Synthesis and Reactivity of 4-Aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones

Thomas Kurz,*[a] Mehdi Khankischpur[b]

[a] Institute of Pharmaceutical and Medicinal Chemistry, Heinrich-Heine Universität Düsseldorf, Universitätsstr. 1, 40225 Düsseldorf, Germany
Fax +49(211)8113847; E-mail: Thomas.Kurz@uni-duesseldorf.de

[b] Institute of Pharmacy, University of Hamburg, Bundesstr. 45, 20146 Hamburg, Germany

Received 5 June 2009; revised 24 July 2009

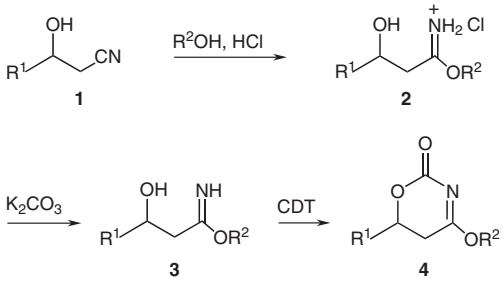
Abstract: The synthesis of previously unreported 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones, as well as their transformation into various novel 4-functionalized 5,6-dihydro-2*H*-1,3-oxazine-2-ones and 1,3-oxazinane-2-ones is described.

Key words: β-hydroxyimidates, cyclization, nitrogen-containing heterocycles, N-nucleophiles, oxazinanes

The development of simple and efficient methods for the preparation of new analogs of bioactive heterocyclic compounds represents an important task in organic and medicinal chemistry. Among nitrogen–oxygen containing heterocycles, functionalized 1,3-oxazin(an)es are of interest for organic and medicinal chemists because they are present in various biologically active compounds and natural products.[1,2] Recently, 1,3-oxazinane-2-ones have attracted considerable interest in medicinal chemistry especially due to their potent antibacterial activity.[3] As cyclic imides, 1,3-oxazinane-2,4-diones are structurally related to bioactive heterocycles like glutarimides and barbiturates. 1,3-Oxazinane-2,4-diones exhibit anti-convulsive, sedative, hypnotic and narcotic properties. 1,3-Oxazinane-2,4-diones are, for instance, accessible starting from 2,2-disubstituted 3-hydroxycarboxylic acids by multi-step syntheses.[4] The promising biological properties of the latter heterocycles, as well as their versatile synthetic applications, prompted us to develop a synthetic pathway for the preparation of novel 4-functionalized 1,3-oxazin(an)es.[5]

We now describe the first synthesis of 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4**, as well as their transformation into various novel 4-functionalized 5,6-dihydro-2*H*-1,3-oxazine-2-ones **5** and 4-functionalized 1,3-oxazinane-2-ones **6** and **7**, by treatment of heterocycles **4** with different nitrogen nucleophiles. Our retro-synthetic analysis led to β-hydroxyimidates as suitable starting materials for the preparation of the key intermediates **4** (Scheme 1).

Novel β-hydroxyimidate hydrochlorides (**2a–j**) were synthesized by Pinner reactions of β-hydroxynitriles **1**,[6] primary alcohols and hydrogen chloride in anhydrous dichloromethane at 0 °C, in 30–96% yield (Table 1). The β-hydroxyimidate hydrochlorides **2** are characterized by strong C=N absorption bands at 1637–1656 cm^{-1}. Without further purification, the crude imidate hydrochlorides **2** were converted directly into the corresponding imidate bases **3** by treatment with a saturated aqueous solution of potassium carbonate. During the reaction the structures of imidate bases **3** were determined by IR spectroscopy [IR: 1635–1660 (C=N) cm^{-1}] and TLC. Subsequent cyclic carbonylation of imidate bases using CDT [1,1′-carbonyldi(1,2,4-triazole)] as carbonylating agent afforded the previously unknown 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazin-2-ones (**4a–j**) in 55–71% yield, after recrystallisation from appropriate solvents (Table 1).



Scheme 1 Synthesis of imidates (**2**) and 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones (**4**)

Heterocycles **4** contain a cyclic carbamate as well as a semi-cyclic imidate functionality and display two sharp IR absorption bands at 1718–1727 cm^{-1} and at 1590–1610 cm^{-1}. The structure of compound **4f** was also confirmed by X-ray structure analysis (Figure 1).[7]

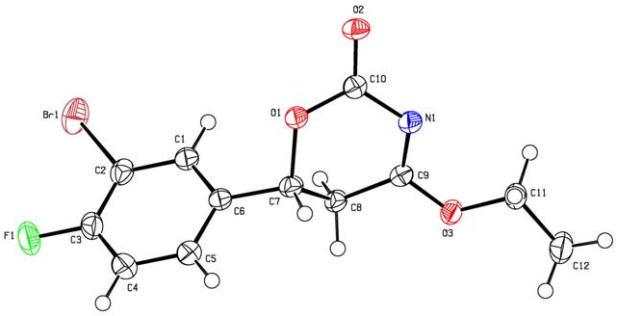


Figure 1 X-ray crystal structure of compound **4f**

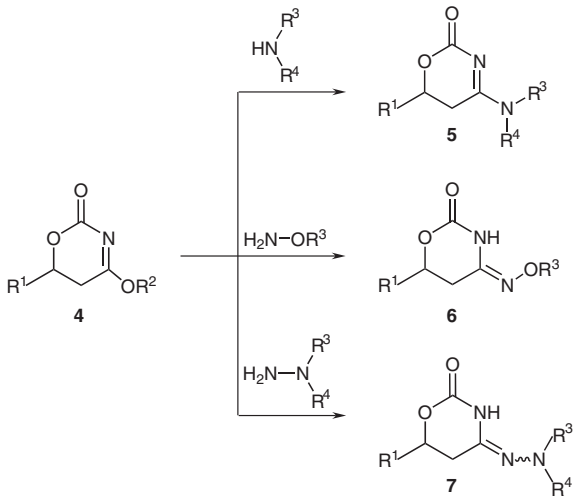
SYNTHESIS 2009, No. 23, pp 4068–4074
Advanced online publication: 23.09.2009
DOI: 10.1055/s-0029-1217023; Art ID: T11609SS

Table 1 Imidate Hydrochlorides **2** and 4-Aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4**.

