SUPPORTING INFORMATION

Synthesis of α-Thiooximes by Addition of Thiols to N,N-bis(oxy)enamines. A Comparative Study of S-, N- and O-nucleophiles in Michael Reaction with Nitrosoalkene Species

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1. General experimental

All reactions were carried out in oven-dried (150°C) glassware. NMR spectra were recorded at room temperature with residual solvents peaks as an internal standard. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), br (broad). Peaks in FTIR-spectra data are reported in cm$^{-1}$ with the following relative intensities: s (strong), m (medium), w (weak), br (broad), sh (shoulder). HRMS were measured on electrospray ionization (ESI) instrument with a time-of-flight (TOF) detector. Concentrations in optical rotation angles are given in g/100 mL. $[\alpha]_D$ values are given in 10$^{-1}$ deg cm$^2$ g$^{-1}$.

Column chromatography was performed using Kieselgel 40-60µm 60A. Analytical thin-layer chromatography was performed on silica gel plates with QF-254. Visualization was accomplished with UV light and solution of ninhydrine/acetic acid in ethanol or solution of anisaldehyde/H$_2$SO$_4$ in ethanol. DMF was distilled from CaH$_2$ under reduced pressure. CH$_2$Cl$_2$ was distilled from CaH$_2$. THF distilled first from LiAlH$_4$ prior use. Methanol, hexane, toluene, pentane, diethyl ether, methyl tert-butyl ether, and ethyl acetate were distilled without drying agents. All thiols, NaBH$_3$CN, benzoic acid, $p$-ethylphenol and diethylamine were commercial grade and were used as received. $N,N$-Bis(oxy)enamines 2a, 1 2b, 1 2c, 2 2d, 3 2e, 4 2f, 3 2i, 1 6a, 3 and 6b$^3$ were prepared following the previously described methods from corresponding aliphatic nitro compounds or nitroalkenes, respectively (see Table S1 for structures of $N,N$-bis(oxy)enamines 2 and 6).

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**Table S1**

\[
\begin{array}{c}
\text{Table S1} \\
\text{R}^1 - \text{R} \xrightarrow{TMSX, Et}_3\text{N, CH}_2\text{Cl}_2 \xrightarrow{X = \text{Cl, Br, OTf}} \text{R}^1 \text{N} - \text{OTMS}
\end{array}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>Me</td>
</tr>
<tr>
<td>2b</td>
<td>H</td>
</tr>
<tr>
<td>2c</td>
<td>Ph</td>
</tr>
<tr>
<td>2d</td>
<td>CO\textsubscript{2}Me</td>
</tr>
<tr>
<td>2e</td>
<td>Ph</td>
</tr>
<tr>
<td>2f</td>
<td>CO\textsubscript{2}Et</td>
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<tr>
<td>2g</td>
<td>Me</td>
</tr>
</tbody>
</table>

*Cyclic N,N-bis(oxy)enamines 6:*

- **6a**
  - **Synthesis:**
    - **Reagents:** SnCl\textsubscript{4}, CH\textsubscript{2}Cl\textsubscript{2} at -90°C
    - **Yield:** 94%
  - **Product:** 6a, 84%

- **6b**
  - **Synthesis:**
    - **Reagents:** (CH\textsubscript{3})\textsubscript{3}S\textsuperscript{+}I\textsubscript{−}, NaH, CuI in DMF
    - **Yield:** 48%
  - **Product:** 6b, 86%
2. General procedures for the synthesis of α-thiooximes 1

**General procedure for the addition of thiophenols to N,N-bis(oxy)enamines 2 (method 1).**

To a stirred solution of N,N-bis(oxy)enamine 2 (1 mmol) in toluene (6 mL) was added p-thiocresol (124 mg, 1 mmol) or pyridine-2-thiol (111 mg, 1 mmol). After keeping for 24 h at r.t., methanol (5 mL) was added and the mixture was stirred for additional 1 h at r.t. and concentrated in vacuum (c.a. 45°C). The residue was subjected to a column chromatography on silica gel.

**General procedure for the addition of aliphatic thiols to N,N-bis(oxy)enamines 2 (method 2).**

A solution of thiol (1 mmol) in dimethylformamide (1.5 mL) was added to the corresponding N,N-bis(oxy)enamine 2 (1 mmol; 2 mmol for product 1n) with vigorous stirring. After keeping for 24 h at r.t., methanol (5 mL) was added and the mixture was stirred for additional 1 h at r.t. and concentrated in vacuum (c.a. 45°C). The residue was dried in vacuum (1 Torr, c.a. 50°C) to remove DMF and then subjected to a column chromatography on silica gel.
3. Characterization of α-thiooximes 1

![Diagram of 1-(p-Tolylthio)propan-2-one oxime (1a).]

1-(p-Tolylthio)propan-2-one oxime (1a).

Yield: 74% (method 1). White crystals. Mp = 81-83°C (pentane-Et₂O). Rᵣ = 0.29 (AcOEt-hexane = 1 : 1).

Dynamic mixture of mixture of E/Z-isomers, ratio 3 : 1.

\[ \text{δ} \text{H NMR (300 MHz, Chloroform-}d\text{, }E\text{-isomer)} \delta 8.35-8.23 \text{ (br, 1H, NOH), 7.31-7.24 (d, } J = 8.1 \text{ Hz, 2H, HC-3), 7.09 (d, } J = 8.1 \text{ Hz, 2H, HC-2), 3.56 (s, 2H, CH₂), 2.32 (s, 3H, } H_3C\text{-Ar), 1.99 (s, 3H, } H_3C\text{-C=N).} \]

\[ \text{δ} \text{C NMR (50 MHz, DEPT135, CDCl₃, } E\text{-isomer)} \delta 155.09 \text{ (C=N), 137.19 (C-4), 131.39 and 129.84 (C-2 and C-3), 131.00 (C-1), 39.93 (CH₂), 21.16 (H₃C-Ar), 12.89 (H₃C-C=N).} \]

\[ \text{δ} \text{H NMR (300 MHz, Chloroform-}d\text{, }Z\text{-isomer)} \delta 8.53-8.38 \text{ (br, 1H, NOH), 7.31 (d, } J = 8.1 \text{ Hz, 2H, HC-3), 7.09 (d, } J = 8.1 \text{ Hz, 2H, HC-2), 3.79 (s, 2H), 2.32 (s, 3H, } H_3C\text{-Ar), 1.92 (s, 3H, } H_3C\text{-C=N).} \]

\[ \text{δ} \text{C NMR (50 MHz, DEPT135, CDCl₃, } Z\text{-isomer)} \delta 154.94 \text{ (C=N), 136.84 (C-4), 131.78 (C-1), 130.33 and 129.84 (C-2 and C-3), 30.68 (CH₂), 21.19 (H₃C-Ar), 19.22 (H₃C-C=N).} \]

FT-IR (KBr): 3239 (s, br), 3104 (s, sh), 3022 (s, sh), 2920 (s), 2870 (s), 1660 (m), 1493 (s), 1448 (s), 1411 (s), 1368 (s), 1270 (m), 1230 (w), 1159 (m), 1091 (m), 1018 (s), 963 (s), 867 (m), 805 (s), 721 (m), 629 (m), 500 (s) cm⁻¹.

HRMS: calcd. for [C₁₀H₁₄NOS]⁺ 196.0793; found 196.0791 ([M+H]⁺).
<table>
<thead>
<tr>
<th>NOH</th>
<th>S</th>
</tr>
</thead>
</table>

**1-(Heptylthio)propan-2-one oxime (1b).**

Yield: 86% (method 2). Oil. $R_f = 0.89$ (AcOEt-hexane = 1 : 1).

Single isomer.

$^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 8.25 (s, 1H, NOH), 3.19 (s, 2H, $CH_2C=N$), 2.44 (t, $J = 7.4$ Hz, 2H, $CH_2S$), 2.00 (s, 3H, $CH_3$), 1.61-1.51 and 1.41-1.24 (2 m, 2H and 8H, 5 $CH_2$), 0.89 (t, $J = 6.8$ Hz, 3H, $CH_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 155.72 (C=N), 36.47 ($CH_2C=N$), 31.80, 31.30, 29.27, 28.94, 28.86 and 22.67 (6 $CH_2$), 14.13 and 12.64 (2 $CH_3$).

