with α-bromoketones proceeds in a complex manner without clear regioselectivity (in contrast to thiourea). Pyrimidone may be considered as a sort of ‘protected’ urea that may be selectively N-phenacylated. Here the protecting group is the fragment of malonaldehyde, which is safely removed by hydrazinolysis at the final step. The role of malonaldehyde as protecting group is not only envisaged: in fact, the common way to obtain 2-pyrimidone is the condensation of urea with malonaldehyde derivatives. Hence, the overall sequence of ‘protection and deprotection’ of urea in the synthesis of 2-aminooxazoles can be described as shown in Scheme 8.

**Table 3** 2-Amino-5-aryloxazoles Prepared

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>4-ClC₆H₄</td>
<td>95</td>
</tr>
<tr>
<td>4b</td>
<td>4-BrC₆H₄</td>
<td>96</td>
</tr>
<tr>
<td>4c</td>
<td>2,4-Cl₂C₆H₃</td>
<td>88</td>
</tr>
<tr>
<td>4d</td>
<td>4-NO₂C₆H₄</td>
<td>93</td>
</tr>
<tr>
<td>4e</td>
<td>3-NO₂C₆H₄</td>
<td>88</td>
</tr>
<tr>
<td>4f</td>
<td>Ph</td>
<td>90</td>
</tr>
<tr>
<td>4g</td>
<td>4-MeC₆H₄</td>
<td>82</td>
</tr>
</tbody>
</table>

Melting points are uncorrected. ¹H and ¹³C NMR spectra were recorded on AM 400 Bruker spectrometer for ¹H at 360 MHz and for ¹³C at 90 or 100 MHz. Chemical shifts are reported in ppm referenced to residual protons in the deuterated solvent. IR spectra were obtained on UR-20 spectrometer in Nujol. Mass spectra were determined on Kratos MS-30 mass spectrometer (El 70 eV). TLC was performed with Silufol UV-254 (Merck). The experimental intensities of diffraction reflections for single crystals of compounds 2a, 3b, 4b were measured on a CAD4 automated diffractometer (MoKα radiation, graphite monochromator, o scan mode) at r.t. All subsequent calculations were carried out with the SHELX97 program package.

2-Pyrimidone hydrochloride was prepared by reaction of urea with malonaldehyde bis(dimethyl acetal) (1,1,3,3-tetramethoxypropane) by a method described in the literature³⁰ [yield: 71%; yellow solid; mp 203–207 °C; (Lit.³¹ mp 210 °C)].

1-(2-Aryl-2-oxoethyl)pyrimidin-2(1H)-ones 2a,b,f–h; 1-[(2-(4-Chlorophenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2a); Typical Procedure: Method A

K₂CO₃ (55.2 g, 0.4 mol) was added under stirring to a suspension of 2-pyrimidone hydrochloride (26.5 g, 0.2 mol) in anhyd acetone.
Yield: 95%; white solid; mp 237–239 °C;

1-(2-Aryl-2-oxoethyl)pyrimidin-2(1H)-ones 2c–e; 1-(2-(2,4-Dichlorophenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2e); Typical Procedure: Method B

2-Pyrimidone hydrochloride (26.5 g, 0.2 mol) was added to a freshly prepared solution of NaOMe obtained by reaction of Na (9.2 g, 0.4 mol) with MeOH (10:1). The mixture was stirred for 30 min, and MeOH was evaporated under reduced pressure. The residue was suspended in anhyd acetone (400 mL), and a solution of 2,4-dichlorophenyl bromide (26.8 g, 0.1 mol) in acetone (200 mL) was added with stirring. The mixture was refluxed for 2 h and treated as described in Method A to give 2e; yield: 17.0 g (60%).