Compound	R^1	R^2	Yield (%)
2a	Ph	Et	74
2b	*t*-Bu	Me	30
2c	4-F-C_6H_4	Et	69
2d	4-Cl-C_6H_4	Et	96
2e	4-Me-C_6H_4	Et	66
2f	3-Br-4-F-C_6H_3	Et	75
2g	1-Naphthyl	Me	80
2h	1-Naphthyl	Et	93
2i	1-Naphthyl	Bn	63
2j	1-Naphthyl	$Ph(CH_2)_2$	86
4a	Ph	Et	65
4b	*t*-Bu	Me	62
4c	4-F-C_6H_4	Et	70
4d	4-Cl-C_6H_4	Et	71
4e	4-Me-C_6H_4	Et	55
4f	3-Br-4-F-C_6H_3	Et	64
4g	1-Naphthyl	Me	70
4h	1-Naphthyl	Et	67
4i	1-Naphthyl	Bn	60
4j	1-Naphthyl	$Ph(CH_2)_2$	71

Next, we investigated the reactivity of the semi-cyclic imidate group of compounds **4** towards primary and secondary amines, O-substituted hydroxylamines and N,N-disubstituted hydrazines (Scheme 2). Treatment of 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4** with either primary or secondary amines, furnished the corresponding 4-amino-5,6-dihydro-2*H*-1,3-oxazine-2-ones (**5a–f**) in 80–87% yield (Table 2). In contrast to imidates **4**, heterocycles **5** exhibit sharp C=O absorption bands at 1663–1687 cm^{-1}. According to H,H-COSY experiments, the heterocyclic amidines **5** contain a 5,6-dihydro-2*H*-1,3-oxazine-2-one ring system as well as an exocyclic amino group in ring position four. In addition, the X-ray crystal structure of compound **5c** confirmed the 4-amino-5,6-dihydro-2*H*-1,3-oxazine-2-one structure.[7]

Reactions of 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4** with O-substituted hydroxylamines at room temperature provided 4-aralkoxy(alkoxy)imino-1,3-oxazinane-2-ones (**6a–f**) as *Z*-isomers in 73–92% yield (Table 2). In contrast to amidines **5**, amidoximes **6** display a sharp C=N absorption band at 1654–1668 cm^{-1}, which is characteristic for exocyclic aralkoxyimino groups. In accordance with the spectroscopic data, the crystal structure of the *Z*-isomer of compound **6f** showed a semi-cyclic amidoxime functionality in which the alkoxyimino group is located at carbon atom four of the 1,3-oxazinane-2-one nucleus (Figure 2).[7] Semi-cyclic amidrazones (**7a–e**) were accessible in 66–87% yield by reacting 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4** with N,N-disubstituted hydrazines under similar reaction conditions (Table 2). According to 1D and 2D NMR experiments, compounds **7a–e** were obtained as mixtures of *E*- and *Z*-isomers. In accordance with amidoximes **6**, heterocycles **7** demonstrate a sharp C=N absorption band at 1648–1656 cm^{-1}, as well as a strong C=O absorption band at 1726–1734 cm^{-1}.



Scheme 2 Synthesis of 4-amino-5,6-dihydro-2*H*-1,3-oxazine-2-ones (**5**) and 4-functionalized 1,3-oxazinane-2-ones (**6** and **7**)

The structures of compounds **4–7** were determined by IR, ^1H and ^{13}C NMR spectroscopy and by elemental analysis. Compounds **2–7** were obtained as racemic mixtures.

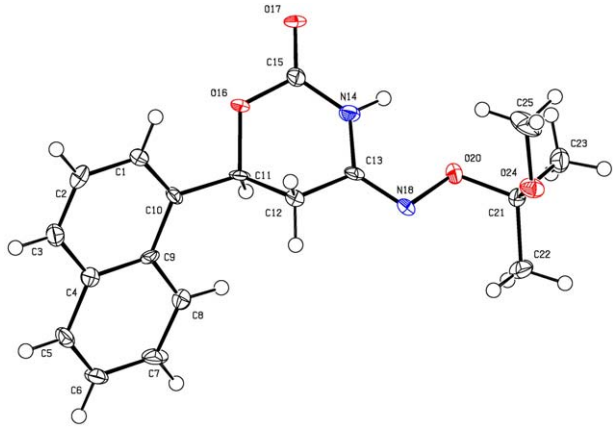


Figure 2 X-ray crystal structure of compound **6f**

In conclusion, we have successfully studied the synthesis of previously unreported 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-ones **4**, as well as their transformation into various novel 4-functionalized 5,6-dihydro-2*H*-

Table 2 4-Amino-5,6-dihydro-2*H*-1,3-oxazine-2-ones **5** and 4-Functionalized 1,3-Oxazinane-2-ones **6** and **7**

Entry	R^1	R^3	R^4	Yield (%)
5a	Ph	$PhCH_2$	H	86
5b	*t*-Bu	2-Cl,6-F-$C_6H_3CH_2$	H	84
5c	4-Cl-C_6H_4	2,6-Cl-$C_6H_3CH_2$	H	87
5d	4-Me-C_6H_4	-$(CH_2)_2O(CH_2)_2$-		85
5e	1-Naphthyl	cyclopentyl	H	80
5f	1-Naphthyl	2-Cl-$C_6H_4CH_2$	H	82
6a	Ph	$PhCH_2$	–	89
6b	4-Cl-C_6H_4	2-F-$C_6H_4CH_2$	–	92
6c	4-Me-C_6H_4	4-Me-$C_6H_4CH_2$	–	88
6d	1-Naphthyl	$PhCH_2$	–	87
6e	1-Naphthyl	$Ph(CH_2)_3$	–	73
6f	1-Naphthyl	$MeO(Me)_2C$	–	82
7a	Ph	-$(CH_2)_2NMe(CH_2)_2$-		76
7b	4-F-C_6H_4	-$(CH_2)_2O(CH_2)_2$-		75
7c	1-Naphthyl	Me	Me	72
7d	1-Naphthyl	-$(CH_2)_5$-		66
7e	1-Naphthyl	-$(CH_2)_2O(CH_2)_2$-		87

1,3-oxazine-2-ones **5** and 4-functionalized 1,3-oxazinane-2-ones **6** and **7**. Currently, we are investigating the biological properties and synthetic applications of heterocycles **5**–**7**.