HRMS: calcd. for $[C_{10}H_{21}NOSNa]^+$ 226.1239; found 226.1236 ($[M+Na]^+$).
**2-(p-Tolylthio)acetaldehyde oxime (1c)**

Yield: 76% (method 1). White crystals. Mp = 63-65°C (pentane-Et₂O). R<br>₂ = 0.38 (AcOEt-hexane = 1 : 3).

Dynamic mixture of E/Z-isomers, ratio 1.3 : 1.

<table>
<thead>
<tr>
<th>Proton NMR (300 MHz, Chloroform-d, E-isomer) δ</th>
<th>Proton NMR (300 MHz, Chloroform-d, Z-isomer) δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.99 (s, 1H, NOH), 7.44 (t, J = 6.4 Hz, 1H, N=CH), 7.32 (d, J = 7.7 Hz, 2H, HC-3), 7.14 (d, J=7.7 Hz, 2H, HC-2), 3.58 (d, J = 6.4 Hz, 2H, CH₂), 2.35 (s, 3H, CH₃).</td>
<td>9.54 (s, 1H, OH), 7.32 (d, J = 7.7 Hz, 2H, HC-3), 7.14 (d, J = 7.7 Hz, 2H, HC-2), 6.84 (t, J = 5.6 Hz, 1H, N=CH), 3.80 (d, J = 5.6 Hz, 2H, CH₂), 2.35 (s, 3H, CH₃).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Carbon NMR (75 MHz, JMOD, Chloroform-d, E-isomer) δ</th>
<th>Carbon NMR (75 MHz, JMOD, Chloroform-d, Z-isomer) δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>147.95 (C=N), 136.81 (C-4), 131.43 and 129.80 (C-2 and C-3), 131.07 (C-1), 33.52 (CH₂), 21.01 (CH₃).</td>
<td>148.58 (C=N), 137.28 (C-4), 131.07 (C-1), 130.12 and 129.84 (C-2 and C-3), 27.59 (CH₂), 21.01 (CH₃).</td>
</tr>
</tbody>
</table>

HRMS: calcd. for [C₉H₁₂NOS]⁺ 182.0636; found 182.0634 ([M+H]+).
1-Phenyl-3-(p-tolylthio)propan-2-one oxime (1d)

Yield: 85% (method 1). White crystals. $R_f = 0.47$ (AcOEt-hexane = 1 : 1).

Dynamic mixture of $E$/Z-isomers, ratio 1.6 : 1. Pure $E$-isomer was obtained by crystallization. Mp = 138-139$^\circ$C (pentane-Et$_2$O).

$^1$H NMR (300 MHz, Chloroform-$d$, $E$-isomer) $\delta$ 7.96 (br, 1H, NOH), 7.41-7.05 (m, 9H, HC-2, HC-3 and $o,m,p$-C$_6$H$_5$), 3.93 (s, 2H, CH$_2$Ph), 3.52 (s, 2H, CH$_2$S), 2.34 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, JMOD, DMSO-$d_6$, $E$-isomer, characteristic signals) $\delta$ 153.11 (C=N), 38.23 (CH$_2$S), 27.59 (CH$_2$Ph), 20.49 (CH$_3$).

$^1$H NMR (300 MHz, Chloroform-$d$, Z-isomer) $\delta$ 7.96 (br, 1H, NOH), 7.39-7.07 (m, 9H, HC-2, HC-3 and $o,m,p$-C$_6$H$_5$), 3.69 (s, 2H, CH$_2$Ph), 3.60 (s, 2H, CH$_2$S), 2.35 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, JMOD, DMSO-$d_6$, Z-isomer, characteristic signals) $\delta$ 153.11 (C=N), 36.65 (CH$_2$Ph) and 31.42 (CH$_2$S), 20.49 (CH$_3$).

$^{13}$C NMR (75 MHz, JMOD, DMSO-$d_6$, both isomers) $\delta$ 136.57 and 135.92 (C-4), 129.93, 129.59, 129.52, 129.31, 128.85, 128.34, 126.40 and 126.16 (C-1, C-2, C-3 and $o,m,p$-C$_6$H$_5$).

Anal. calcd. for C$_{16}$H$_{17}$NOS: C, 70.81; H, 6.31; N, 5.16; S, 11.82. Found: C, 70.36; H, 6.22; N, 5.20; S, 11.18.
**Methyl 4-(hydroxyimino)-5-(p-tolylthio)pentanoate (1e)**

Yield: 94% (method 1). Oil. R<sub>f</sub> = 0.6 (AcOEt-hexane = 1 : 1).

Dynamic mixture of E/Z-isomers, ratio 2.6 : 1.

1H NMR (300 MHz, Chloroform-<sup>d</sup>, E-isomer) δ 9.04-8.97 (br, 1H, NOH), 7.26 (d, J = 8.2 Hz, 2H, HC-3), 7.08 (d, J = 7.9 Hz, 2H, HC-2), 3.69 (s, 3H, OCH<sub>3</sub>), 3.63 (s, 2H, CH<sub>2</sub>S), 2.79-2.72 and 2.69-2.61 (2 m, 2H and 2H, -CH<sub>2</sub>-CH<sub>2</sub>-), 2.30 (s, 3H, CH<sub>3</sub>).

13C NMR (75 MHz, CDCl<sub>3</sub>, E-isomer) δ 173.19 (C=O), 156.13 (C=N), 136.97 (C-4), 131.04 and 129.69 (C-2 and C-3), 130.82 (C-1), 51.73 (OCH<sub>3</sub>), 38.66 (CH<sub>2</sub>S), 29.86 (-CH<sub>2</sub>-CH<sub>2</sub>-C=O), 22.64 (-CH<sub>2</sub>-CH<sub>2</sub>-C=O), 20.97 (CH<sub>3</sub>).

1H NMR (300 MHz, Chloroform-<sup>d</sup>, Z-isomer) δ 9.10-9.04 (br, 1H, NOH), 7.30 (d, J = 8.2 Hz, 2H, HC-3), 7.10 (d, J = 8.2 Hz, 2H, HC-2), 3.80 (s, 2H, CH<sub>2</sub>S), 3.65 (s, 3H, OCH<sub>3</sub>), 2.66-2.60 and 2.56-2.49 (2 m, 2H and 2H, -CH<sub>2</sub>-CH<sub>2</sub>-), 2.31 (s, 3H, CH<sub>3</sub>).

13C NMR (75 MHz, CDCl<sub>3</sub>, Z-isomer) δ 173.19 (C=O), 155.58 (C=N), 136.74 (C-4), 130.82 (C-1), 130.30 and 129.69 (C-2 and C-3), 51.73 (OCH<sub>3</sub>), 30.24 (CH<sub>2</sub>S), 29.98 (-CH<sub>2</sub>-CH<sub>2</sub>-C=O) and 28.07 (-CH<sub>2</sub>-CH<sub>2</sub>-C=O), 20.97 (CH<sub>3</sub>).

HRMS: calcd. for [C<sub>13</sub>H<sub>18</sub>NO<sub>3</sub>S]<sup>+</sup> 268.0999; found 268.1002 ([M+H]<sup>+</sup>).
(Z)-1-Phenyl-2-(p-tolylthio)ethanone oxime (1f)

Yield: 80% (method 1). White crystals. Mp = 84-85°C (pentane-Et<sub>2</sub>O), lit.<sup>7</sup> 84-85°C. R<sub>f</sub> = 0.6 (AcOEt-hexane = 1 : 3).

Single isomer with Z-configuration.

<sup>1</sup>H NMR (300 MHz, Chloroform-d) δ 9.09 (s, 1H, NOH), 7.65-7.58 and 7.43-7.38 (2 m, 2H and 3H, o,m,p-C<sub>6</sub>H<sub>5</sub>), 7.36 (d, J = 7.9 Hz, 2H, HC-3), 7.10 (d, J = 7.9 Hz, 2H, HC-2), 4.23 (s, 2H, CH<sub>2</sub>), 2.33 (s, 3H, CH<sub>3</sub>).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 155.43 (C=N), 137.36 and 134.57 (C-4 and i-C<sub>6</sub>H<sub>5</sub>), 131.72 (C-1), 131.89, 129.69, 129.55, 128.58 and 126.55 (C-2, C-3 and o,m,p-C<sub>6</sub>H<sub>5</sub>), 29.20 (CH<sub>2</sub>), 21.14 (CH<sub>3</sub>).

