Mononuclear Heterocyclic Rearrangement of 5-Arylisoxazole-3-hydroxamic Acids into 3,4-Substituted 1,2,5-Oxadiazoles

Vladimir I. Potkin,*[a] Sergey K. Petkevich,[a] Alexander S. Lyakhov,[b] Ludmila S. Ivashkevich[b]

[a] Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, Surganova Str., 13, Minsk 220072, Belarus
Fax +375(17)2841679; E-mail: potkin@ifoch.bas-net.by

[b] Research Institute for Physical Chemical Problems of Belarusian State University, Leningradskaya Str., 14, Minsk 220030, Belarus

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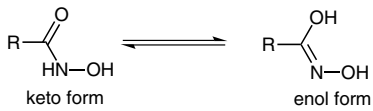
Abstract: By a series of successive transformations, 5-arylisoxazole-3-carboxylic acids (aryl = phenyl, *p*-tolyl, 2,5-dimethylphenyl) have been converted into 5-arylisoxazole-3-hydroxamic acids, which undergo rearrangement by the action of aqueous KOH to form 3,4-substituted 1,2,5-oxadiazoles. The structure of one of them, 1-(2,5-dimethylphenyl)-2-(4-hydroxy-1,2,5-oxadiazol-3-yl)ethanone, has been confirmed by single crystal X-ray analysis.

Key words: isoxazoles, 1,2,5-oxadiazoles, furazans, rearrangement, crystal structure, hydroxamic acids

The chemistry of 1,2,5-oxadiazole (trivial name furazan) is of great interest, because a large number of compounds incorporating furazan cycle possess a wide spectrum of biological activity.[1] Moreover, they attract great attention as energetic materials,[2] dyes, and precursors for organic synthesis of useful products.[3] There are different methods available for the synthesis of furazans. One of them is based on the mononuclear heterocyclic rearrangement of the isoxazoles bearing an oxime group in the 3 position of the heterocycle.[4] Hydroxamic acids can be considered as synthetic equivalents of oximes as they can exist in two tautomeric forms, keto or enol (Scheme 1).[5] The latter is produced in low percentage, is less stable, and contains the oxime moiety.



Scheme 1 Tautomeric forms of hydoxamic acids

The transformation of isoxazolylhydroxamic acids and their derivatives into furazans is not described up till now. We intended to synthesize the 5-arylisoxazole-3-hydroxamic acids (aryl = Ph, 3-MeC_6H_4, 2,5-$Me_2C_6H_3$) **1**–**3** and their *O*-acetyl derivatives **4**–**6**, and to study the possibility of their use in obtaining substituted 1,2,5-oxadiazoles via mononuclear heterocyclic rearrangement. The 5-arylisoxazole-3-carboxylic acids **7**–**9** were taken as starting compounds. Recently, we have reported their synthesis from the corresponding available 5-arylisoxazole-3-carbaldehyde oximes.[6]

