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

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Received 21 August 2006; revised 18 October 2006

Abstract: Stepwise conversion of pyrimidin-2(1H)-one to 2-amino-5-aryloxazoles via oxazolo[3,2-a]pyrimidinium salts is reported. The sequence involves, (i) regioselective N-alkylation of pyrimidinone 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-aminooxazoles.

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

In our previous investigation1 we described a simple route to 5-aryloxazoles IVa bearing a o-aminodiényl residue by ring opening of bicyclic oxazolo[3,2-a]pyrimidinium salts IIIa (Scheme 1), which in turn can easily be obtained from 2-pyrimidone Ia via N-phenacyl-2-pyrimidones 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-phenacetyl derivatives IIb and oxazolo[3,2-a]pyrimidinium salts IIIb may lead to unstable oxazoyl-substituted azadienes 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 1. The overall sequence shown in Scheme 2 has never been realized, although some related reactions have been briefly discussed in the literature.

N-Phenacetylation of Pyrimidin-2(1H)-one (1)

The reaction of 2-pyrimidone 1 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 pyrimidinone 1 only reactions with diethy lacetal of bromocacetaldheyde4 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 o-aminoketones by an alternative strategy, not involving the alklylation step.6

Earlier examined alklylation reactions were carried out in bipolar aprotic solvents with pyrimidinone alkali salts. We studied phenacylation of 1 in two different ways: using K2CO3 as the base (Method A) and starting from the initially prepared sodium salt of 1 (Method B). Various phenacetyl bromides have been used (Scheme 3, Table 1), and in all cases the N-phenacetyl 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-

\[
\text{Scheme 1}
\]

\[
\text{Scheme 2}
\]

SYNTHESIS 2007, No. 2, pp 0263–0270
Advanced online publication: 14.12.2006
DOI: 10.1055/s-2006-958941; Art ID: Z16706SS
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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)

**Scheme 3**

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

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

**Scheme 4**

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Method</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>4-ClC₆H₄</td>
<td>A</td>
<td>90</td>
</tr>
<tr>
<td>3b</td>
<td>4-BrC₆H₄</td>
<td>A</td>
<td>85</td>
</tr>
<tr>
<td>3c</td>
<td>2,4-Cl₂C₆H₃</td>
<td>A</td>
<td>83</td>
</tr>
<tr>
<td>3d</td>
<td>4-NO₂C₆H₄</td>
<td>A</td>
<td>80</td>
</tr>
<tr>
<td>3e</td>
<td>3-NO₂C₆H₄</td>
<td>A</td>
<td>87</td>
</tr>
<tr>
<td>3f</td>
<td>Ph</td>
<td>B</td>
<td>79</td>
</tr>
<tr>
<td>3g</td>
<td>4-MeC₆H₄</td>
<td>B</td>
<td>75</td>
</tr>
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</table>

**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-amino-oxazoles with acetylacetone leading to 5,7-dimethyl-oxazolo[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.

We have tried to perform the cyclization of N-phenacyl-2-pyrimidones 2 using the above protocol in a mixture of Ac₂O and HClO₄. The isolated crystalline substances,
The salts 3 could be easily isolated as perchlorates. The singlet of CH₃ 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).

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 that is even a weaker sulfonation media than oleum.) In the case of N-phenacyl derivative 2f (unsubstituted at benzene ring) partial sulfonation was also observed, however, decrease of temperature and using DMSO for purification has allowed us to obtain 2-phenyl derivative 3f pure.

In order to avoid the sulfonation problem, we have tried to perform cyclization of SO₃-sensitive compounds 2f–h in a mixture of triflic acid and P₂O₅ (Scheme 5). In this case the desired salts 3f,g were obtained in good yields (Table 2, Method B), whereas the compound 2h decomposed completely.