Anal. calcd. for C<sub>15</sub>H<sub>15</sub>NOS: C, 70.01; H, 5.87; N, 5.44; S, 12.46. Found: C, 69.92; H, 5.93; N, 5.42; S, 12.07.

<sup>1</sup>H NMR spectra are in accordance with published data.<sup>8</sup>

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(Z)-Ethyl 2-(hydroxyimino)-3-(p-tolylthio)propanoate (1g)

Yield: 24% (method 1). White crystals. Mp = 60-62°C (pentane-Et₂O), lit.³ 61-62°C. Rᵣ = 0.36 (AcOEt-hexane = 1 : 3).

Single isomer with Z-configuration.

¹H NMR (300 MHz, Chloroform-d) δ 9.55 (s, 1H, OH), 7.40 (d, J = 7.7 Hz, 2H, o-C₆H₄CH₃), 7.10 (d, J = 7.7 Hz, 2H, m-C₆H₄CH₃), 4.26 (m, J = 7.1, 2H, CH₂O), 3.97 (s, 2H, CH₂S), 2.33 (s, 3H, CH₃-Ar), 1.30 (t, J = 7.1, 3H, CH₃CH₂).

¹³C NMR (75.47 MHz, JMOD, Chloroform-d) δ 162.69 (C=O), 149.48 (C=N), 137.77 (C-4), 132.63 and 129.69 (C-2 and C-3), 130.93 (C-1), 62.10 (CH₂O), 27.66 (CH₂S), 21.15 (CH₃-Ar), 14.03 (CH₃CH₂).

HRMS: calcd. for [C₁₂H₁₅NO₃SNa]⁺ 276.0663; found 276.0665 ([M+Na]⁺).

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2-(p-Tolylthio)propanal oxime (1h)

Yield: 25% (method 1). Oil. R<sub>f</sub> = 0.71 (AcOEt-hexane = 1 : 1).

Dynamic mixture of E/Z-isomers, ratio 2.7 : 1.

<table>
<thead>
<tr>
<th>Compound</th>
<th>1H NMR (300 MHz, Chloroform-d, E-isomer)</th>
<th>13C NMR (75 MHz, CDCl&lt;sub&gt;3&lt;/sub&gt;, E-isomer)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>δ 8.17 (br s, 1H, NOH), 7.36 (d, J = 5.7 Hz, 1H, N=CH), 7.33 (d, J = 7.0 Hz, 2H, HC-3), 7.13 (d, J = 7.0 Hz, 1H, HC-2), 3.80 (m, 1H, CH-S), 2.34 (s, 3H, H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 1.43 (d, J = 6.8 Hz, 1H, CH-C&lt;sub&gt;3&lt;/sub&gt;), 152.44 (C=N), 138.15 (C-4), 133.88 and 129.76 (C-2 and C-3), 129.02 (C-1), 42.63 (CH-S), 21.19 (H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 17.97 (CH-CH&lt;sub&gt;3&lt;/sub&gt;), 153.25 (C=N), 137.68 (C-4), 132.72 and 129.71 (C-2 and C-3), 129.26 (C-1), 35.90 (CH-S), 21.16 (H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 17.63 (CH-CH&lt;sub&gt;3&lt;/sub&gt;), 153.25 (C=N), 137.68 (C-4), 132.72 and 129.71 (C-2 and C-3), 129.26 (C-1), 35.90 (CH-S), 21.16 (H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 17.63 (CH-CH&lt;sub&gt;3&lt;/sub&gt;), 153.25 (C=N), 137.68 (C-4), 132.72 and 129.71 (C-2 and C-3), 129.26 (C-1), 35.90 (CH-S), 21.16 (H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 17.63 (CH-CH&lt;sub&gt;3&lt;/sub&gt;), 153.25 (C=N), 137.68 (C-4), 132.72 and 129.71 (C-2 and C-3), 129.26 (C-1), 35.90 (CH-S), 21.16 (H&lt;sub&gt;3&lt;/sub&gt;C-Ar), 17.63 (CH-CH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>HRMS: calcd. for [C&lt;sub&gt;10&lt;/sub&gt;H&lt;sub&gt;14&lt;/sub&gt;NOS]&lt;sup&gt;+&lt;/sup&gt; 196.0791; found 196.0795 ([M+H]&lt;sup&gt;+&lt;/sup&gt;)</td>
</tr>
</tbody>
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1-(Pyridin-2-ylthio)propan-2-one oxime (II)

Yield: 79% (method 1). White crystals. Mp = 64-66°C (pentane-Et₂O). Rᵥ = 0.48 (AcOEt-hexane = 1 : 1)

Mixture of E/Z-isomers, ratio 3.2 : 1.0

¹H NMR (300 MHz, Chloroform-d, E-isomer) δ 8.46 (d, J = 3.3 Hz, 1H, HC-6), 8.05-7.85 (br, 1H, NOH), 7.51 (ddd, J = 8.0, 7.6, 1.8 Hz, 1H, HC-4), 7.25 (d, J = 8.0 Hz, 1H, HC-3), 7.02 (m, 1H, HC-5), 4.05 (s, 2H, CH₂S), 2.00 (s, 3H, CH₃).

¹³C NMR (50 MHz, DEPT135, Chloroform-d, E-isomer) δ 157.70 and 155.43 (C-2 and C=N), 149.48 (С-6), 136.23 (С-4), 122.35 and 119.91 (C-3 and C-5), 34.23 (CH₂), 12.90 (CH₃).

¹H NMR (300 MHz, Chloroform-d, Z-isomer) δ 8.75-8.55 (br, 1H, NOH), 8.46 (d, J = 3.3 Hz, 1H, HC-6), 7.51 (ddd, J = 8.0, 7.6, 1.8 Hz, 1H, HC-4), 7.25 (d, J = 8.0 Hz, 1H, HC-3), 7.02 (m, 1H, HC-5), 4.12 (s, 2H, CH₂S), 2.00 (s, 3H, CH₃).

¹³C NMR (50 MHz, DEPT135, Chloroform-d, Z-isomer) δ 157.80 and 155.43 (C-2 and C=N), 149.28 (C-6), 136.44 (C-4), 122.00 and 119.91 (C-3 and C-5), 25.52 (CH₂), 19.41 (CH₃).

HRMS: calcd. for [C₈H₁₁NO₂S]⁺ 183.0582; found 183.0587 ([M+H]⁺).
**1-(Heptylthio)-3-phenylpropan-2-one oxime (1j)**

Yield: 69% (method 2). Oil. R<sub>f</sub> = 0.75 (AcOEt-hexane = 1 : 3)

Mixture of E/Z-isomers, ratio 4 : 1.

**H NMR (300 MHz, Chloroform-d, E-isomer)** δ 9.25-9.15 (br, 1H, NOH), 7.48-7.19 (m, 5H, o,m,p-C<sub>6</sub>H<sub>5</sub>), 3.96 (s, 2H, CH<sub>2</sub>Ph), 3.16 (s, 2H, CH<sub>2</sub>C=N), 2.48 (t, J = 7.4 Hz, 2H, CH<sub>2</sub>S), 1.65-1.53 and 1.47-1.18 (2 m, 2H and 8H, 5 CH<sub>2</sub>), 0.91 (t, J = 6.5 Hz, 3H, CH<sub>3</sub>).

**13C NMR (75 MHz, CDCl<sub>3</sub>, E-isomer, characteristic signals)** δ 157.00 (C=N), 136.27 (i-C<sub>6</sub>H<sub>5</sub>), 129.32, 128.68 and 126.65 (o,m,p-C<sub>6</sub>H<sub>5</sub>), 38.50 (CH<sub>2</sub>C=N), 14.14 (CH<sub>3</sub>).

**H NMR (300 MHz, Chloroform-d, Z-isomer)** δ 9.14-9.07 (br, 1H, NOH), 7.48-7.19 (m, 5H, o,m,p-C<sub>6</sub>H<sub>5</sub>), 3.73 (s, 2H, CH<sub>2</sub>Ph), 3.34 (s, 2H, CH<sub>2</sub>C=N), 2.54 (t, J = 7.4 Hz, 2H, CH<sub>2</sub>S), 1.65-1.53 and 1.47-1.18 (2 m, 2H and 8H, 5 CH<sub>2</sub>), 0.91 (t, J = 6.5 Hz, 3H, CH<sub>3</sub>).