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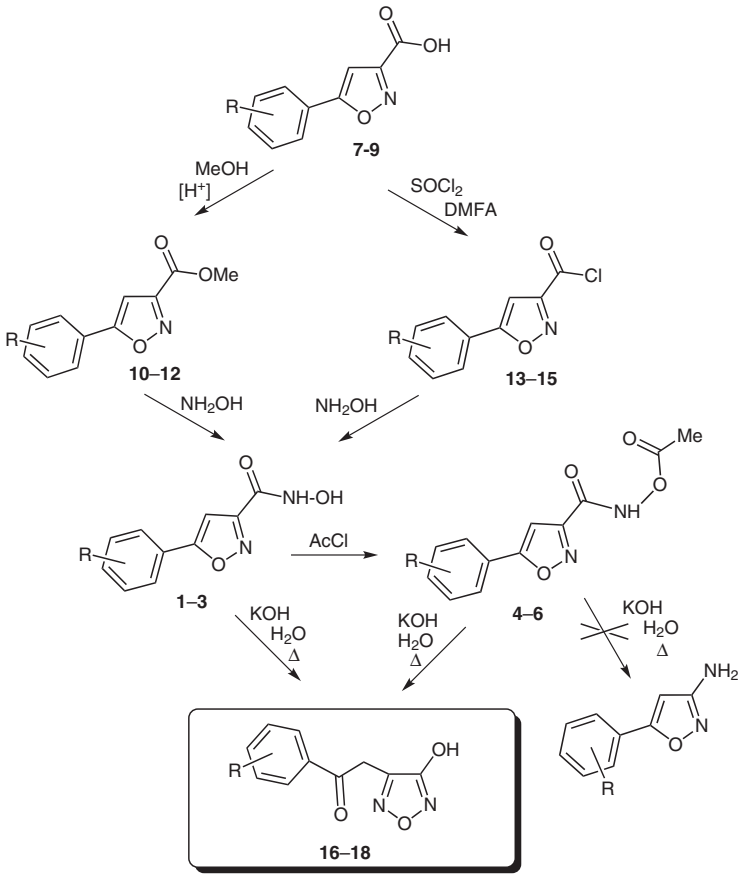
Two approaches were tested for the synthesis of arylisoxazole-3-hydroxamic acids **1**–**3**. One of them included the amidation of methyl 5-arylisoxazole-3-carboxylates **10**–**12** by reaction with hydroxylamine. Another path consisted in acylation of hydroxylamine by the action of 5-arylisoxazole-3-carbonyl chlorides **13**–**15**, easily obtained by the reaction of acids **7**–**9** with thionyl chloride. The former approach was found to be more preferable, as it allows to obtain the target hydroxamic acids **1**–**3** in higher yields (75–88% instead of 51–60% in the latter approach) and with higher purity. Thus, the first approach was used in practice. Acetylation of hydroxamic acids proceeded selectively on the hydroxy group and led to the corresponding acetyl derivatives **4**–**6** in 83–96% yields (Scheme 2).

At first it was planned to convert the *O*-acetylhydroxamic acids **4**–**6** into 3-amino-5-arylisoxazoles by heating with aqueous alkali. The conversion of *O*-acylhydroxamic acids to isocyanates and further to amines or ureas is well known as Lossen rearrangement.[7] However, the process proceeded quite differently and led to 1-aryl-2-(4-hydroxy-1,2,5-oxadiazol-3-yl)ethanones **16**–**18**, that is, substituted furazans (Scheme 2).

The hydrolysis of acylated fragment was supposed to be the first step of the process and further mononuclear rearrangement of the enol form of hydroxamic acids into the furazan systems occurred. To test this hypothesis, arylisoxazole-3-hydroxamic acids **1**–**3** were subjected to heating in aqueous alkali (KOH) and the reaction resulted in the formation of the corresponding substituted furazans **16**–**18**. Yields of the furazans obtained from the hydroxamic acids **1**–**3** (70–76%, method A), were slightly higher than those of the products obtained from the acetylated derivatives **4**–**6** (54–62%, method B). Given the findings, a sequence of the arylisoxazole-3-hydroxamic acid molecules transformations in mononuclear heterocyclic rearrangement is suggested, which is presented in Scheme 3.

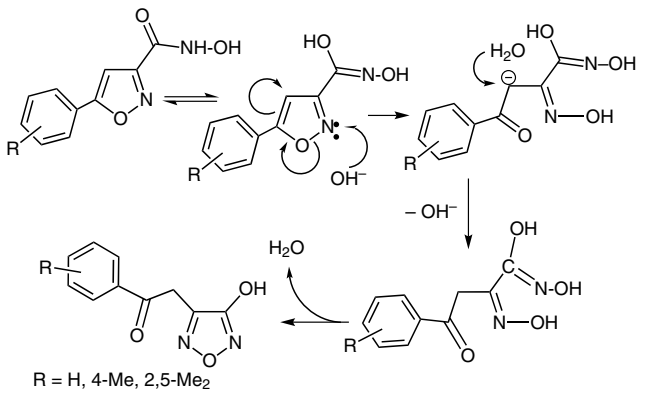
The structure of furazan derivatives **16**–**18** was confirmed by IR, ^{1}H, and ^{13}C NMR spectra as well as by single crystal X-ray analysis at 296 K for compound **18**. Single crystals of **18** suitable for X-ray analysis were obtained by slow evaporation of a dichloromethane–hexane (2:1) solution of the compound.