1-(2-(4-Chlorophenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2a)

Yield: 90%; white solid; mp 230–231 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1700, 1660 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 5.48 \) (s, 2 H, CH₂), 6.51 (m, 1 H, H-5), 7.68 (m, 2 H, Ar-H, BB'), 8.07 (m, 2 H, Ar-H, AA'), 8.13 (m, 1 H, H-4), 8.62 (m, 1 H, H-6).

13C NMR (90 MHz, DMSO-d₆): 56.1 (CH₃), 103.8 (C-5), 129.1 (C-3'), Ar), 129.8 (C-2'), Ar), 133.0 (C-1'), Ar), 139.0 (C-4', Ar), 150.5 [C-4 (6)], 155.5 (C-2), 166.7 [C-6 (4)], 191.6 (C=O).


1-(2-(4-Methoxyphenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2f)

Yield: 65%; pale yellow solid; mp 215–217 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1695, 1615 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 5.54 \) (s, 2 H, CH₂), 6.41 (m, 1 H, H-5), 7.72 (m, 2 H, Ar-H, BB'), 7.99 (m, 2 H, Ar-H, AA'), 8.08 (m, 1 H, H-4), 8.57 (m, 1 H, H-6).

Anal. Calcd for C₁₂H₁₀N₂O₂: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.65; H, 5.49; N, 12.38.

1-(2-(2-Aryl-2-oxoethyl)pyrimidin-2(1H)-one (2b)

Yield: 95%; white solid; mp 237–239 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1700, 1660 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 5.43 \) (s, 2 H, CH₂), 6.41 (m, 1 H, H-5), 7.72 (m, 2 H, Ar-H, BB'), 7.99 (m, 2 H, Ar-H, AA'), 8.08 (m, 1 H, H-4), 8.57 (m, 1 H, H-6).

Anal. Calcd for C₁₂H₁₀BrN₂O₂: C, 57.96; H, 3.65; N, 11.27. Found: C, 57.67; H, 3.42; N, 11.29.

1-(2-(4-Methylphenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2g)

Yield: 60%; white solid; mp 205–207 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1710, 1680 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 5.27 \) (s, 2 H, CH₂), 6.42 (m, 1 H, H-5), 7.51 (d, \( J_{H-H} = 8.2 \) Hz, 1 H, H-5'-Ar), 7.57 (s, 1 H, H-3'-Ar), 7.91 (d, \( J_{H-H} = 8.2 \) Hz, 1 H, H-6'-Ar), 8.19 (m, 1 H, H-4), 8.57 (m, 1 H, H-6).

Anal. Calcd for C₁₃H₁₂N₂O₂: C, 50.91; H, 2.85; N, 9.89. Found: C, 50.74; H, 2.83; N, 9.75.

1-(2-(2-Aryl-2-oxoethyl)pyrimidin-2(1H)-one (2h)

Yield: 81%; white solid; mp 197–199 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1690, 1660 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 3.29 \) (s, 3 H, CH₃), 5.45 (s, 2 H, CH₂), 6.50 (m, 1 H, H-5), 7.40 (m, 2 H, Ar-H, BB'), 7.95 (m, 2 H, Ar-H, AA'), 8.14 (m, 1 H, H-4), 8.62 (m, 1 H, H-6).

13C NMR (90 MHz, DMSO-d₆): \( \delta = 21.2 \) (CH₃), 56.0 (CH₂), 103.6 (C-5), 128.0 (C-2', Ar), 129.4 (C-3', Ar), 131.9 (C-1', Ar), 144.6 (C-4', Ar), 150.6 [C-4 (6)], 155.5 (C-2), 166.7 [C-6 (4)], 191.9 (C=O).

Anal. Calcd for C₁₃H₁₂N₂O₂: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.65; H, 5.49; N, 12.38.

1-(2-(2-Methylphenyl)-2-oxoethyl)pyrimidin-2(1H)-one (2i)

Yield: 70%; white solid; mp 173–175 °C; \( R_f = 0.15 \) (CHCl₃–MeOH, 10:1).

IR (Nujol): 1700, 1640 cm⁻¹.