**13C NMR (75 MHz, CDCl<sub>3</sub>, Z-isomer, characteristic signals)** δ 157.84 (C=N), 136.54 (i-C<sub>6</sub>H<sub>5</sub>), 129.25, 128.68 and 126.92 (o,m,p-C<sub>6</sub>H<sub>5</sub>), 34.05 (CH<sub>2</sub>Ph), 14.14 (CH<sub>3</sub>).

**13C NMR (75 MHz, CDCl<sub>3</sub>, both isomers, unassignned signals)** δ 32.35, 31.80, 31.54, 31.51, 29.52, 29.24, 28.95, 28.88, 28.87, 25.21, 22.67 (8 CH<sub>2</sub>).

**HRMS**: calcd. for [C<sub>16</sub>H<sub>26</sub>NOS]<sup>+</sup> 280.1734; found 280.1730 ([M+H]<sup>+</sup>).
2-(Heptylthio)-1-phenylethanone oxime (1k)

Yield: 77% (method 2). White crystals. Mp = 27-29°C (pentane-Et₂O). Rₘ = 0.65 (AcOEt-hexane = 1 : 1).

Dynamic mixture of E/Z-isomers, ratio 2.1 : 1.

¹H NMR (300 MHz, Chloroform-d, E-isomer) δ 8.33 (s, 1H, NOH), 7.55 (dd, J = 7.9, 1.9 Hz, 2H, o-C₆H₅), 7.51-7.39 (m, 3H, m,p-C₆H₅), 3.58 (s, 2H, CH₂C=N), 2.54 (t, J = 7.4 Hz, 2H, CH₂S), 1.65-1.55 and 1.45-1.19 (2 m, 2H and 8H, 5 CH₂), 0.90 (t, J = 6.3 Hz, 3H, CH₃).

¹³C NMR (75 MHz, CDCl₃, E-isomer) δ 155.15 (C=N), 132.23 (i-C₆H₅), 129.32 and 128.25 (o,m,p-C₆H₅), 36.05 (CH₂C=N), 31.78, 31.71, 29.24, 28.92, 28.86 and 22.65 (6 CH₂), 14.13 (CH₃).

¹H NMR (300 MHz, Chloroform-d, Z-isomer) δ 8.79 (s, 1H, NOH), 7.69 (dd, J = 6.7, 2.5 Hz, 2H, o-C₆H₅), 7.51-7.39 (m, 3H, m,p-C₆H₅), 3.88 (s, 2H, CH₂C=N), 2.59 (t, J = 7.6 Hz, 2H, CH₂S), 1.65-1.55 and 1.45-1.19 (2 m, 2H and 8H, 5 CH₂), 0.90 (t, J = 6.3 Hz, 3H, CH₃).

¹³C NMR (75 MHz, CDCl₃, Z-isomer, characteristic signals) δ 128.60 and 126.49 (o,m,p-C₆H₅), 32.74 (CH₂C=N), 24.76 (CH₂S).

Anal. calcd. for C₁₅H₂₃NOS: C, 67.88; H, 8.73; N, 5.28; S, 12.08. Found: C, 67.70; H, 8.76; N, 5.23; S, 11.26.
**(E)-1-((2-Hydroxyethyl)thio)propan-2-one oxime (1I)**

Yield: 91% (method 2). White crystals. Mp = 79-80°C (pentane-Et<sub>2</sub>O). R<sub>f</sub> = 0.12 (AcOEt-hexane = 1 : 1).

Single isomer with *E*-configuration

1H NMR (300 MHz, Chloroform-<sup>d</sup>) δ 8.47-8.29 (s, 1H, NOH), 3.75 (t, *J* = 6.1 Hz, 2H, CH<sub>2</sub>OH), 3.25 (s, 2H, CH<sub>2</sub>C=N), 2.85-2.75 (br, 1H, OH), 2.69 (t, *J* = 6.1 Hz, 2H, CH<sub>2</sub>S), 2.02 (s, 3H, CH<sub>3</sub>).

13C NMR (75 MHz, CDCl<sub>3</sub>) δ 155.79 (C=N), 60.94 (CH<sub>2</sub>OH), 35.98 (CH<sub>2</sub>C=N), 34.07 (CH<sub>2</sub>S), 12.82 (CH<sub>3</sub>).

FTIR (KBr): 3384 (s), 3205 (s), 2919 (s), 2883 (s), 1663 (m, sh), 1464 (s), 1422 (s, sh), 1370 (s, sh), 1273 (w), 1225 (m), 1193 (w), 1166 (m), 1065 (s), 1032 (s), 972 (s), 826 (m), 807 (m), 632 (m) cm<sup>−1</sup>.

Anal. calcd. for C<sub>5</sub>H<sub>11</sub>NO<sub>2</sub>S: C, 40.25; H, 7.43; N, 9.39; S, 21.49. Found: C, 40.52; H, 7.65; N, 9.35; S, 21.74.
(E)-Methyl 2-((tert-butoxycarbonyl)amino)-3-((2-(hydroxyimino)propyl)thio)propanoate (1m)

Yield: 61% (method 2). White crystals. Mp = 44-46°C (pentane-Et<sub>2</sub>O). R<sub>f</sub> = 0.4 (AcOEt-hexane = 1 : 1)

[α]<sub>D</sub> = -24.3 (c = 1, CH<sub>3</sub>OH, 22°C)

Single isomer with E-configuration

<sup>1</sup>H NMR (300 MHz, Chloroform-<em>d</em>) δ 8.93 (s, 1H, NOH), 5.50 (d, <em>J</em> = 8.5 Hz, 1H, NH), 4.56 (m, 1H, CH), 3.76 (s, 3H, OCH<sub>3</sub>), 3.22 (s, 2H, CH<sub>2</sub>C=N), 2.95 (dd, <em>J</em> = 13.6, 4.9 Hz, 1H, CH<sub>2</sub>S), 2.83 (dd, <em>J</em> = 13.6, 6.1 Hz, 1H, CH<sub>2</sub>S), 1.97 (s, 3H, CH<sub>3</sub>), 1.45 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C).

<sup>13</sup>C NMR (75 MHz, JMOD, CDCl<sub>3</sub>) δ 171.67 (O-C=O), 155.25 and 154.73 (N-C=O and C=N), 80.24 ((CH<sub>3</sub>)<sub>3</sub>CO), 53.21 and 52.60 (CH and OCH<sub>3</sub>), 36.88 (CH<sub>2</sub>C=N), 33.52 (CH<sub>2</sub>S), 28.34 ((CH<sub>3</sub>)<sub>3</sub>CO), 12.61 (CH<sub>3</sub>).

HRMS: calcd. for [C<sub>12</sub>H<sub>22</sub>N<sub>2</sub>O<sub>5</sub>SNa]<sup>+</sup> 329.1144; found 329.1142 ([M+Na]<sup>+</sup>).
(E,E)-1-(((3-(2-(hydroxyimino)propyl)thio)propyl)thio)propan-2-one oxime (1n).  

Yield: 83% (method 2). Oil, which solidified upon standing. R_f = 0.09 (AcOEt-hexane = 1:3).

Single isomer with E,E-configuration.

^{1}H NMR (300 MHz, Chloroform-d) δ 9.78-9.53 (br, 2H, 2 NOH), 3.22 (s, 4H, 2 CH$_2$C=N), 2.46 (t, J = 7.6 Hz, 4H, 2 -CH$_2$-CH$_2$-CH$_2$-), 2.00 (s, 6H, 2 CH$_3$), 1.87-1.71 (m, 2H, -CH$_2$-CH$_2$-CH$_2$-).

^{13}C NMR (75 MHz, CDCl$_3$) δ 156.09 (2 C=N), 36.21, 29.89 and 29.57 (5 CH$_2$), 12.85 (2 CH$_3$).

HRMS: calcd. for [C$_9$H$_{19}$N$_2$O$_2$S$_2$]$^+$ 251.0883; found 251.0882 ([M+H]$^+$).

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4. Reaction of enamine 6a with n-heptanethiol. To a stirred solution of enamine 6a (146 mg, 0.5 mmol) in DMF (0.75 mL) was added n-heptanethiol (79 µL, 0.5 mmol). After keeping for 24 h at r.t., methanol (3 mL) was added and the mixture was stirred for additional 1 h at r.t. and concentrated in vacuum (c.a. 45°C). The residue was dried in vacuum (1 Torr, c.a. 50°C) to remove DMF and then subjected to a column chromatography on silica gel to give 164 mg (94%) of oxime 7a.