Melting points (uncorrected) were determined on a Mettler FP 62 apparatus. Elemental analyses were carried out with a Heraeus CHN-O-Rapid instrument. IR spectra were recorded on a Shimadzu FT-IR 8300. ^{1}H NMR (400 MHz) und ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AMX 400 spectrometer using TMS as an internal standard and DMSO-d_6 as solvent.

Preparation of 2a–j; General Procedure

To a solution of the appropriate β-hydroxynitrile[6] **1** (15 mmol) in anhydrous CH_2Cl_2 (150 mL), HCl gas was added at 0 °C according to the Pinner synthesis. After 5–7 d at –10 °C, most CH_2Cl_2 (120 mL) was removed under reduced pressure and anhydrous Et_2O (100–150 mL) was added. The solid imidate hydrochlorides **2a–j** were isolated by filtration, suspended in anhydrous Et_2O and filtered. The structures of imidate hydrochlorides **2a–j** were confirmed by IR spectroscopy. All imidate hydrochlorides were used for the synthesis of compounds **4** without further purification.

Ethyl 3-Hydroxy-3-phenylpropanimidoate Hydrochloride (2a)

Colorless solid (74%); mp 127.0 °C.

IR (KBr): 1637 cm^{-1}.

Methyl 3-Hydroxy-4,4-dimethylpentanimidoate Hydrochloride (2b)

Colorless solid (30%); mp 121.0 °C.

IR (KBr): 1646 cm^{-1}.

Ethyl 3-(4-Fluorophenyl)-3-hydroxypropanimidoate Hydrochloride (2c)

Colorless crystals (69%); mp 135.2 °C.

IR (KBr): 1637 cm^{-1}.

Ethyl 3-(4-Chlorophenyl)-3-hydroxypropanimidoate Hydrochloride (2d)

Colorless solid (96%); mp 123.5 °C.

IR (KBr): 1638 cm^{-1}.

Ethyl 3-Hydroxy-3-(4-methylphenyl)propanimidoate Hydrochloride (2e)

Colorless solid (66%); mp 119.8 °C.

IR (KBr): 1654 cm^{-1}.

Ethyl 3-(3-Bromo-4-fluorophenyl)-3-hydroxypropanimidoate Hydrochloride (2f)

Colorless solid (75%); mp 126.4 °C.

IR (KBr): 1637 cm^{-1}.

Methyl 3-Hydroxy-3-naphthalen-1-ylpropanimidoate Hydrochloride (2g)

Colorless solid (80%); mp 211.0 °C.

IR (KBr): 1656 cm^{-1}.

Ethyl 3-Hydroxy-3-naphthalen-1-ylpropanimidoate Hydrochloride (2h)

Colorless solid (93%); mp 112.0 °C.

IR (KBr): 1654 cm^{-1}.

Benzyl 3-Hydroxy-3-naphthalen-1-ylpropanimidoate Hydrochloride (2i)

Colorless solid (63%); mp 188.4 °C.

IR (KBr): 1639 cm^{-1}.

2-Phenylethyl 3-Hydroxy-3-naphthalen-1-ylpropanimidoate Hydrochloride (2j)

Colorless solid (86%); mp 129.0 °C.

IR (KBr): 1654 cm^{-1}.

Preparation of 4a–j; General Procedure

The crude imidate hydrochlorides **2** (2.5 mmol) were converted into the corresponding imidate bases by treatment with ice-cold, sat. aq K_2CO_3 (40 mL) and subsequent extraction with Et_2O (3 × 15 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After structure conformation by IR spectroscopy and TLC, the remaining oil was dissolved in anhydrous CH_2Cl_2 (15 mL). 1,1′-Carbonyldi-(1,2,4-triazole) (CDT; 451 mg, 2,75 mmol) was added at 5 °C and the reaction mixture was stirred at r.t. for 1 h. The resulting suspension was washed with H_2O (3 × 10 mL), dried over $MgSO_4$ and filtered. The solvent was removed and the remaining residue was crystallized from Et_2O–*n*-hexane to afford compounds **4a–j** as solid products. Recrystallization from EtOAc–*n*-hexane provided analytically pure products.

4-Ethoxy-6-phenyl-5,6-dihydro-2*H*-1,3-oxazin-2-one (4a)

Yield: 356 mg (65%); colorless crystals; mp 86.5 °C.

IR (KBr): 1725, 1596 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.31 (t, *J* = 7.2 Hz, 3 H), 2.89 (dd, *J* = 16.8, 4.3 Hz, 1 H), 3.01 (dd, *J* = 16.7, 11.4 Hz, 1 H), 4.38 (q,

J = 7.2 Hz, 2 H), 5.53 (dd, *J* = 11.5, 4.3 Hz, 1 H), 7.36–7.46 (m, 5 H).

^{13}C NMR (DMSO-d_6): δ = 13.7, 31.8, 64.0, 75.1, 126.4, 127.3, 128.6, 137.8, 155.6, 178.2.

Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.71; H, 6.11; N, 6.53.

6-*tert*-Butyl-4-methoxy-5,6-dihydro-2*H*-1,3-oxazin-2-one (4b)
Yield: 282 mg (62%); colorless solid; mp 119.2 °C.

IR (KBr): 1725, 1608 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 0.91 (s, 9 H), 2.49–2.65 (m, 2 H), 3.87 (s, 3 H), 4.09 (dd, *J* = 12.6, 4.3 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 25.2, 26.6, 33.7, 55.4, 81.4, 156.4, 179.8.

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.23; H, 8.07; N, 7.44.

4-Ethoxy-6-(4-fluorophenyl)-5,6-dihydro-2*H*-1,3-oxazin-2-one (4c)
Yield: 415 mg (70%); colorless crystals; mp 114.4 °C.

IR (KBr): 1721, 1591 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.31 (t, *J* = 7.1 Hz, 3 H), 2.87 (dd, *J* = 16.7, 4.2 Hz, 1 H), 3.03 (dd, *J* = 16.7, 11.8 Hz, 1 H), 4.39 (q, *J* = 7.0 Hz, 2 H), 5.53 (dd, *J* = 12.0, 4.1 Hz, 1 H), 7.24–7.30 (m, 2 H), 7.48–7.53 (m, 1 H).

^{13}C NMR (DMSO-d_6): δ = 13.7, 31.8, 64.1, 74.6, 115.4 (d, $^2J_{C,F}$ = 21.1 Hz), 128.8 (d, $^3J_{C,F}$ = 8.2 Hz), 134.0 (d, $^4J_{C,F}$ = 2.7 Hz), 162.1 (d, $^1J_{C,F}$ = 245.6 Hz), 178.2.