1H NMR (360 MHz, DMSO-d₆): \( \delta = 3.90 \) (s, 3 H, OCH₃), 5.40 (s, 2 H, CH₂), 6.41 (m, 1 H, H-5), 7.05 (m, 2 H, Ar-H, BB'), 8.01 (m, 2 H, Ar-H, AA'), 8.08 (m, 1 H, H-4), 8.56 (m, 1 H, H-6).

Anal. Calcd for C₁₃H₁₂N₂O₂: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.88; H, 4.88; N, 11.56.

Attempted Cyclization of 2a

HClO₄ (0.3 mL) was carefully added under good cooling to Ac₂O (10 mL). Pyrimidone 2a (0.746 g, 0.003 mol) was added, the colorless mixture was stirred for 30 min, and then kept for 24 h at r.t. The obtained precipitate was filtered, dried and recrystallized from
EtOH to afford the perchlorate of 2a; yield: 1.00 g (96%); white solid; mp 325–327 °C.

1H NMR (360 MHz, DMSO-d6): δ = 5.73 (s, 2 H, CH2), 6.98 (m, 1 H, H-5), 7.59 (m, 2 H, Ar-H, BB'), 8.09 (m, 2 H, Ar-H, AA'), 8.86 (m, 1 H, H-4), 8.91 (m, 1 H, H-6). Anal. Calcd for C12H10Cl2N2O6: C, 45.80; H, 3.52; N, 8.90. Found: C, 45.69; H, 3.43; N, 8.80.

Treatment of 2a with conc H2SO4 and PPA led to the same perchlorate. In the case of TiCl4 or POCl3 no identifiable products were isolated.

2-Aryloxazolo[3,2-d]pyrimidinum Perchlorates 3a–f; 2-(4-Chlorophenyl)oxazolo[3,2-d]pyrimidinum Perchlorate (3a);
Typical Procedure; Method A
Dried 4-chlorophenacylpyrimidone (2a; 4.28 g, 0.02 mol) was carefully added to a stirred mixture of fuming H2SO4 [32 mL; prepared from 17 mL, 34 g] fuming H2SO4 (17 mL, 34 g). [For 2c the mixture was kept for 24 h, and for 2d, 72 h at r.t.). After that the mixture was carefully poured into crushed ice (500 g). Then HClO4 (10 mL, 65%) was added. The product was isolated by suction filtration, washed with H2O, then with EtOH and Et2O, and dried in vacuum over P2O5 to afford 3a; yield: 5.23 g (79%); white solid; mp 268–270 °C.

1H NMR (360 MHz, DMSO-d6): δ = 7.64 (m, 2 H, Ar-H, BB), 8.06 (m, 2 H, Ar-H, AA'), 8.14 (dd, J2,3 = 4.5 Hz, J3,4 = 6.3 Hz, 1 H, 1 H-6), 9.31 (s, 1 H, H-3), 9.34 (dd, J3,4 = 4.5 Hz, J4,5 = 1.7 Hz, 1 H, 1 H-7), 9.66 (dd, J4,5 = 6.3 Hz, J5,6 = 1.8 Hz, 1 H, H-5). Anal. Calcd for C12H7Cl3N2O5: C, 39.43; H, 1.93; N, 7.66. Found: C, 39.14; H, 1.91; N, 7.75.

2-(4-Nitrophenyl)oxazolo[3,2-d]pyrimidinum Perchlorate (3d)
Yield: 80%; pale yellow solid; mp 271–273 °C.

1H NMR (360 MHz, CF3CO2D): δ = 8.86 (m, 1 H, H-3’-Ar), 8.33 (m, 1 H, H-6), 9.13 (m, 1 H, H-2’-Ar), 9.32 (m, 1 H, H-4’-Ar), 9.67 (m, 2 H, H-3’-Ar + H-5’-Ar), 10.13 (m, 1 H, H-7), 10.19 (m, 1 H, H-5).