1-(Heptylthio)-5-hydroxy-5-methyl-3-phenylhexan-2-one oxime (7a)

White crystals. Mp = 53-55°C (pentane-Et2O). Rf = 0.59 (AcOEt-hexane = 1 : 1).

Single isomer with unknown configuration

$^1$H NMR (300 MHz, Chloroform-d) δ 11.08 (br s, 1H, NOH), 7.30 (m, 5H, o,m,p-C$_6$H$_5$), 6.98-6.25 (br, 1H, OH), 4.21 (dd, J = 11.3, 3.6 Hz, 1H, CH$_2$C$_6$H$_5$), 4.08 (d, J = 13.2 Hz, 1H, CH$_2$C=N), 2.63-2.43 (m, 3H, CH$_2$S and CH$_2$C-OH), 2.37 (d, J = 13.2 Hz, 1H, CH$_3$C=N), 1.83 (dd, J = 15.2, 3.6 Hz, 1H, CH$_3$C-OH), 1.70-1.60 and 1.47-1.16 (2 m, 8H, 5 CH$_2$), 1.37 and 1.28 (2 s, 3H and 3H, 2 CH$_3$), 0.90 (t, J = 6.7 Hz, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 159.02 (C=N), 142.77 (i-C$_6$H$_5$), 129.01, 128.13 and 127.11 (o,m,p-C$_6$H$_5$), 70.43 ((CH$_3$)$_2$C-OH), 47.49 (CH$_2$C-OH), 46.19 (CH-C$_6$H$_5$), 32.49, 31.79, 29.66, 28.98, 28.90, 25.86 and 22.66 (7 CH$_2$), 31.95 and 27.56 (2 CH$_3$), 14.14 (CH$_3$).

Anal. calcd. for C$_{20}$H$_{33}$NO$_2$S: C, 68.33; H, 9.46; N, 3.98; S, 9.12. Found: C, 68.22; H, 9.65; N, 4.02; S, 8.87.
5. Reaction of enamine 6a with p-thiocresol. To a stirred solution of enamine 6a (146 mg, 0.5 mmol) in toluene (3 mL) was added p-thiocresol (62 mg, 0.5 mmol). After keeping for 24 h at r.t., the mixture was concentrated in vacuum. The residue was subjected to a column chromatography on silica gel (elucent hexane-AcOEt = 10 : 1 \rightarrow 5 : 1 \rightarrow 3 : 1 \rightarrow 1 : 1). Two fractions were collected. The first one contained 51 mg (31%) of cyclic product 8b, second fraction contained 115 mg (67%) of oxime 7b.

**6,6-Dimethyl-4-phenyl-3-((p-tolylthio)methyl)-5,6-dihydro-4H-1,2-oxazine (8b)**

Mp = 79-82°C (pentane-Et2O). \( R_f = 0.7 \) (AcOEt-hexane = 1 : 3)

\(^1\)H NMR (300 MHz, Chloroform-d) \( \delta \) 7.44-7.21 (m, 7H, HC-3’ and o,m,p-C\(_6\)H\(_5\)), 7.10 (d, \( J = 8.0 \) Hz, 2H, HC-2’), 3.82 (d, \( J = 14.1 \) Hz, 1H, CH\(_2\)S), 3.75 (dd, \( J = 8.0, 12.0 \) Hz, 1H, HC-4), 3.20 (d, \( J = 14.1 \) Hz, 1H, CH\(_2\)S), 2.33 (s, 3H, CH\(_3\)-Ar), 2.05 (dd, \( J = 13.6, 8.0 \) Hz, 1H, H\(_\text{ax}\)C-5), 1.90 (dd, \( J = 13.6, 12.0 \) Hz, 1H, H\(_\text{eq}\)C-5), 1.31 and 0.96 (2 s, 3H and 3H, 2 CH\(_3\)).

\(^{13}\)C NMR (75 MHz, DEPT135, CDCl\(_3\)) \( \delta \) 155.58 (C=N), 140.17 and 136.69 (C-4’ and i-C\(_6\)H\(_5\)), 131.15 (C-1’), 130.54, 129.76, 129.10, 128.63 and 127.34 (C-2’, C-3’ and o,m,p-C\(_6\)H\(_5\)), 74.49 (C-6), 40.90 and 37.27 (2 CH\(_2\)), 37.45 (C-4), 28.47, 22.16 and 21.09 (3 CH\(_3\)).

HRMS: calcd. for [C\(_{20}\)H\(_{24}\)NOS]\(^+\) 326.1573; found 326.1571 ([M+H]\(^+\)).
5-Hydroxy-5-methyl-3-phenyl-1-(p-tolylthio)hexan-2-one oxime (7b)

White crystals. Mp = 111-112°C (pentane-Et₂O). Rᵣ = 0.24 (AcOEt-hexane = 1 : 3).

Single isomer with unknown configuration

¹H NMR (300 MHz, Chloroform-­d) δ 11.24 (s, 1H, NOH), 7.43-7.21 (m, 5H, o,m,p-­C₆H₅), 7.19-7.04 (m, 4H, HC-2 and HC-3), 6.67 (br s, 1H, OH), 4.40 (d, J = 13.4 Hz, 1H, CH₂S), 3.97 (dd, J = 10.9, 3.9 Hz, 1H, CH-­C₆H₅), 2.83 (d, J = 13.4 Hz, 1H, CH₂S), 2.43 (dd, J = 15.3, 11.0 Hz, 1H, CH₂), 2.33 (s, 3H, CH₃-­Ar), 1.76 (dd, J = 15.2, 3.9 Hz, 1H, CH₂), 1.22 and 1.17 (2 s, 3H and 3H, 2 CH₃).

¹³C NMR (75 MHz, JMOD, CDCl₃) δ 158.33 (C=N), 142.52 and 136.74 (C-­4 and i-­C₆H₅), 132.14 (C-­1), 130.45, 129.77, 128.99, 128.21 and 127.12 (C-­2, C-­3 and o, m, p-­C₆H₅), 70.31 ((CH₃)₂C-­OH), 47.71 (CH₂), 46.83 (CH-­C₆H₅), 29.26 (CH₂S), 31.85, 27.36 and 21.10 (3 CH₃).

HRMS: calcd. for [C₂₀H₂₆NO₂S]⁺ 344.1676; found 344.1679 ([M+H]⁺).

Anal. calcd. for C₂₀H₂₅NO₂S: C, 69.93; H, 7.34; N, 4.08; S, 9.34. Found: C, 69.99; H, 7.38; N, 4.15; S, 9.31.
6. Reaction of enamine 6b with p-thiocresol. To a stirred solution of enamine 6b (140 mg, 0.5 mmol) in toluene (3.2 mL) was added p-thiocresol (62 mg, 0.5 mmol). After keeping for 24 h at r.t., the mixture was concentrated in vacuum. The residue was subjected to a column chromatography on silica gel (eluent hexane-AcOEt = 10 : 1 → 5 : 1 → 3 : 1) to give 97 mg (62%) of isoxazoline 8c, further elution provided 18 mg (16%) of minor 3-(methoxymethyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole (see below).

![Chemical Structure](image)

4-(4-Methoxyphenyl)-3-((p-tolylthio)methyl)-4,5-dihydroisoxazole (8c)

White crystals. Mp = 90-92°C (pentane-Et2O). Rf = 0.56 (AcOEt-hexane = 1 : 1).

$^1$H NMR (300 MHz, Chloroform-d) δ 7.28 (d, $J$ = 8.0 Hz, 2H, HC-3), 7.13 (d, $J$ = 8.0 Hz, 2H, HC-2’), 7.09 (d, $J$ = 8.0 Hz, 2H, HC-2), 6.89 (d, $J$ = 8.0 Hz, 2H, HC-3’), 4.52 (dd, $J$ = 10.7, 7.3 Hz, 1H, CH$_2$O), 4.52 (dd, $J$ = 10.7, 5.9 Hz, 1H, CH$_2$O), 4.29 (dd, $J$ = 6.6, 6.5 Hz, 1H, CH), 3.95 (d, $J$ = 14.4 Hz, 1H, CH$_2$S), 3.83 (s, 3H, OCH$_3$), 3.23 (d, $J$ = 14.4 Hz, 1H, CH$_2$S), 2.35 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, CDC$_3$) δ 159.36 and 158.55 (C=N and C-4’), 137.42 (C-4), 133.66 (C-1’), 130.60 (C-1), 131.11, 129.98 and 128.91 (C-2, C-3 and C-2’), 114.65 (C-3’), 77.10 (CH$_2$O), 55.40 and 53.70 (CH and OCH$_3$), 30.0 (CH$_2$), 21.15 (CH$_3$).