**Cyclization Mechanism**

The formation of fused oxazoles 3 from 2 resembles closure of N-acyl-α-aminoacarbonyl compounds to oxazoles (known as Robinson–Gabriel cyclization in the case of monocycles). The influence of the nature of acid on the results of the cyclization of 2 to 3 may bring some light to the mechanism of this conversion. Clearly, the oxygen in the bicyclic oxazoles 3 originates from the amide group in pyrimidones 2; this mechanism was proved by isotope label for monocyclic case,¹⁰ and there is no evidence for its change in the case of bicyclic analogs. Therefore, protonation of the ketone oxygen in phenacyl derivatives 2 is required. However, 2-pyrimidones 2 have the concurrent basic center – the second nitrogen atom in the ring. As we have seen, use of H₂SO₄, PPA or HClO₄–Ac₂O systems led only to the salts of 2, whereas the use of stronger acids (super acids) like H₂SO₄–SO₃ or CF₃SO₃H resulted in successful cyclization. This may indicate that the real cyclization mechanism requires somewhat unusual assumption on the formation of dications IX as the reaction intermediates (Scheme 6).

As an indirect proof of this hypothesis, one could consider the changes in the color of reaction mixtures: usual acids caused no changes, whereas super acids brought to solutions bright (yellow to red) colors. The same colors appeared when the final solid perchlorates 3 were dissolved in triflic acid.

**Conversion of Oxazolo[3,2-a]pyrimidinium Salts 3 to 2-Amino-5-aryloxazoles 4**

Although the structures of the type 3 are known for decades, there are no examples of their reactions with nucleophiles. We found that in reactions with hydrazine bicyclic salts 3a–g 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 ambident 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
compounds 4 it would be necessary to start from hardly available 2-halogen derivatives of arylacetic aldehydes. The are only few alternative methodologies to prepare 2-amino-5-aryloxazoles: Curtius rearrangement of oxazolyl-2-carboxylic acids hydrazides,\textsuperscript{17} multistep synthesis starting from \(N\)-(tosylmethyl)-\(N\)\(^{\prime}\)-tritylcarbodiimide,\textsuperscript{18} and condensation of \(\alpha\)-bromoketones with \(N\)-cyanourea.\textsuperscript{19} Hence the strategy proposed in this communication, involving simple sequence with high yields and requiring cheap materials, may serve as a competitive complementary route to the class of compounds 4.

Closer inspection of the suggested strategy may clarify, that actual use of 2-pyrimidone as the source of NCO fragment of 2-aminooxazole is nothing else but applying the idea of protecting group. Indeed, reaction of urea with \(\alpha\)-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, most 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.

Figure 3  X-ray crystal structure of the compound 4b

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>4-ClC(_6)H(_4)</td>
<td>95</td>
</tr>
<tr>
<td>4b</td>
<td>4-BrC(_6)H(_4)</td>
<td>96</td>
</tr>
<tr>
<td>4c</td>
<td>2,4-Cl(_2)C(_6)H(_3)</td>
<td>88</td>
</tr>
<tr>
<td>4d</td>
<td>4-NO(_2)C(_6)H(_4)</td>
<td>93</td>
</tr>
<tr>
<td>4e</td>
<td>3-NO(_2)C(_6)H(_4)</td>
<td>88</td>
</tr>
<tr>
<td>4f</td>
<td>Ph</td>
<td>90</td>
</tr>
<tr>
<td>4g</td>
<td>4-MeC(_6)H(_4)</td>
<td>82</td>
</tr>
</tbody>
</table>

Table 3  2-Amino-5-aryloxazoles Prepared

Melting points are uncorrected. \(^1\)H and \(^13\)C NMR spectra were recorded on AM 400 Bruker spectrometer for \(^1\)H at 360 MHz and for \(^13\)C 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 (EI 70 eV). TLC was performed with Silufol UV-254 (Merck). The experimental intensities of diffraction reflections for single crystals of compounds 2a\textsuperscript{20} 3b,\textsuperscript{21} and 4b\textsuperscript{22} were measured on a CAD4 automated diffractometer (MoK\(_\alpha\) radiation, graphite monochromator, \(\omega\) 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 literature\textsuperscript{26} (yield: 71%; yellow solid; mp 203–207 °C; (Lit.\textsuperscript{23} 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

\(K_2\)CO\(_3\) (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; treated as described in Method A to give 2a: yield: 22.3 g (60%).