Anal. Calcd for $C_{12}H_{12}FNO_3$: C, 60.76; H, 5.10; N, 5.90. Found: C, 60.82; H, 5.12; N, 5.81.

6-(4-Chlorophenyl)-4-ethoxy-5,6-dihydro-2*H*-1,3-oxazin-2-one (4d)
Yield: 450 mg (71%); colorless crystals; mp 115.5 °C.

IR (KBr): 1721, 1592 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.31 (t, *J* = 7.2 Hz, 3 H), 2.90 (dd, *J* = 16.7, 4.6 Hz, 1 H), 3.00 (dd, *J* = 16.7, 11.4 Hz, 1 H), 4.38 (q, *J* = 6.6 Hz, 2 H), 5.55 (dd, *J* = 11.4, 4.3 Hz, 1 H), 7.43–7.57 (m, 4 H).

^{13}C NMR (DMSO-d_6): δ = 13.7, 31.7, 64.1, 74.4, 128.3, 128.6, 133.3, 136.8, 155.4, 178.0.

Anal. Calcd for $C_{12}H_{12}ClNO_3$: C, 56.82; H, 4.77; N, 5.52. Found: C, 56.56; H, 4.83; N, 5.58.

4-Ethoxy-6-(4-methylphenyl)-5,6-dihydro-2*H*-1,3-oxazin-2-one (4e)
Yield: 321 mg (55%); colorless crystals; mp 93.5 °C.

IR (KBr): 1718, 1596 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.31 (t, *J* = 7.1 Hz, 3 H), 2.31 (s, 3 H), 2.84 (dd, *J* = 16.8, 4.3 Hz, 1 H), 2.99 (dd, *J* = 16.8, 11.4 Hz, 1 H), 4.37 (q, *J* = 7.3 Hz, 2 H), 5.47 (dd, *J* = 11.4, 4.1 Hz, 1 H), 7.23 (d, *J* = 7.9 Hz, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H).

^{13}C NMR (DMSO-d_6): δ = 14.1, 21.1, 32.2, 64.4, 75.5, 126.8, 129.5, 135.2, 138.5, 156.1, 178.6.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.95; H, 6.53; N, 5.95.

6-(3-Bromo-4-fluorophenyl)-4-ethoxy-5,6-dihydro-2*H*-1,3-oxazin-2-one (4f)
Yield: 506 mg (64%); colorless crystals; mp 130.5 °C.

IR (KBr): 1720, 1591 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.32 (t, *J* = 7.1 Hz, 3 H), 2.91 (dd, *J* = 16.8, 4.1 Hz, 1 H), 3.05 (dd, *J* = 16.8, 11.9 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 5.54 (dd, *J* = 11.8, 3.9 Hz, 1 H), 7.45 (t, *J* = 8.6 Hz, 1 H), 7.50–7.55 (m, 1 H), 7.83 (dd, *J* = 6.7, 2.2 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 13.7, 31.6, 64.1, 73.9, 108.1 (d, $^2J_{C,F}$ = 20.8 Hz), 116.9 (d, $^2J_{C,F}$ = 22.3 Hz), 128.1 (d, $^3J_{C,F}$ = 8.5 Hz), 131.8, 136.0 (d, $^4J_{C,F}$ = 3.1 Hz), 155.3, 158.2 (d, $^1J_{C,F}$ = 245.8 Hz), 178.1.

Anal. Calcd for $C_{12}H_{11}BrFNO_3$: C, 45.59; H, 3.51; N, 4.43. Found: C, 45.55; H, 3.74; N, 4.21.

4-Methoxy-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (4g)
Yield: 447 mg (70%); colorless solid; mp 124.0 °C.

IR (KBr): 1727, 1610 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.01 (dd, *J* = 16.7, 4.4 Hz, 1 H), 3.19 (dd, *J* = 16.5, 11.8 Hz, 1 H), 3.96 (s, 3 H), 6.37 (dd, *J* = 11.8, 4.0 Hz, 1 H), 7.55–7.63 (m, 4 H), 7.96–8.01 (m, 2 H), 8.16–8.21 (m, 1 H).

^{13}C NMR (DMSO-d_6): δ = 31.1, 55.1, 72.3, 123.3, 124.0, 125.3, 126.0, 126.6, 128.7, 129.2, 130.0, 133.0, 133.3, 155.7, 179.0.

Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.36; H, 5.17; N, 5.36.

4-Ethoxy-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (4h)
Yield: 451 mg (67%); colorless solid; mp 83.0 °C.

IR (KBr): 1720, 1596 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.34 (t, *J* = 7.1 Hz, 3 H), 2.98 (dd, *J* = 16.8, 4.1 Hz, 1 H), 3.18 (dd, *J* = 16.5, 11.7 Hz, 1 H), 4.43 (q, *J* = 7.1 Hz, 2 H), 6.37 (dd, *J* = 11.6, 3.9 Hz, 1 H), 7.55–7.66 (m, 4 H), 7.96–8.02 (m, 2 H), 8.17–8.21 (m, 1 H).

^{13}C NMR (DMSO-d_6): δ = 13.8, 31.3, 64.1, 72.2, 123.3, 124.0, 125.4, 126.0, 126.7, 128.7, 129.2, 130.1, 133.1, 133.3, 155.9, 178.5.

Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.20; H, 5.73; N, 5.36.

4-(Benzyloxy)-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (4i)
Yield: 497 mg (60%); colorless solid; mp 138.0 °C.

IR (KBr): 1718, 1591 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.07 (dd, *J* = 16.7, 4.0 Hz, 1 H), 3.26 (dd, *J* = 16.7, 11.6 Hz, 1 H), 5.40–5.52 (m, 2 H), 6.41 (dd, *J* = 11.5, 3.9 Hz, 1 H), 7.38–7.46 (m, 3 H), 7.47–7.52 (m, 2 H), 7.55–7.62 (m, 3 H), 7.63–7.67 (m, 1 H), 7.96–8.02 (m, 2 H), 8.20 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 40.7, 65.7, 68.4, 123.2, 124.3, 125.7, 126.1, 126.8, 127.7, 128.3, 128.6, 129.4, 130.7, 133.3, 136.1, 137.5, 155.6, 169.6.

Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.21; H, 5.17; N, 4.23. Found: C, 75.93; H, 5.27; N, 3.97.

6-Naphthalen-1-yl-4-(2-phenylethoxy)-5,6-dihydro-2*H*-1,3-oxazin-2-one (4j)
Yield: 613 mg (71%); colorless crystals; mp 123.3 °C.

IR (KBr): 1718, 1590 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.99 (dd, *J* = 16.8, 4.3 Hz, 1 H), 3.06 (t, *J* = 6.8 Hz, 2 H), 3.18 (dd, *J* = 16.8, 11.3 Hz, 1 H), 4.53–4.67 (m, 2 H), 6.36 (dd, *J* = 11.3, 4.3 Hz, 1 H), 7.21–7.32 (m, 5 H), 7.53–7.62 (m, 4 H), 7.96–8.02 (m, 2 H), 8.17 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 31.1, 33.9, 68.3, 72.2, 123.3, 124.0, 125.3, 126.0, 126.4, 126.6, 128.4, 128.9, 129.2, 130.1, 132.9, 133.3, 137.6, 155.7, 178.4.

Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.63; H, 5.74; N, 4.09.

Preparation of 5a–f, 6a–f and 7a-e; General Procedure

To a solution of the appropriate 4-aralkoxy(alkoxy)-5,6-dihydro-2*H*-1,3-oxazine-2-one **4** (1.5 mmol) in anhydrous CH_2Cl_2 (10 mL), the appropriate amine, O-substituted hydroxylamine or *N*,*N*-disubstituted hydrazine (2 mmol) was added at 5 °C. After stirring at r.t. for 8 h, the solvent was removed and the remaining residue was crystallized from EtOAc–*n*-hexane.

4-(Benzylamino)-6-phenyl-5,6-dihydro-2*H*-1,3-oxazin-2-one (5a)

Yield: 362 mg (86%); colorless crystals; mp 114.5 °C.

IR (KBr): 3287, 1663, 1591 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.67–2.89 (m, 2 H), 4.45–4.63 (m, 2 H), 5.39 (dd, *J* = 9.7, 4.6 Hz, 1 H), 7.22–7.44 (m, 10 H), 8.97 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 32.5, 43.8, 74.5, 126.6, 127.5, 128.0, 128.7, 128.8, 128.9, 138.0, 139.3, 157.3, 168.7.

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.52; H, 5.84; N, 9.99.

6-*tert*-Butyl-4-[(2-chloro-6-fluorobenzyl)amino]-5,6-dihydro-2*H*-1,3-oxazin-2-one (5b)

Yield: 394 mg (84%); colorless crystals; mp 125.7 °C.

IR (KBr): 3226, 1687, 1582 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 0.89 (s, 9 H), 2.28–2.48 (m, 2 H), 3.86 (dd, *J* = 12.7, 3.0 Hz, 1 H), 4.52–4.70 (m, 2 H), 7.30 (t, *J* = 8.6 Hz, 1 H), 7.37–7.50 (m, 2 H), 8.65 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 25.2, 26.2, 33.7, 36.4, 80.3, 115.0, 122.7 (d, $^2J_{C,F}$ = 18.3 Hz), 126.0, 131.2, 135.4 (d, $^3J_{C,F}$ = 6.1 Hz), 157.7, 161.7 (d, $^1J_{C,F}$ = 248.7 Hz), 169.3.

Anal. Calcd for $C_{17}H_{18}ClFN_2O_2$: C, 57.60; H, 5.80; N, 8.96. Found: C, 57.75; H, 5.99; N, 8.93.

6-(4-Chlorophenyl)-4-[(2,6-dichlorobenzyl)amino]-5,6-dihydro-2*H*-1,3-oxazin-2-one (5c)

Yield: 501 mg (87%); colorless crystals; mp 134.0 °C.

IR (KBr): 3215, 1686, 1576 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.67–2.85 (m, 2 H), 4.65–4.79 (m, 2 H), 5.40 (dd, *J* = 9.7, 4.6 Hz, 1 H), 7.40–7.50 (m, 5 H), 7.52–7.58 (m, 2 H), 8.73 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 31.9, 41.0, 73.9, 128.7, 128.9, 128.9, 129.0, 131.3, 132.2, 133.4, 136.2, 138.2, 156.8, 168.3.

Anal. Calcd for $C_{17}H_{13}Cl_3N_2O_2$: C, 53.22; H, 3.42; N, 7.30. Found: C, 53.31; H, 3.43; N, 7.22.

6-(4-Methylphenyl)-4-morpholin-4-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (5d)

Yield: 350 mg (85%); colorless crystals; mp 161.7 °C.

IR (KBr): 1686, 1561 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.31 (s, 3 H), 2.69 (dd, *J* = 16.4, 11.7 Hz, 1 H), 3.10 (dd, *J* = 16.4, 3.6 Hz, 1 H), 3.50–3.77 (m, 7 H), 3.91 (ddd, *J* = 13.1, 5.6, 3.1 Hz, 1 H), 5.22 (dd, *J* = 11.7, 3.4 Hz, 1 H), 7.22 (d, *J* = 7.8 Hz, 2 H), 7.32 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (DMSO-d_6): δ = 20.7, 29.3, 43.7, 46.2, 65.6, 66.0, 73.8, 126.3, 128.9, 136.0, 137.6, 156.8, 168.1.

Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.39; H, 6.69; N, 10.15.

4-(Cyclopentylamino)-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (5e)

Yield: 370 mg (80%); colorless solid; mp 133.0 °C.

IR (KBr): 3226, 1677, 1590 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.36–1.46 (m, 1 H), 1.50–1.72 (m, 5 H), 1.84–2.00 (m, 2 H), 2.78–2.93 (m, 2 H), 4.25–4.40 (m, 1 H), 6.14 (dd, *J* = 10.3, 4.3 Hz, 1 H), 7.52–7.62 (m, 4 H), 7.90–8.02 (m, 2 H), 8.14 (d, *J* = 7.8 Hz, 1 H), 8.51 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 23.9, 23.9, 31.9, 32.3, 52.1, 71.5, 123.6, 123.8, 125.7, 126.3, 126.8, 129.1, 129.1, 130.2, 133.7, 134.8, 157.4.

Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 73.86; H, 6.79; N, 8.91.

4-[(2-Chlorobenzyl)amino]-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (5f)

Yield: 449 mg (82%); colorless crystals; mp 130.5 °C.