Compound **18** was found to crystallize in the monoclinic space group $P2_1/c$ ($Z = 4$). The asymmetric unit comprises one molecule of 1-(2,5-dimethylphenyl)-2-(4-hydroxy-



R = H (**1**,**4**,**7**,**10**,**13**,**16**), 4-Me (**2**,**5**,**8**,**11**,**14**,**17**), 2,5-Me_2 (**3**,**6**,**9**,**12**,**15**,**18**)

Scheme 2 Preparation of 3,4-substituted 1,2,5-oxadiazoles



Scheme 3 A probable route of mononuclear rearrangement of 5-arylisoxazole-3-hydroxamic acids

1,2,5-oxadiazol-3-yl)ethanone (Figure 1). The furazan and benzene rings are planar within 0.0035(10) and 0.0059(12) Å, respectively. In the molecule, the dihedral angle between the least squares planes of the rings is of 64.08(6)°. Bond lengths and valence angles (Table 1) lie in the expected ranges.[8]

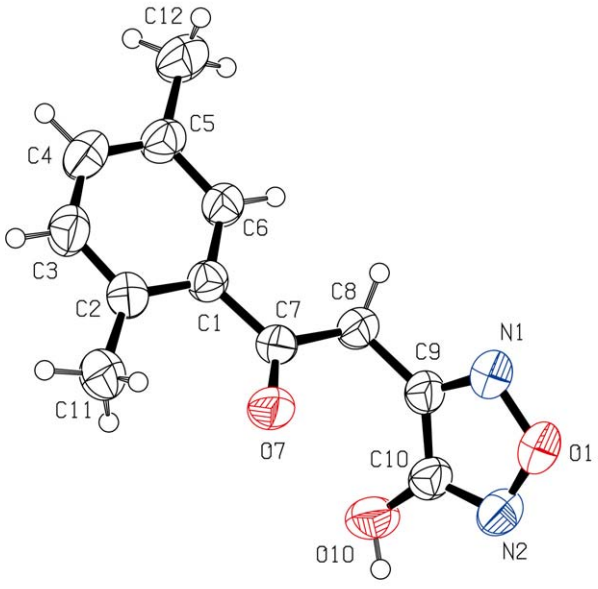


Figure 1 The molecular structure of **18**, showing the atom-numbering scheme and displacement ellipsoids drawn at the 50% probability level

Table 1 Selected Bond Lengths and Angles for Furazan **18**

Bond lengths (Å)		Angles (°)	
O(1)–N(1)	1.3880(19)	N(1)–C(9)–C(10)	108.36(14)
O(1)–N(2)	1.391(2)	N(1)–O(1)–N(2)	110.74(12)
C(10)–N(2)	1.296(2)	C(9)–N(1)–O(1)	105.97(14)
C(9)–C(10)	1.423(2)	C(10)–N(2)–O(1)	104.31(13)
C(9)–N(1)	1.293(2)	N(2)–C(10)–C(9)	110.61(15)
C(10)–O(10)	1.331(2)	N(1)–C(9)–C(8)	121.39(15)
C(8)–C(9)	1.487(2)	N(2)–C(10)–O(10)	124.86(15)
C(7)–C(8)	1.521(2)	O(7)–C(7)–C(1)	122.50(13)
C(7)–O(7)	1.2178(17)	O(7)–C(7)–C(8)	119.20(13)

The carbonyl and hydroxy groups of neighboring molecules are involved in intermolecular hydrogen bonds O10–H10···O7[a] (symmetry code as in Figure 2) responsible for the formation of centrosymmetric dimers, with only van der Waals interactions between them.

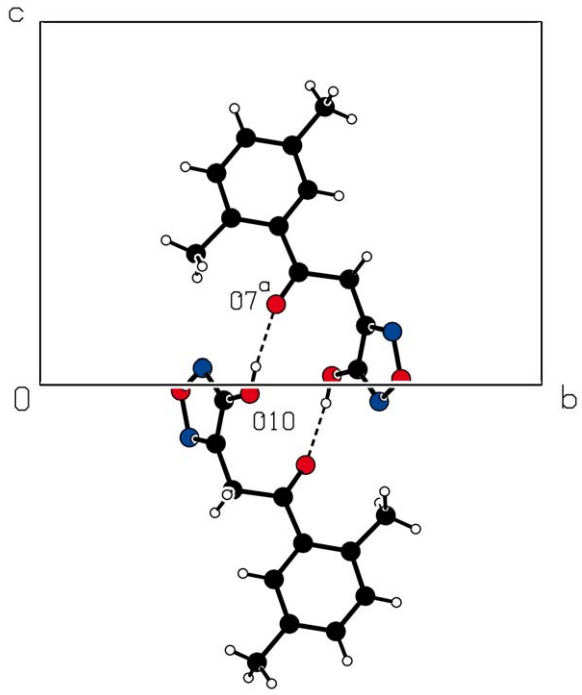


Figure 2 A hydrogen-bonded dimer in the crystal structure of **18**; symmetry code (a): 1–*x*, 1–*y*, 1–*z*