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

A mixture of 2-mercaptopyrimidone hydrochloride (26.5 g, 0.2 mol) and dry acetone (200 mL) was added with stirring. The mixture was refluxed for 2 h and then kept 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-dichlorophenacyl 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 2c: yield: 17.0 g (60%).

IR (Nujol): 1710, 1680 cm–1.

Yield: 65%; pale yellow solid; mp 215–217 °C; yield: 17.0 g (60%).

IR (Nujol): 1695, 1615 cm–1.

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

IR (Nujol): 1700, 1660 cm–1.

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

IR (Nujol): 1700, 1660 cm–1.

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

IR (Nujol): 1700, 1680 cm–1.

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

IR (Nujol): 1695, 1655 cm–1.

Yield: 63%; white solid; mp 162–164 °C; Rf = 0.15 (CHCl3–MeOH; 10:1).

IR (Nujol): 1710, 1670 cm–1.

Yield: 79%; white solid; mp 184–186 °C; Rf = 0.15 (CHCl3–MeOH; 10:1).

IR (Nujol): 1690, 1660 cm–1.

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

IR (Nujol): 1700, 1660 cm–1.

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

IR (Nujol): 1700, 1640 cm–1.

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

Synthesis of 2-Aminooxazoles

PAPER
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 C₁₂H₈Cl₂N₂O₅: C, 43.53; H, 2.44; N, 8.46. Found: C, 43.69; H, 3.43; N, 8.80.

Treatment of 2a with concd 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-chlorohenacylpyrimidone (2a; 4.28 g, 0.02 mol) was carefully added to a stirred mixture of fuming H₂SO₄ (25 mL, d = 1.84) and commercial (60 mass% of SO₃) fuming H₂SO₄ (17 mL, 34 g). [For 2e–f: fuming sulfuric acid (40 mL) with 30 mass% of SO₃ was used for mixing]. The temperature was kept in the range –5 to 0 °C. The mixture (orange to red) was stirred below 0 °C until the compound was completely dispersed and then kept for 5 h under r.t. (For 2e the mixture was kept for 24 h, and for 2d, 2 e, 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 the perchlorate 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 (d, J₆,₅ = 4.5 Hz, J₅,₇ = 1.8 Hz, 1 H, H-6), 9.31 (s, 1 H, H-3), 9.34 (d, J₆,₅ = 4.5 Hz, J₅,₇ = 1.7 Hz, 1 H, H-1), 9.66 (d, J₆,₅ = 6.3 Hz, J₅,₇ = 1.8 Hz, 1 H, H-5).

13C NMR (100 MHz, DMSO-d₆): δ = 111.8 (C-3), 118.6 (C-6), 122.6 (C-1', Ar), 127.7 (C-2', Ar), 130.1 (C-3', Ar), 137.1 (C-4', Ar), 142.4 [C-7 (5)], 150.8 (C-2), 153.2 (C-9), 162.6 [C-5 (7)].

Anal. Calcd for C₁₂H₈Cl₂N₂O₅: C, 48.58; H, 3.06; N, 9.44. Found: C, 48.52; H, 2.98; N, 9.46.

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 (d, J₆,₅ = 4.5 Hz, J₅,₇ = 1.8 Hz, 1 H, H-6), 9.31 (s, 1 H, H-3), 9.36 (d, J₆,₅ = 4.6 Hz, J₅,₇ = 1.8 Hz, 1 H, H-1), 9.68 (d, J₆,₅ = 6.3 Hz, J₅,₇ = 1.8 Hz, 1 H, H-5).