IR (KBr): 3227, 1676, 1597 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.97–3.09 (m, 2 H), 4.57 (dd, *J* = 15.6, 5.0 Hz, 1 H), 4.69 (dd, *J* = 15.6, 5.5 Hz, 1 H), 6.24 (dd, *J* = 9.5, 4.5 Hz, 1 H), 7.31–7.37 (m, 3 H), 7.46–7.50 (m, 1 H), 7.53–7.63 (m, 4 H), 7.93–8.02 (m, 2 H), 8.16 (d, *J* = 8.0 Hz, 1 H), 8.98 (t, *J* = 5.3 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 31.7, 42.0, 71.7, 123.6, 123.9, 125.7, 126.3, 126.9, 127.7, 129.1, 129.2, 129.5, 129.6, 129.8, 130.2, 132.7, 133.7, 134.6, 135.0, 157.2, 169.2.

Anal. Calcd for $C_{21}H_{17}ClN_2O_2$: C, 69.14; H, 4.70; N, 7.68. Found: C, 69.43; H, 4.84; N, 7.74.

(4*Z*)-6-Phenyl-1,3-oxazinane-2,4-dione 4-(*O*-Benzyloxime) (6a)

Yield: 396 mg (89%); colorless solid; mp 188.5 °C.

IR (KBr): 3220, 1718, 1666 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.77 (dd, *J* = 15.7, 3.0 Hz, 1 H), 2.92 (dd, *J* = 15.5, 10.7 Hz, 1 H), 4.99 (s, 2 H), 5.58 (dd, *J* = 10.5, 2.9 Hz, 1 H), 7.28–7.44 (m, 10 H), 10.32 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 30.0, 74.8, 76.1, 126.2, 127.4, 127.6, 128.1, 128.5, 128.6, 137.7, 138.1, 142.6, 149.4.

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 68.87; H, 5.56; N, 9.22.

(4*Z*)-6-(4-Chlorophenyl)-1,3-oxazinane-2,4-dione 4-[*O*-(2-Fluorobenzyl)oxime] (6b)

Yield: 481 mg (92%); colorless solid; mp 114.5 °C.

IR (KBr): 3233, 1719, 1668 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.75–2.95 (m, 2 H), 5.04 (s, 2 H), 5.61 (dd, *J* = 10.8, 3.0 Hz, 1 H), 7.15–7.22 (m, 2 H), 7.34–7.40 (m, 1 H), 7.45–7.50 (m, 4 H), 7.52–7.56 (m, 1 H), 10.37 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 29.9, 68.4 (d, *J* = 3.8 Hz), 75.4, 115.0 (d, $^2J_{C,F}$ = 21.6 Hz), 124.2 (d, $^4J_{C,F}$ = 3.1 Hz), 124.7 (d, $^2J_{C,F}$ = 14.6 Hz), 128.2, 128.6, 129.7 (d, $^3J_{C,F}$ = 8.5 Hz), 130.6 (d, $^3J_{C,F}$ = 3.8 Hz), 133.3, 136.7, 142.8, 149.2, 160.0 (d, $^1J_{C,F}$ = 245.1 Hz).

Anal. Calcd for $C_{17}H_{14}ClFN_2O_3$: C, 58.55; H, 4.05; N, 8.03. Found: C, 58.55; H, 4.34; N, 7.84.

(4*Z*)-6-(4-Methylphenyl)-1,3-oxazinane-2,4-dione 4-[*O*-(4-Methylbenzyl)oxime] (6c)

Yield: 428 mg (88%); colorless solid; mp 173.5 °C.

IR (KBr): 3279, 1719, 1657 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.29 (s, 3 H), 2.31 (s, 3 H), 2.71 (dd, *J* = 15.6, 3.3 Hz, 1 H), 2.88 (dd, *J* = 15.7, 10.7 Hz, 1 H), 4.93 (s, 2 H), 5.51 (dd, *J* = 10.5, 3.0 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.29 (dd, *J* = 13.5, 8.0 Hz, 4 H), 10.24 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 20.7, 20.7, 30.0, 74.6, 76.1, 126.2, 127.7, 128.6, 129.0, 134.7, 135.0, 136.6, 138.0, 142.5, 149.5.

Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.23; H, 6.37; N, 8.49.

(4*Z*)-6-Naphthalen-1-yl-1,3-oxazinane-2,4-dione 4-(*O*-Benzyloxime) (6d)

Yield: 452 mg (87%); colorless solid; mp 141.5 °C.

IR (KBr): 3310, 1721, 1662 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.89 (dd, *J* = 15.8, 2.9 Hz, 1 H), 3.10 (dd, *J* = 15.7, 10.9 Hz, 1 H), 5.03 (s, 2 H), 6.41 (dd, *J* = 10.6, 2.5 Hz, 1 H), 7.27–7.33 (m, 1 H), 7.36 (t, *J* = 7.3 Hz, 2 H), 7.41–7.45 (m, 2 H), 7.52–7.66 (m, 4 H), 7.98 (t, *J* = 7.1 Hz, 2 H), 8.17 (d, *J* = 7.8 Hz, 1 H), 10.42 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 29.4, 73.1, 74.8, 123.3, 123.8, 125.3, 126.0, 126.7, 127.4, 127.7, 128.1, 128.7, 129.3, 130.0, 132.9, 133.3, 138.1, 142.8, 149.6.

Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.86; H, 5.37; N, 8.15.

6-Naphthalen-1-yl-4-[(3-phenylpropoxy)amino]-5,6-dihydro-2*H*-1,3-oxazin-2-one (6e)

Yield: 410 mg (73%); colorless solid; mp 134.5 °C.

IR (KBr): 3229, 1718, 1654 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.85–1.96 (m, 2 H), 2.72 (t, *J* = 7.6 Hz, 2 H), 2.90 (dd, *J* = 15.7, 2.5 Hz, 1 H), 3.11 (dd, *J* = 15.7, 11.1 Hz, 1 H), 3.95 (t, *J* = 6.2 Hz, 2 H), 6.42 (dd, *J* = 10.7, 2.1 Hz, 1 H), 7.14–7.22 (m, 1 H), 7.22–7.33 (m, 4 H), 7.53–7.64 (m, 3 H), 7.67 (d, *J* = 7.1 Hz, 1 H), 7.99 (t, *J* = 7.4 Hz, 2 H), 8.18 (d, *J* = 7.8 Hz, 1 H), 10.29 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 29.5, 30.3, 31.4, 72.3, 73.2, 123.3, 123.8, 125.3, 125.7, 126.0, 126.7, 128.2, 128.4, 128.7, 129.3, 129.9, 133.0, 133.3, 141.9, 142.3, 149.8.