13C NMR (90 MHz, DMSO-d6): δ = 113.3 (C-3), 118.6 (C-6), 120.7 (C-2’), 125.2 (C-1’), 125.6 (C-6’-Ar), 131.6 (C-4’, Ar), 131.8 (C-5’, Ar), 142.7 (C-7’), 146.8 (C-3’, Ar), 149.6 (C-2), 153.3 (C-9), 163.3 (C-7’). Anal. Calcd for C12H10Cl2N2O6: C, 45.80; H, 3.52; N, 8.90. Found: C, 45.69; H, 3.43; N, 8.80.

2-(4-Bromophenyl)oxazolo[3,2-d]pyrimidinum Perchlorate (3b)
Yield: 85%; white solid; mp 279–281 °C.

1H NMR (360 MHz, DMSO-d6): δ = 7.81 (m, 2 H, Ar-H, BB), 8.02 (m, 2 H, Ar-H, AA'), 8.14 (dd, J2,3 = 4.6 Hz, J3,4 = 6.3 Hz, 1 H, 1 H-6), 9.31 (s, 1 H, H-3), 9.36 (dd, J3,4 = 4.6 Hz, J4,5 = 1.8 Hz, 1 H, 1 H-7), 9.68 (dd, J4,5 = 6.3 Hz, J5,6 = 1.8 Hz, 1 H, H-5). Anal. Calcd for C12H7Cl3N2O5: C, 39.43; H, 1.93; N, 7.66. Found: C, 39.14; H, 1.91; N, 7.75.

2-(3-Nitrophenyl)oxazolo[3,2-d]pyrimidinum Perchlorate (3e)
Yield: 87%; white solid; mp 248–250 °C.

1H NMR (360 MHz, CF3CO2D): δ = 8.66 (m, 1 H, H-3’-Ar), 8.83 (m, 1 H, H-6), 9.13 (m, 1 H, H-2’-Ar), 9.32 (m, 1 H, H-4’-Ar), 9.67 (m, 2 H, H-3’-Ar + H-5’-Ar), 10.13 (m, 1 H, H-7), 10.19 (m, 1 H, H-5).

13C NMR (90 MHz, DMSO-d6): δ = 111.2 (C-3), 118.4 (C-6), 123.6 (C-2’), 125.9 (C-1’), 125.9 (C-2’-Ar), 129.8 (C-3’-Ar), 132.3 (C-4’, Ar), 142.2 (C-7’), 151.8 (C-2), 152.3 (C-9), 162.4 (C-5 [7]). Anal. Calcd for C12H10Cl2N2O6: C, 45.80; H, 3.52; N, 8.90. Found: C, 45.69; H, 3.43; N, 8.80.

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Synthesis of 2-Aminooxazoles

Yield: 88%; orange solid; mp 201–203 °C; 5-(3-Nitrophenyl)-1,3-oxazol-2-amine (4e)

MS (EI, 70 eV):
1H NMR (360 MHz, DMSO-d6): δ = 6.57 (br s, 2 H, NH2), 7.01 (s, 1 H, H-4), 7.26 (m, 2 H, Ar-H, BB′), 7.41 (m, 2 H, Ar-H, AA′).
13C NMR (90 MHz, DMSO-d6): δ = 123.4 (C-2′, Ar), 123.9 (C-4′, Ar), 128.8 (C-3′, Ar), 130.2 (C-4′, Ar), 142.0 (C-5′), 161.5 (C-2).

5-(4-Bromophenyl)-1,3-oxazol-2-amine (4b)

Rf = 0.4 (CHCl3-MeOH, 10:1). The solution was cooled to r.t. and poured into cold H2O (100 mL). The product was isolated by suction filtration and recrystallized from EtOH to afford 4b; yield: 1.65 g (95%); white solid; mp 220–221 °C (Lit.18a mp 220–222 °C);


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