Anal. calcd. for C$_{18}$H$_{19}$NO$_2$S: C, 68.98; H, 6.11; N, 4.47; S, 10.23. Found: C, 69.26; H, 5.82; N, 4.57; S, 10.13.
3-(Methoxymethyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole

Oil. R<sub>f</sub> = 0.34 (AcOEt-hexane = 1 : 1).

<sup>1</sup>H NMR (300 MHz, Chloroform-<sup>d</sup>) δ 7.14 (d, <i>J</i> = 8.5 Hz, 2H, HC-2), 6.90 (d, <i>J</i> = 8.5 Hz, 2H, HC-3), 4.66 (dd, <i>J</i> = 9.8, 7.3 Hz, 1H, CH), 4.47-4.33 (m, 2H, CH<sub>2</sub>), 3.95 (d, <i>J</i> = 12.6 Hz, 1H, CH<sub>2</sub>), 3.82 (s, 3H, OCH<sub>3</sub>), 3.31 (s, 3H, CH<sub>2</sub>OC).  <br><br>1<sup>3</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 159.28 and 158.84 (C=N and C=O), 130.19 (C-1), 128.69 (C-2), 114.59 (C-3), 76.85 (CH<sub>2</sub>), 65.31 (CH<sub>2</sub>OC), 58.56, 55.37 and 53.49 (2 OCH<sub>3</sub> and CH).  

HRMS calcd. for [C<sub>12</sub>H<sub>16</sub>NO<sub>3</sub>]<sup>+</sup> 222.1125; found 222.1131 ([M+H]<sup>+</sup>).
7. Reduction of oxime 1a to amine 3a. To a stirred solution of oxime 1a (0.15 g, 0.76 mmol) in THF (6.8 mL) was added a suspension of LiAlH₄ (0.14 g, 3.7 mmol) in THF (6.8 mL). The resulting mixture was heated at 50°C for 3 h with intensive stirring. After cooling to r.t., AcOEt (5 mL), methanol (5 mL), water (0.3 mL) and 20% aqueous NaOH solution (0.3 mL) were added successively. The resulting mixture was stirred for 15 min, diluted with diethyl ether (50 mL) and anhydrous Na₂SO₄ (c.a. 2 g) was added. The solution was filtered from precipitate and filter cake was washed with diethyl ether (2×25 mL). The filtrate was concentrated in vacuum and the residue was subjected to column chromatography on silica gel (AcOEt-hexane = 1 : 10 → 1 : 5 → 1 : 3 → 1 : 1 → 1 : 0 → AcOEt-CH₃OH = 3 : 1 → 1 : 1) to give 0.042 g (31%) of amine 3a as yellowish oil.

1-(p-Tolythio)propan-2-amine (3a).

Oil. Rₐ = 0.05 (AcOEt-CH₃OH = 5 : 1).

¹H NMR (300 MHz, Chloroform-d) δ 7.30 (d, J = 7.9 Hz, 2H, HC-3), 7.11 (d, J = 7.9 Hz, 2H, HC-2), 3.90 (br s, 2H, NH₂), 3.09 (m, 1H, CH₃-CH), 3.00 (dd, J = 13.1, 5.9 Hz, 1H, CH₂), 2.81 (dd, J = 13.1, 7.8 Hz, 1H, CH₂), 2.33 (s, 3H, CH₃), 1.20 (d, J = 6.3 Hz, 3H, CH₃-CH).

¹³C NMR (75 MHz, CDCl₃) δ 136.67 (C-4), 130.65 (C-1), 130.69 and 129.87 (C-2 and C-3), 46.23 (CH), 44.08 (CH₂), 22.09 and 21.07 (2 CH₃).

¹H NMR data are in agreement with previously published spectra.¹¹

8. Reduction of oxime 1a to hydroxylamine 4a. To a stirred solution of oxime 1a (45 mg, 0.23 mmol) in glacial acetic acid (1.1 mL) was added NaBH$_3$CN (44 mg, 0.7 mmol). After 1.5 h of stirring at r.t., second portion of NaBH$_3$CN (29 mg, 0.46 mmol) was added and the mixture was stirred for additional 30 min. The resulting solution was diluted with ethyl acetate (10 mL) and poured into a mixture of ethyl acetate (50 mL) and saturated solution of Na$_2$CO$_3$ (50 mL). The aqueous layer was back-extracted with ethyl acetate (50 mL). Combined organic layers were washed with saturated solution of Na$_2$CO$_3$ (50 mL), water (50 mL), and brine (50 mL), dried (Na$_2$SO$_4$), and evaporated in vacuum. The residue was subjected to column chromatography on silica gel (AcOEt-hexane = 1 : 10 → 1 : 5 → 1 : 3) to give 40 mg (89%) of hydroxylamine 4a.

**N-(1-(p-tolylthio)propan-2-yl)hydroxylamine (4a)**

Oil. R$_f$ = 0.35 (AcOEt-hexane = 1 : 3)

$^1$H NMR (300 MHz, Chloroform-d) $\delta$ 7.31 (d, $J$ = 8.3 Hz, 2H, HC-3), 7.12 (d, $J$ = 8.3 Hz, 2H, HC-2), 6.2-5.4 (br, 2H, NH and OH), 3.18-3.05 and 3.01-2.91 (2 m, 2H and 1H, CH$_3$ and CH$_2$), 2.33 (s, 3H, CH$_3$-Ar), 1.19 (d, $J$ = 6.3 Hz, 3H, CH$_3$CH).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 136.49 (C-4), 132.23 (C-1), 130.32 and 129.83 (C-2 and C-3), 56.03 (CH-N), 38.06 (CH$_2$S), 21.03 and 17.27 (2 CH$_3$).

HRMS: calcd. for [C$_{10}$H$_{16}$NOS]$^+$ 198.0948; found 198.0947 ([M+H]$^+$).
9. Reduction of oxime 1d to hydroxylamine 4d. To a stirred solution of oxime 1d (73 mg, 0.27 mmol) in glacial acetic acid (1.2 mL) was added NaNH$_3$CN (51 mg, 0.81 mmol). After 1.5 h of stirring at r.t., second portion of NaNH$_3$CN (34 mg, 0.54 mmol) was added and the mixture was stirred for additional 30 min. The resulting solution was diluted with ethyl acetate (10 mL) and poured into a mixture of ethyl acetate (50 mL) and saturated solution of NaN$_2$CO$_3$ (50 mL). The aqueous layer was back-extracted with ethyl acetate (50 mL). Combined organic layers were washed with saturated solution of NaN$_2$CO$_3$ (50 mL), water (50 mL), and brine (50 mL), dried (Na$_2$SO$_4$), and evaporated in vacuum. The residue was subjected to column chromatography on silica gel (AcOEt-hexane = 1 : 10 → 1 : 5 → 1 : 3) to give 59 mg (80%) of hydroxylamine 4d.

N-(1-Phenyl-3-(p-tolylthio)propan-2-yl)hydroxylamine (4d)

White crystals. Mp = 74-76°C (pentane-Et$_2$O). R$_f$ = 0.67 (AcOEt-hexane = 1 : 3).

$^1$H NMR (300 MHz, Chloroform-d) $\delta$ 7.38-7.15 (m, 7H, HC-3 and o,m,p-C$_6$H$_5$), 7.09 (d, $J$ = 8.2 Hz, 2H, HC-2), 6.45 (br s, 2H, NH and OH), 3.21 (m, 1H, CH-N), 3.12 (dd, $J$ = 13.5, 6.9 Hz, 1H, CH$_2$S), 3.02 (dd, $J$ = 13.5, 5.2 Hz, 1H, CH$_2$S), 2.97 (dd, $J$ = 13.7, 6.1 Hz, 1H, CH$_2$C$_6$H$_5$), 2.88 (dd, $J$ = 13.7, 6.7 Hz, 1H, CH$_2$C$_6$H$_5$), 2.33 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 138.02 and 136.40 (C-4 and i-C$_6$H$_5$), 132.05 (C-1), 129.94, 129.86, 129.38, 128.69 and 126.67 (C-2, C-3 and o,m,p-C$_6$H$_5$), 61.96 (CH-N), 37.15 and 35.44 (2 CH$_2$), 21.06 (CH$_3$).