Anal. Calcd for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48. Found: C, 73.45; H, 6.07; N, 7.45.

4-[(1-Methoxy-1-methylethoxy)amino]-6-naphthalen-1-yl-5,6-dihydro-2*H*-1,3-oxazin-2-one (6f)

Yield: 404 mg (82%); colorless solid; mp 175.7 °C.

IR (KBr): 3243, 1735, 1666 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.39 (s, 3 H), 1.42 (s, 3 H), 2.96 (dd, *J* = 15.8, 2.9 Hz, 1 H), 3.13 (s, 3 H), 3.15 (dd, *J* = 15.9, 10.6 Hz, 1 H), 6.42 (dd, *J* = 10.4, 2.6 Hz, 1 H), 7.54–7.65 (m, 3 H), 7.68 (d, *J* = 7.1 Hz, 1 H), 7.99 (t, *J* = 7.2 Hz, 2 H), 8.19 (d, *J* = 8.1 Hz, 1 H), 10.30 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 23.5, 23.9, 29.6, 48.4, 73.2, 102.7, 123.4, 123.8, 125.3, 126.0, 126.7, 128.7, 129.3, 130.0, 133.0, 133.3, 143.0, 149.8.

Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.55; H, 6.20; N, 8.60.

(4*E*/*Z*)-4-[(4-Methylpiperazin-1-yl)imino]-6-phenyl-1,3-oxazinan-2-one (7a)

Yield: 329 mg (76%); colorless solid; mp 111.0 °C; ratio *E*/*Z* = 65:35.

IR (KBr): 3277, 1734, 1648 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ (*E*-isomer) = 2.17 (s, 3 H), 2.33–2.60 (m, 8 H), 2.78 (dd, *J* = 16.1, 3.0 Hz, 1 H), 2.96 (dd, *J* = 15.8, 11.0 Hz, 1 H), 5.58 (dd, *J* = 10.7, 2.4 Hz, 1 H), 7.37–7.48 (m, 5 H), 9.57 (br s, 1 H); (*Z*-isomer) = 2.13 (s, 3 H), 2.33–2.60 (m, 8 H), 2.90 (dd, *J* = 16.7, 11.2 Hz, 1 H), 3.35 (dd, *J* = 16.7, 3.1 Hz, 1 H), 5.46 (dd, *J* = 11.3, 3.3 Hz, 1 H), 7.37–7.48 (m, 5 H), 10.26 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ (*E*/*Z*) = 28.3, 32.4, 45.4, 45.5, 53.5, 53.9, 54.0, 54.7, 75.1, 76.1, 126.3, 126.4, 128.5, 128.6, 128.6, 137.7, 138.1, 151.4.

Anal. Calcd for $C_{15}H_{20}N_4O_2$: C, 62.48; H, 6.99; N, 19.43. Found: C, 62.74; H, 7.26; N, 19.12.

(4*E*/*Z*)-6-(4-Fluorophenyl)-4-(morpholin-4-ylimino)-1,3-oxazinan-2-one (7b)

Yield: 330 mg (75%); colorless solid; mp 174.5 °C; ratio *E*/*Z* = 70:30.

IR (KBr): 3283, 1726, 1656 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ (*E*-isomer) = 2.46–2.64 (m, 4 H), 2.77 (dd, *J* = 15.8, 3.0 Hz, 1 H), 2.99 (dd, *J* = 15.9, 11.2 Hz, 1 H), 3.72 (t, *J* = 4.6 Hz, 4 H), 5.60 (dd, *J* = 11.0, 3.0 Hz, 1 H), 7.23–7.30 (m, 2 H), 7.49–7.56 (m, 2 H), 9.87 (br s, 1 H); (*Z*-isomer) = 2.46–2.64 (m, 4 H), 2.92 (dd, *J* = 16.7, 11.4 Hz, 1 H), 3.41 (dd, *J* = 16.7, 3.1 Hz, 1 H), 3.63 (t, *J* = 4.1 Hz, 4 H), 5.48 (dd, *J* = 11.3, 3.0 Hz, 1 H), 7.23–7.30 (m, 2 H), 7.49–7.56 (m, 2 H), 10.41 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ (*E*/*Z*) = 28.3, 32.4, 54.7, 55.5, 65.2, 65.4, 74.5, 75.5, 115.4 (d, $^2J_{C,F}$ = 21.6 Hz), 128.7 (d, $^3J_{C,F}$ = 8.5 Hz), 128.8 (d, $^3J_{C,F}$ = 8.5 Hz), 133.9 (d, $^4J_{C,F}$ = 3.1 Hz), 134.3 (d, $^4J_{C,F}$ = 3.1 Hz), 149.4, 149.8, 162.1 (d, $^1J_{C,F}$ = 245.1 Hz).

Anal. Calcd for $C_{14}H_{16}FN_3O_3$: C, 57.33; H, 5.50; N, 14.33. Found: C, 57.24; H, 5.71; N, 14.21.

(4*E*/*Z*)-4-(Dimethylhydrazono)-6-naphthalen-1-yl-1,3-oxazinan-2-one (7c)

Yield: 316 mg (72%); colorless solid; mp 142.5 °C; ratio *E*/*Z* = 68:32.

IR (KBr): 3243, 1733, 1645 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ (*E*-isomer) = 2.38 (s, 6 H), 2.89 (dd, *J* = 15.8, 3.0 Hz, 1 H), 3.11 (dd, *J* = 15.1, 11.0 Hz, 1 H), 6.37–6.45 (m, 1 H), 7.53–7.69 (m, 4 H), 7.99 (t, *J* = 8.2 Hz, 2 H), 8.18 (d, *J* = 8.0 Hz, 1 H), 9.83 (br s, 1 H); (*Z*-isomer) = 2.35 (s, 6 H), 3.05 (dd, *J* = 16.8, 11.0 Hz, 1 H), 3.54 (dd, *J* = 16.5, 3.3 Hz, 1 H), 6.30 (dd, *J* = 10.8, 3.0 Hz, 1 H), 7.53–7.69 (m, 4 H), 7.99 (t, *J* = 8.2 Hz, 2 H), 8.18 (d, *J* = 8.0 Hz, 1 H), 10.14 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ (*E*/*Z*) = 27.6, 31.7, 46.8, 47.6, 72.0, 73.9, 123.3, 123.6, 123.8, 125.3, 125.3, 125.9, 126.0, 126.6, 128.7, 129.1, 129.2, 129.9, 130.0, 133.0, 133.3, 133.5.