In conclusion, we have successfully developed an efficient synthetic approach for the preparation of 3,4-substituted 1,2,5-oxadiazoles (furazans) based on mononuclear heterocyclic rearrangement of accessible 5-arylisoxazole-3-hydroxamic acids. The furazans formed contain reactive exocyclic hydroxy and keto groups and can be used in further target transformations.

All reagents were of analytical grade and used as purchased without further purification. Melting points were determined on Boetius heating table. The IR spectra were recorded on a Nicolet Protégé spectrometer, using KBr discs. The NMR spectra were recorded on a Bruker Avance-500 spectrometer. GC-MS analysis was carried out on Hewlett Packard 5890/5972 spectrometer.

Methyl 5-Arylisoxazole-3-carboxylates 10–12; General Procedure

To a solution of the corresponding 5-arylisoxazol-3-carboxylic acid **7–9** (10 mmol) in anhyd MeOH (50 mL) was added concd H_2SO_4 (2 drops) and the mixture was refluxed for 4 h. The solution was allowed to cool to r.t., then H_2O (200 mL) was added, the product extracted with CH_2Cl_2 (50 mL), and the extract was dried ($CaCl_2$). After removal of the solvent by rotary evaporation, the residue was recrystallized from hexane.

Methyl 5-Phenylisoxazole-3-carboxylate (10)

Yield: 1.75 g (86%); white solid; mp 80–82 °C.

IR (KBr): 3148, 3131, 3059, 2952, 2922, 1728, 1613, 1592, 1572, 1477, 1447, 1426, 1296, 1252 1143, 1005, 948, 936, 809, 782, 767, 685, 675 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, OCH_3), 6.85 (s, 1 $H_{isoxazole}$), 7.39 (m, 3 H_{arom}), 7.71 (m, 2 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.89 (OCH_3), 99.99 ($CH_{isoxazole}$), 125.95 (2 CH_{arom}), 129.20 (2 CH_{arom}), 130.88 (1 CH_{arom}), 126.60, 156.74, 160.45 (3 C_q), 171.79 (C=O).

GC-MS (EI, 70 eV): *m*/*z* = 203 [M^+].

Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.16; H, 4.75; N, 6.95.

Methyl 5-(*p*-Tolyl)isoxazole-3-carboxylate (11)

Yield: 1.93 g (89%); white solid; mp 116–117 °C.

IR (KBr): 3139, 3030, 2954, 2926, 1727, 1616, 1595, 1522, 1474, 1447, 1425, 1412, 1248, 1143, 1005, 947, 938, 809, 782, 676, 502 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.98 (s, 3 H, OCH_3), 6.85 (s, 1 $H_{isoxazole}$), 7.26 (d, *J* = 8.0 Hz, 2 H_{arom}), 7.66 (d, *J* = 8.0 Hz, 2 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.59 (CH_3), 52.94 (OCH_3), 99.39 ($CH_{isoxazole}$), 125.94 (2 CH_{arom}), 129.90 (2 CH_{arom}), 123.94, 141.36, 156.69, 160.61 (4 C_q), 172.07 (C=O).

GC-MS (EI, 70 eV): *m*/*z* = 217 [M^+].

Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.54; H, 5.29; N, 6.57.

Methyl 5-(2,5-Dimethylphenyl)isoxazole-3-carboxylate (12)

Yield: 2.17 g (94%); white solid; mp 53–54 °C.