FT-IR (KBr): 3329 (s, br), 3029 (m, sh), 2911 (m), 2897 (m), 1493 (s), 1421 (s), 1144 (m, sh), 1087 (m), 1028 (m), 920 (s), 805 (s), 747 (s), 701 (s), 491 (s) cm$^{-1}$.

HRMS: calcd. for [C$_{16}$H$_{20}$NOS]$^+$ 274.1260; found 274.1260 ([M+H]$^+$).
10. **Oxidation of oxime 1a to sulfone 5a.** To a stirred solution of oxime 1a (112 mg, 0.57 mmol) in CH$_2$Cl$_2$ (12 mL) was added mCPBA (284 mg, 1.24 mmol, 75% purity). The mixture was stirred for 1 h at r.t. and then evaporated. The residue was dissolved in CH$_2$Cl$_2$ (5 mL) and washed with a saturated solution of NaHCO$_3$ (2 × 5 mL) and brine (5 mL). Water phase was back-extracted with CH$_2$Cl$_2$ (5 mL). Combined organic layers were dried over Na$_2$SO$_4$ and concentrated in vacuum. The residue was subjected to a column chromatography on silica gel (AcOEt-hexane = 1 : 10 → 1 : 5 → 1 : 3 → 1 : 1) to give 51 mg (40%) of sulfone 5a as oil, which crystallized upon standing.

![1-Tosylpropan-2-one oxime (5a)](image)

**1-Tosylpropan-2-one oxime (5a)**

White solid. Mp = 88-92°C. R$_f$ = 0.51 (AcOEt-hexane = 1 : 1).

Dynamic mixture of E,Z-isomers (ratio 4 : 1).

$^1$H NMR (300 MHz, Chloroform-d, E-isomer) δ 8.42-8.31 (br s, 1H, NOH), 7.73 and 7.35 (2 d, J = 8.3 Hz, 2H and 2H, HC-2 and HC-3), 3.92 (s, 2H, CH$_2$), 2.45 (s, 3H, CH$_3$-Ar), 2.02 (s, 3H, CH$_3$=N).

$^{13}$C NMR (75 MHz, CDCl$_3$, E-isomer) δ 148.80 (C=N), 145.18 (C-4), 135.36 (C-1), 129.91 and 128.36 (C-2 and C-3), 62.18 (CH$_2$), 21.69 (CH$_3$-Ar), 14.52 (CH$_3$C=N).

$^1$H NMR (300 MHz, Chloroform-d, Z-isomer) δ 8.12-8.00 (br s, 1H, NOH), 7.79 and 7.35 (2 d, J = 8.0 Hz, 2H and 2H, HC-2 and HC-3), 4.23 (s, 2H, CH$_2$), 2.45 (s, 3H, CH$_3$-Ar), 2.08 (s, 3H, CH$_3$=N).

$^{13}$C NMR (75 MHz, CDCl$_3$, Z-isomer, characteristic signals) δ 129.75 and 128.24 (C-2 and C-3), 54.77 (CH$_2$), 21.69 (CH$_3$-Ar), 20.34 (CH$_3$C=N).

HRMS: calcd. for [C$_{10}$H$_{13}$NO$_5$SNa]$^+$ 250.0508; found 250.0509 ([M+Na]$^+$).
11. Synthesis of \((E)\)-1-(diethylamino)propan-2-one oxime.\textsuperscript{12,13} To a stirred solution of \(N,N\text{-bis(oxy)enamine}\) 2a (1 mmol) in CH\(_2\)Cl\(_2\) (3 mL) was added diethylamine (0.1 mL, 1 mmol). After keeping for 24 h at r.t., methanol (5 mL) was added and the mixture was stirred for additional 1 h at r.t. and concentrated in vacuum (c.a. 45°C). The residue was subjected to a column chromatography on silica gel (AcOEt-hexane = 1 : 10 \(\rightarrow\) 1 : 5 \(\rightarrow\) 1 : 3 \(\rightarrow\) 1 : 1 \(\rightarrow\) 0 : 1) to give 104 mg of 1-(diethylamino)propan-2-one oxime (72%) as a white solid.

| NOH | White solid. Mp = 40-41°C (pentane-Et\(_2\)O), lit.\textsuperscript{12} 44-45 °C, lit.\textsuperscript{13}. 40 °C. \(R_f\) = 0.4 (AcOEt-hexane = 1 : 1).

Single isomer with \(E\)-configuration.

\(^1\text{H NMR (300 MHz, CDCl}_3\) \(\delta 9.23\text{-}8.50 \text{(br, 1H, NOH), 3.11 (s, 2H, CH}_2\text{C=}=N), 2.56 \text{(q, } J = 7.2 \text{ Hz, 4H, 2 CH}_2\text{CH}_3), 1.95 \text{(s, 3H, CH}_3), 1.05 \text{(t, } J = 7.2 \text{ Hz, 6H, 2 CH}_2\text{CH}_3).}

\(^{13}\text{C NMR (75 MHz, CDCl}_3\) \(\delta 157.08 \text{(C=}=N), 57.21 \text{ and 47.04 (CH}_2\text{C=}=N \text{ and 2 CH}_2\text{CH}_3), 12.58 \text{ and 11.38 (CH}_3 \text{ and 2 CH}_2\text{CH}_3).}

HRMS: calcd. for [C\(_7\)H\(_{17}\)N\(_2\)O\(^+\)] 145.1335; found 145.1338 ([M+H]\(^+\)).


12. Synthesis of 1-(benzyloxy)propan-2-one oxime. To N,N-bis(oxy)enamine 2a (233 mg, 1 mmol) was added benzyl alcohol (0.21 mL, 2 mmol) and the mixture was kept for 24 h at r.t. with occasional shaking. Then, a solution of tetrabutylammonium fluoride (261 mg, 1 mmol) in methanol (4 mL) was added with stirring. After keeping for another 24 h, the solution was concentrated in vacuum and the residue was subjected to a column chromatography on silica gel (AcOEt-hexane = 1 : 10 → 1 : 5 → 1 : 3) to give 67 mg (38%) of 1-(benzyloxy)propan-2-one oxime as a colorless liquid together with unreacted benzyl alcohol.

![Oxime Structure](image)

Colorless liquid.

Mixture of E/Z-isomers, ratio 10 : 1

$^1$H NMR (300 MHz, E-isomer, Chloroform-d) δ 8.53 (br s, 1H, NOH), 7.42-7.27 (m, 5H, Ph), 4.52 (s, 2H, OCH$_2$Ph), 4.08 (s, 2H, OCH$_2$C=N), 1.99 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, E-isomer, CDCl$_3$) δ 156.09 (C=N), 137.76 (i-Ph), 128.51, 127.93 and 127.87 (o,m,p-Ph), 72.34 and 71.42 (2 CH$_2$), 11.58 (CH$_3$).

$^1$H NMR (300 MHz, Z-isomer, Chloroform-d) δ 8.75 (br s, 1H, NOH), 7.42-7.27 (m, 5H, Ph), 4.56 and 4.42 (2 s, 2 H and 2 H, 2 CH$_2$O), 2.01 (s, 3H, CH$_3$).

$^{13}$C NMR (75 MHz, Z-isomer, characteristic signals, CDCl$_3$) δ $^{13}$C NMR (75 MHz, CDCl$_3$) δ 73.31 and 65.39 (2 CH$_2$), 16.75 (CH$_3$).