13C NMR (90 MHz, DMSO-d₆): δ = 111.8 (C-3), 118.5 (C-6), 122.9 (C-1', Ar), 125.9 (C-4', Ar), 127.8 (C-2', Ar), 132.8 (C-3', Ar), 142.3 [C-7 (5)], 150.8 (C-2), 153.2 (C-9), 162.6 [C-5 (7)].

Anal. Calcd for C₁₂H₈Br₂N₂O₅: C, 34.53; H, 2.44; N, 8.46. Found: C, 34.33; H, 2.40; N, 8.53.

2-(4-Dichlorophenyl)oxazolo[3,2-d]pyrimidinum Perchlorate (3e)

Yield: 83%; white solid; mp 325–327 °C.

1H NMR (360 MHz, DMSO-d₆): δ = 7.49 (d, J₆,₅ = 8.9 Hz, J₅,₇ = 1.8 Hz, 1 H, H-5), 7.82 (d, J₆,₅ = 4.5 Hz, 1 H, H-3'), 8.16 (m, 2 H, H-5',Ar + H-6',Ar), 9.41 (d, J₆,₅ = 4.4 Hz, J₅,₇ = 1.8 Hz, 1 H, H-1), 9.45 (s, 1 H, H-3), 9.61 (d, J₆,₅ = 6.2 Hz, J₅,₇ = 1.8 Hz, 1 H, H-5).

13C NMR (90 MHz, DMSO-d₆): δ = 115.2 (C-3), 118.8 (C-6), 121.4 (C-1', Ar), 128.9 (C-3', Ar), 130.7 (C-6', Ar), 131.0 (C-5', Ar), 132.2 (C-2', Ar), 137.4 (C-4', Ar), 142.4 [C-7 (5)], 147.2 (C-2), 152.8 (C-9), 163.6 [C-5 (7)].

Anal. Calcd for C₁₂H₈Cl₂N₂O₅: 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, DMSO-d₆): δ = 8.17 (dd, J₆,₅ = 4.5 Hz, J₅,₇ = 6.3 Hz, 1 H, H-6), 7.36 (m, 2 H, Ar-H, BB'), 8.46 (m, 2 H, Ar-H, AA'), 9.41 (dd, J₆,₅ = 4.5 Hz, J₅,₇ = 1.8 Hz, 1 H, H-7), 9.50 (s, 1 H, H-3), 9.73 (dd, J₆,₅ = 6.3 Hz, J₅,₇ = 1.8 Hz, 1 H, H-5).

Anal. Calcd for C₁₂H₈N₃O₇: 271.4; found: 271.2 (C-5 (7)).

V. L. Alifanov, E. V. Babaev

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

MS (EI, 70 eV):
\[ \text{Ar}, 141.0 (C-5), 148.4 (C-3) \]

13C NMR (90 MHz, DMSO-d6):
\[ \text{Ar}, 126.1 (C-4), 127.8 (C-6) \]


Yield: 96%; white solid; mp 220–221 °C (Lit. 19b mp 220–222 °C); 5-(4-Bromophenyl)-1,3-oxazol-2-amine (4b)

MS (EI, 70 eV):
\[ \text{Ar}, 130.4 (C-4) \]

1H NMR (360 MHz, DMSO-d6):
\[ \delta = 6.61 (br s, 2 H, NH_2), 7.04 (s, 1 H, H-4), 7.35 (m, 2 H, Ar-H, BB) \]

MS (EI, 70 eV): m/z (%) = 138 (100), 238 (100).

Yield: 88%; white solid; mp 202–204 °C; Rf = 0.4 (CHCl3–MeOH, 10:1).

5-(4-Nitrophenyl)-1,3-oxazol-2-amine (4d)

1H NMR (360 MHz, DMSO-d6):
\[ \delta = 7.58 (d, J = 8.6 Hz, 1 H, H-4) \]

MS (EI, 70 eV): m/z (%) = 175 (47), 205 (100).

References


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