IR (KBr): 3171, 3008, 2957, 2925, 1735, 1726, 1575, 1505, 1471, 1451, 1424, 1384, 1295, 1248 1189, 1180, 1154, 1116, 1002, 936, 820, 806, 775 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 2.45 (s, 3 H, CH_3), 4.00 (s, 3 H, OCH_3), 6.81 (s, 1 $H_{isoxazole}$), 7.17 (m, 2 H_{arom}), 7.54 (m, 1 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.92 (CH_3), 21.02 (CH_3), 52.97 (OCH_3), 102.93 ($CH_{isoxazole}$), 128.97 (CH_{arom}), 131.51 (2 CH_{arom}), 125.89, 133.30, 136.09, 156.39, 160.70 (5 C_q), 172.03 (C=O).

GC-MS (EI, 70 eV): *m*/*z* = 231 [M^+].

Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.69; H, 5.78; N, 6.12.

5-Arylisoxazole-3-hydroxamic Acids 1–3; General Procedure

A solution of hydroxylamine hydrochloride (1.39 g, 20 mmol) and Et_3N (20.02 g, 20 mmol) in MeOH (40 mL) was stirred at r.t. for 30 min. The corresponding ester **10–12** (10 mmol) was then added and

the mixture was refluxed for 8 h. After cooling to r.t., the reaction mixture was diluted with H_2O (250 mL), the precipitate was filtered, washed with H_2O (3 × 25 mL), dried in vacuo, and recrystallized from $CHCl_3$.

5-Phenylisoxazole-3-hydroxamic Acid (1)
Yield: 1.59 g (78%); white solid; mp 167–169 °C.

IR (KBr): 3327, 3160, 3068, 1664, 1608, 1570, 1538, 1449, 1261, 1167, 1050, 1003, 948, 868, 769, 694 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 7.15 (s, 1 $H_{isoxazole}$), 7.52 (m, 3 H_{arom}), 7.90 (m, 2 H_{arom}), 8.69 (s, 1 H, OH), 10.86 (s, 1 H, NH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 99.36 ($CH_{isoxazole}$), 125.94 (2 CH_{arom}), 129.53 (2 CH_{arom}), 130.86 (CH_{arom}), 126.90, 156.64, 158.28 (3 C_q), 170.97 (C=O).

Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.03; H, 4.35; N, 13.91.

5-(*p*-Tolyl)isoxazole-3-hydroxamic Acid (2)
Yield: 1.92 g (88%); white solid; mp 168–170 °C.

IR (KBr): 3286, 3164, 3033, 2923, 1650, 1614, 1594, 1542, 1509, 1450, 1388, 1263, 1159, 1046, 1034, 947, 869, 807 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 2.36 (s, 3 H, CH_3), 7.07 (s, 1 $H_{isoxazole}$), 7.33 (d, *J* = 8.0 Hz, 2 H_{arom}), 7.77 (d, *J* = 8.0 Hz, 2 H_{arom}), 8.76 (s, 1 H, OH), 10.81 (s, 1 H, NH).

^{13}C NMR (125 MHz, acetone-d_6): δ = 20.64 (CH_3), 98.73 ($CH_{isoxazole}$), 125.89 (2 CH_{arom}), 129.93 (2 CH_{arom}), 124.21, 141.25, 156.73, 158.20 (4 C_q), 171.15 (C=O).

Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.87; H, 4.93; N, 12.75.

5-(2,5-Dimethylphenyl)isoxazole-3-hydroxamic Acid (3)
Yield: 1.74 g (75%); white solid; mp 149–151 °C.

IR (KBr): 3363, 3159, 2922, 2869, 1689, 1660, 1568, 1531, 1509, 1443, 1425, 1376, 1262, 1137, 1042, 1001, 957, 873, 854, 814 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 2.36 (s, 3 H, CH_3), 2.46 C (s, 3 H, CH_3), 6.95 (s, 1 $H_{isoxazole}$), 7.26 (m, 2 H_{arom}), 7.58 (s, 1 H_{arom}), 8.73 (s, 1 H, OH), 10.92 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.13 (CH_3), 21.29 (CH_3), 103.18 ($CH_{isoxazole}$), 129.97 (CH_{arom}), 132.48 (CH_{arom}), 132.68 (CH_{arom}), 127.29, 134.46, 137.20, 157.75, 158.95 (5 C_q), 172.24 (C=O).

Anal. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.23; H, 5.44; N, 12.18.