HRFAB-MS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}N_3O_2$: 284.1399; found: 284.1389.

Anal. Calcd for $C_{16}H_{17}N_3O_3 \cdot 0.5H_2O$: C, 65.74; H, 6.21; N, 14.37. Found: C, 65.38; H, 6.10; N, 14.27.

(4*E*/*Z*)-6-Naphthalen-1-yl-4-(piperidin-1-ylimino)-1,3-oxazinan-2-one (7d)

Yield: 320 mg (66%); colorless solid; mp 157.3 °C; ratio *E*/*Z* = 63:37.

IR (KBr): 3265, 1730, 1654 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ (*E*-isomer) = 1.39 (br s, 2 H), 1.63–1.68 (m, 4 H), 2.51–2.62 (m, 4 H), 2.91 (dd, *J* = 15.9, 2.9 Hz, 1 H), 3.15 (dd, *J* = 15.8, 10.8 Hz, 1 H), 6.42 (dd, *J* = 10.4, 2.4 Hz, 1 H), 7.55–7.68 (m, 4 H), 7.99 (t, *J* = 8.2 Hz, 2 H), 8.17–8.22 (m, 1 H), 9.60 (br s, 1 H); (*Z*-isomer) = 1.31 (br s, 2 H), 1.46–1.55 (m, 4 H), 2.52–2.56 (m, 4 H), 3.06 (dd, *J* = 16.6, 11.0 Hz, 1 H), 3.52 (dd, *J* = 16.6, 3.3

Hz, 1 H), 6.28 (dd, *J* = 10.9, 2.9 Hz, 1 H), 7.54–7.67 (m, 4 H), 7.99 (t, *J* = 8.2 Hz, 2 H), 8.17–8.21 (m, 1 H), 10.38 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ (*E*/*Z*) = 23.1, 23.4, 24.5, 24.9, 27.6, 31.7, 55.6, 56.4, 72.1, 73.2, 123.3, 123.8, 123.9, 125.3, 125.3, 125.9, 126.0, 126.6, 126.6, 128.7, 129.1, 129.3, 130.0, 132.9, 133.3, 133.6, 149.2, 150.0.

Anal. Calcd for $C_{19}H_{21}N_3O_2$: C, 70.57; H, 6.55; N, 12.99. Found: C, 70.22; H, 6.74; N, 12.74.

(4*E*/*Z*)-4-(Morpholin-4-ylimino)-6-naphthalen-1-yl-1,3-oxazinan-2-one (7e)

Yield: 425 mg (87%); colorless solid; mp 187.0 °C; ratio *E*/*Z* = 59:41.

IR (KBr): 3267, 1728, 1654 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ (*E*-isomer) = 2.61 (t, *J* = 4.3 Hz, 4 H), 2.92 (dd, *J* = 15.9, 3.1 Hz, 1 H), 3.16 (dd, *J* = 16.1, 10.8 Hz, 1 H), 3.75 (t, *J* = 4.6 Hz, 4 H), 6.43 (dd, *J* = 10.8, 3.0 Hz, 1 H), 7.54–7.65 (m, 3 H), 7.68 (d, *J* = 7.0 Hz, 1 H), 7.99 (t, *J* = 7.9 Hz, 2 H), 8.16–8.23 (m, 1 H), 9.94 (br s, 1 H); (*Z*-isomer) = 2.54–2.67 (m, 4 H), 3.11 (dd, *J* = 16.8, 11.3 Hz, 1 H), 3.55–3.60 (m, 1 H), 6.30 (dd, *J* = 11.0, 3.0 Hz, 1 H), 7.55–7.69 (m, 4 H), 7.99 (t, *J* = 7.9 Hz, 2 H), 8.16–8.23 (m, 1 H), 10.50 (br s, 1 H).

^{13}C NMR (DMSO-d_6): δ (*E*/*Z*) = 27.7, 31.8, 54.3, 54.8, 55.6, 65.2, 65.4, 65.7, 72.2, 73.1, 123.3, 123.4, 123.8, 124.1, 125.3, 125.3, 126.0, 126.6, 126.7, 128.7, 129.2, 129.3, 130.0, 132.9, 133.3, 133.4, 149.7, 150.0, 155.7.

Anal. Calcd for $C_{18}H_{19}N_3O_3$: C, 66.45; H, 5.89; N, 12.91. Found: C, 66.52; H, 6.10; N, 12.76.

Acknowledgment

The authors thank Prof. Dr. J. Kopf and Miss Isabelle Nevoigt for their valuable help in the preparation of the X-ray crystal structures. Moreover, the authors thank Prof. Dr. D. Geffken for his support.

References

(1) Kupchan, S. M.; Komoda, Y.; Court, W. A.; Thomas, G. J.; Smith, R. M.; Karim, A.; Gilmore, C. J.; Haltwanger, R. C.; Bryan, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 1354.
(2) (a) Hayes, K. *J. Am. Chem. Soc.* **1955**, *77*, 2333. (b) Bassus, J.; Pacheca, H.; Chareire, M.; Cier, M. *Eur. J. Med. Chem.* **1974**, *9*, 416.
(3) (a) Wang, G.; Ella-Menye, J.-R.; Sharma, V. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2177. (b) Ella-Menye, J.-R.; Sharma, V.; Wang, G. *J. Org. Chem.* **2005**, *70*, 463. (c) Wang, G. *Anti-Infect. Agents Med. Chem.* **2008**, *7*, 32.
(4) Testa, E.; Fontanella, L.; Cristiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1028.
(5) Church, T. L.; Byrne, C. M.; Lobkoovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 8156.
(6) Kaiser, E. M.; Hauser, C. R. *J. Org. Chem.* **1968**, *33*, 3402.
(7) Crystallographic data for compounds **4f**, **5c** and **6f** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 726927 (**4f**), CCDC 726928 (**5c**) and CCDC 726929 (**6f**).