HRMS: calcd. for [C$_{10}$H$_{14}$NO$_2$]$^+$ 180.1019; found 180.1018 ([M+H]$^+$).
13. General procedure for competitive experiments with enamine 2a. A solution of nucleophile 1 (0.25 mmol) and nucleophile 2 (0.25 mmol) in toluene (1.5 mL) or in DMF (0.4 mL) was added to $N,N$-bis(oxy)enamine 2a with vigorous stirring. After keeping for 24 h at r.t., methanol (c.a. 2 mL) was added and the mixture was stirred for additional 1 h at r.t. and concentrated in vacuum (c.a. 45 °C) and dried (0.5 Torr). The residue was analyzed by $^1$H NMR with internal standard. NMR data of all products are in agreement with spectra of authentic samples. Results are summarized in Figure 1. Primary data is given below.
14. Primary data for Figure 1

(A) Competitive experiments with benzoic acid and p-thiocresol

\[
\text{ benzoyl } + \text{ TMSO-NOTMS } \rightarrow \text{ product } (2a) \rightarrow \text{ products after 24 h in toluene or DMF } \\

toluene 45\% \quad 6\%
DMF 7\% \quad 62\%
\]

(B) Competitive experiments with p-ethylphenol and p-thiocresol

\[
\text{ ethylphenol } + \text{ TMSO-NOTMS } \rightarrow \text{ product } (2a) \rightarrow \text{ products after 24 h in toluene or DMF } \\

toluene 6\% \quad 75\%
DMF 35\% \quad 48\%
\]

(C) Competitive experiments with diethylamine and p-thiocresol

\[
\text{ diethylamine } + \text{ TMSO-NOTMS } \rightarrow \text{ product } (2a) \rightarrow \text{ products after 24 h in toluene or DMF } \\

toluene 31\% \quad 66\%
DMF 30\% \quad 70\%
\]

(D) Competitive experiments with 1-heptanethiol and p-thiocresol

\[
\text{ heptanethiol } + \text{ TMSO-NOTMS } \rightarrow \text{ product } (2a) \rightarrow \text{ products after 24 h in toluene or DMF } \\

toluene 1\% \quad 57\%
DMF 12\% \quad 65\%
\]
(E) Competitive experiments with benzoic acid and p-ethylphenol

\[
\begin{align*}
\text{H} & \text{O} \\
\text{C} & \text{O} \\
\text{H} & \text{TMS} \equiv \text{N} & \text{OTMS} \quad 2a \\
\text{Toluene} & \quad 24 \text{ h} \\
\text{DMF} & \quad 11\% & \quad 36\% \\
\end{align*}
\]

(F) Competitive experiments with diethylamine and p-ethylphenol

\[
\begin{align*}
\text{H} & \text{N} \\
\text{H} & \text{TMS} \equiv \text{N} & \text{OTMS} \\
\text{Toluene} & \quad 24 \text{ h} \\
\text{DMF} & \quad 1\% & \quad 64\% \\
\end{align*}
\]

(G) Competitive experiments with diethylamine and benzoic acid

\[
\begin{align*}
\text{H} & \text{N} \\
\text{C} & \text{O} \\
\text{H} & \text{TMS} \equiv \text{N} & \text{OTMS} \\
\text{Toluene} & \quad 24 \text{ h} \\
\text{DMF} & \quad 8\% & \quad 81\% \\
\end{align*}
\]

(H) Competitive experiments with p-ethylphenol and benzyl alcohol

\[
\begin{align*}
\text{H} & \text{OH} \\
\text{C} & \text{O} \\
\text{H} & \text{TMS} \equiv \text{N} & \text{OTMS} \\
\text{Toluene} & \quad 24 \text{ h} \\
\text{DMF} & \quad 21\% & \quad 1\% \\
\end{align*}
\]

All yields are average of two experiments
15. Assignment of oxime group geometry in products 1

Most of oximes 1 were identified as mixtures of several isomers with one isomer being predominant. The ratio of isomers may change upon storage of the compound in pure state or in the solution, yet the main isomer always remains predominant.

Determination of oxime group geometry (E or Z) in previously unknown oximes 1 was performed based on $^1$H and $^{13}$C NMR spectroscopy data. For the majority of oximes 1 signals of both E- and Z-isomers were observed in NMR spectra (the difference of chemical shifts is 0.2 – 0.5 ppm in $^1$H and 3 – 9 ppm in $^{13}$C NMR). In these cases the assignment of signals to E- or Z-isomer was made according to a known relationship between the chemical shift of atoms 0.5 ppm in $^1$H and 3 – 9 ppm in $^{13}$C NMR). In these cases the assignment of signals to E- or Z-isomer was made according to a known relationship between the chemical shift of atoms attached to oximino group and its configuration (see at the top of Figure S1 and ref. 14).

Figure S1

![Figure S1](image)

However, these regularities cannot be used, if a single isomer is observed in NMR spectra. At the same time, chemical shifts of hydrogen ($H_\alpha$) and carbon ($C_\alpha$) in E- and Z-isomers in oximes 1 were found to be in a narrow range. Therefore, the configuration of oximino group in individual isomers of oximes 1 was established by a comparison of observed chemical shifts of $H_\alpha$ and/or $C_\alpha$ with statistic data summarized in Table S2. 15

| Table S2. Ranges of chemical shifts of $H_\alpha$ and $C_\alpha$ atoms in NMR spectra of oximes 1 |
|-----------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| E-isomer                          | Z-isomer                        | E-isomer                        | Z-isomer                        |
| $\delta$ ($H_\alpha$)             | 3.5-3.6                         | 3.7-4.2                         | 3.2-3.6                         | 3.3-3.9                         |
| $\delta$ ($C_\alpha$)             | 34-40                           | 28-31                           | 36-37                           | 33                              |

16. Copies of NMR and FT-IR spectra

NY198.301.{1H}/1
Avance-300, 1H CDCl3

\[
\text{E/Z} = 3 : 1
\]
1a
E/Z = 3 : 1
NOH

1a

E/Z = 3 : 1
NOH

E/Z = 3 : 1

Bruker

Wavenumber cm⁻¹

Transmittance [%]

3500 3000 2500 2000 1500 1000 500

3229 3104 3022 2920 2370 2300 2186 1899 1788 1771 1660 1589 1586 1550 1493 1471 1448 1398 1370 1270 1211 1199 1159 1100 1054 1018 936 809 721 606 500

1a

E/Z = 3 : 1
HO\(^\cdot\)N\(^-\)
S

1b

E-isomer
HO

S

1b

E-isomer

Avance-300, C-13, CDCl3
$\text{E/Z = 1.3 : 1.0}$
1c
E/Z = 1.3 : 1.0
E/Z = 1.6 : 1.0
(CDCl₃)
1d
dynamic mixture of E/Z isomers (DMSO-d$_6$)
Ka81.101{(1H)/1
/tern vari034

N-OH

E-isomer
(CDCl3)
$\text{NOH}$

$1e$

$E/Z = 2.6 : 1.0$
NY252.401.(13C)MOD/135
/TIEN SI-232

E/Z = 2.6 : 1.0
NY305.401.(1H)/1
/TERN i2311

Z-isomer
KA74.301.{1H}/1
/TERN i1956

1g
Zisomer

S49
$\text{OH}$

$\text{Zisomer}$

\[ \text{1g} \]
NOH

$E/Z = 2.7 : 1.0$
NY274.201.13C.JMOD/135
Avance-300, C-13, CDCl3

$\text{E/Z} = 2.7 : 1.0$
NOH

E/Z = 3.2 : 1
$\text{E/Z} = 3.2 : 1$
NY235.601 (13C)MOD/135
/TIEN SI-232

E/Z = 3.2 : 1
NOH

1j

E/Z = 4 : 1
$1k$

$E/Z = 2.1 : 1$
$\text{NOH}$

$1k$

$E/Z = 2.1 : 1$

$\text{S}$

$\text{Z}$
NY258.501.(1H)/1
NMR/S0590080

\[
\begin{align*}
\text{HO-} & \quad \text{S} \quad \text{HO} \\
\end{align*}
\]

11

*E*-isomer
HO
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{O}
\end{array}
\text{O}

1m
\text{E-isomer}

NY316.601.(1H)/1
/TERN SHAPAS1028
NY467.301.(1H)/1
/TERN vin1499

**1n**

*E,E*-isomer
NY202.501.13C3/135
/TIEN SI-232

7b
3a
$E/Z = 4 : 1$
$\text{HON}$

$\text{SO}_2$

$\text{C}$

$\text{E/Z} = 4 : 1$

$5a$

$\text{NMR/50684595}$

$\text{KA102.113.1(13C)} \text{MOD/135}$
NY466.201.(13C)3MOD/135
NMR/50684595

S89
NOH

E/Z = 10 : 1

NY492.101.(13C)3MOD/135
NMR/50684595

S91