***O*-Acetyl Derivatives of 5-Arylisoxazole-3-hydroxamic Acids 4–6; General Procedure**
AcCl (0.86 g, 11 mmol) was slowly added dropwise at r.t. to a stirred solution of the corresponding 5-arylisoxazole-3-hydroxamic acid **1**–**3** (10 mmol) in anhyd pyridine (10 mL). After completion of the addition, the reaction mixture was stirred at 50–55 °C for 3 h. The mixture was cooled to r.t. and diluted with H_2O (100 mL). The product was extracted with $CHCl_3$ (40 mL), the extract was dried ($CaCl_2$), and concentrated up to 10 mL. Then 50 mL of hexane was added and precipitate was filtered and dried in vacuo.

***N*-Acetoxy-5-phenylisoxazole-3-carboxamide (4)**
Yield: 2.04 g (83%); white solid; mp 143–145 °C.

IR (KBr): 3208, 3128, 2936, 1795, 1705, 1609, 1590, 1572, 1519, 1497, 1448, 1370, 1253, 1185, 1048, 1004, 947, 880, 765, 689 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 7.00 (s, 1 $H_{isoxazole}$), 7.47 (m, 3 H_{arom}), 7.77 (m, 2 H_{arom}), 9.96 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.30 (CH_3), 99.47 ($CH_{isoxazole}$), 126.11 (2 CH_{arom}), 129.31 (2 CH_{arom}), 131.12 (CH_{arom}), 126.47, 156.60, 156.83 (3 C_q), 168.33 (C=O), 171.97 (C=O).

Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.77; H, 4.26; N, 11.40.

***N*-Acetoxy-5-(*p*-tolyl)isoxazole-3-carboxamide (5)**
Yield: 2.50 g (96%); white solid; mp 152–154 °C.

IR (KBr): 3216, 3132, 2924, 1797, 1705, 1613, 1593, 1567, 1508, 1447, 1367, 1253, 1182, 1045, 1000, 947, 879, 815, 807, 763 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 6.95 (s, 1 $H_{isoxazole}$), 7.28 (d, *J* = 8.0 Hz, 2 H_{arom}), 7.67 (d, *J* = 8.0 Hz, 2 H_{arom}), 10.23 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.27 (CH_3), 21.60 (CH_3), 98.82 ($CH_{isoxazole}$), 126.02 (2 CH_{arom}), 129.94 (2 CH_{arom}), 123.69, 141.60, 156.57, 156.67 (4 C_q), 168.27 (C=O), 172.18 (C=O).

Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 60.00; H, 4.65; N, 10.76. Found: C, 60.11; H, 4.95; N, 10.68.

***N*-Acetoxy-5-(2,5-dimethylphenyl)isoxazole-3-carboxamide (6)**
Yield: 2.28 g (83%); white solid; mp 115–117 °C.

IR (KBr): 3223, 3162, 2924, 2867, 1801, 1709, 1673, 1573, 1506, 1452, 1434, 1370, 1248, 1174, 1039, 1003, 962, 944, 881, 848, 813 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.46 (s, 3 H, CH_3), 6.91 (s, 1 $H_{isoxazole}$), 7.20 (m, 2 H_{arom}), 7.54 (s, 1 H_{arom}), 10.33 (s, 1 H, NH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.89 (CH_3), 21.51 (CH_3), 21.60 (CH_3), 102.88 ($CH_{isoxazole}$), 129.57 (CH_{arom}), 132.12 (CH_{arom}), 132.20 (CH_{arom}), 126.24, 134.01, 136.69, 156.96, 157.24 (5 C_q), 168.89 (C=O), 172.65 (C=O).

Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.57; H, 5.38; N, 10.32.

Rearrangement of 5-Arylisoxazole-3-hydroxamic Acids and Their *O*-Acetyl Derivatives into 3,4-Substituted 1,2,5-Oxadiazoles 16–18; General Procedures
Method A: The corresponding 5-arylisoxazole-3-hydroxamic acid **1**–**3** (5 mmol) was added to a solution of KOH (0.84 g, 15 mmol) in H_2O (30 mL), and the mixture was stirred at 55–60 °C for 7 h. The reaction mixture was diluted with H_2O (200 mL), extracted with CH_2Cl_2 (50 mL), and the extract dried ($CaCl_2$). The solvent was removed under reduced pressure and the residue was purified by recrystallization from a mixture CH_2Cl_2–hexane (1:3).

Method B: The corresponding *O*-acetyl-5-arylisoxazole-3-hydroxamic acid **4**–**6** (5 mmol) was added to a solution of KOH (1.4 g, 25 mmol) in H_2O (40 mL), and the mixture was stirred at 55 °C for 9 h. The reaction mixture was diluted with H_2O (300 mL), acidified with 4 M HCl to pH 6, extracted with CH_2Cl_2 (50 mL), and the extract dried ($CaCl_2$). The solvent was removed under reduced pressure and the residue was purified by recrystallization from a mixture CH_2Cl_2–hexane (1:3).

2-(4-Hydroxy-1,2,5-oxadiazol-3-yl)-1-phenylethanone (16)
Yield: 1.43 g (70%, method A); 1.10 g (54%, method B); white solid; mp 83–85 °C.

IR (KBr): 3353, 2921, 1693, 1597, 1582, 1548, 1450, 1385, 1330, 1216, 1182, 1002, 929 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.43 (s, 2 H, CH_2), 7.47 (m, 3 H_{arom}), 7.92 (m, 2 H_{arom}), 9.50 (s, 1 H, OH)

^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.52 (CH_2), 128.35 (2 CH_{arom}), 128.73 (CH_{arom}), 129.97 (CH_{arom}), 134.97, 143.03, 163.05 (3 C_q), 194.28 (C=O).

Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 59.11; H, 4.27; N, 13.88.

2-(4-Hydroxy-1,2,5-oxadiazol-3-yl)-1-(*p*-tolyl)ethanone (17)
Yield: 1.55 g (71%, method A); 1.31 g (60%, method B); white solid; mp 93–95 °C.

IR (KBr): 3220, 3951, 2922, 1685, 1606, 1574, 1552, 1519, 1444, 1407, 1397, 1330, 1225, 1185, 1008, 929 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 4.51 (s, 2 H, CH_2), 7.27 (d, J = 8.0 Hz, 2 H_{arom}), 8.00 (d, J = 8.0 Hz, 2 H_{arom}), 9.96 (s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.91 (CH_3), 32.92 (CH_2), 129.37 (2 CH_{arom}), 130.41 (2 CH_{arom}), 126.64, 132.83, 144.88, 163.35 (4 C_q), 194.67 (C=O).

Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.76; H, 4.87; N, 12.91.

1-(2,5-Dimethylphenyl)-2-(4-hydroxy-1,2,5-oxadiazol-3-yl)ethanone (18)

Yield: 1.76 g (76%, method A); 1.44 g (62%, method B); white solid; mp 100–102 °C.

IR (KBr): 3238, 2976, 2921, 1668, 1599, 1566, 1541, 1495, 1386, 1338, 1231, 1176, 1009, 980 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 2.52 (s, 3 H, CH_3), 4.53 (s, 2 H, CH_2), 7.22 (d, J = 8.0 Hz, 1 H_{arom}), 7.31 (d, J = 8.0 Hz, 1 H_{arom}), 7.65 (s, 1 H_{arom}), 10.40 (s, 1 H, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.08 (CH_3), 21.54 (CH_3), 35.38 (CH_2), 130.31 (CH_{arom}), 132.70 (CH_{arom}), 135.10 (CH_{arom}), 134.16, 135.95, 137.14, 143.22, 163.11 (5 C_q), 198.41 (C=O).

Anal. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.15; H, 5.34; N, 12.11.

X-ray Crystal Structure Analysis[9]

X-ray data of **18** were collected on a diffractometer Nicolet R3m at 293(2) K. The crystal structure was solved by direct methods using the program SIR2004.[10] The structure was refined with the program SHELXL.[11] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed in calculated positions and refined in 'riding' model approximation, with $U_{iso}(H) = 1.5U_{eq}(C,O)$ for the methyl and hydroxy groups, and $U_{iso}(H) = 1.2U_{eq}(C)$ for others. The package PLATON[12] was used for molecular graphics.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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(9) CCDC 903835 contains the supplementary crystallographic data for **18**. These data can be obtained via http://www.ccdc.cam.ac.uk/conts/retrieving.html, free of charge or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; e-mail: deposit@ccdc.cam.ac.uk or fax: +44(1223)336033.
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