Journal of Fluorine Chemistry 131 (2010) 229–233

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

# Optically active 4-aryl-4-trifluoromethyl-4H-1,3-oxa(thia)zines

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ARTICLE INFO

*Article history:*
Received 30 July 2009
Received in revised form 16 September 2009
Accepted 18 September 2009
Available online 28 September 2009

*Keywords:*
Optically active compounds
β-Aminoketones
4H-1,3-oxazines
4H-1,3-thiazines
Trifluoromethyl group

ABSTRACT

S(−)-4-Aryl-4-(N-acylamino)-5,5,5-trifluoropentan-2-ones have been reacted with phosphorus pentachloride and pentasulfide to yield S(−)-4-aryl-4-trifluoromethyl-4H-1,3-oxazines and S(+)-4-aryl-4-trifluoromethyl-4H-1,3-thiazines, respectively.



## 1. Introduction

Monocyclic 1,3-oxazines [1,2] and 1,3-thiazines [3] attract much interest both as versatile synthons in heterocyclic chemistry and as compounds with manifold biological activities. Although the synthetic approaches to various 4H-1,3-oxa(thia)zines have been thoroughly developed, there is still little evidence about their trifluoromethyl-substituted derivatives [4,5]. Among a few known examples are 4,4-bis(perfluoroalkyl)-4H-1,3-oxa(thia)zines obtained by cycloaddition of perfluoroalkyl ketone N-acylimines to ketenes and alkenes [6] or alkynes [7]. If performed with hexafluoroacetone N-thioacylimines and phenylacetylene, this reaction provides 4,5-dihydrothiazoles as by-products along with expected 4,4-bis(trifluoromethyl)-4H-1,3-thiazines [8].

Recently we have shown that chiral β-trifluoromethyl-β-aminoketones can be successfully applied in the synthesis of optically active heterocycles containing a quaternary endocyclic chiral centre, e.g., 4-trifluoromethyl-substituted 3,4-dihydropyrimidin-2(1*H*)-(thi)ones and 3,4-dihydro-1,3-oxazin-2-ones [9]. Here we report a synthetic method for new optically active 4-trifluoromethyl derivatives of 1,3-oxa(thia)zines based on a very facile cyclocondensation of easily available chiral S(−)-N-[1-aryl-3-oxo-1-(trifluoromethyl)butyl]amides **1a**–**h** with phosphorus pentachloride or pentasulfide.

## 2. Results and discussion

Compounds **1a**–**h** are readily obtained in 80–87% yields by acylation of 4-amino-4-aryl-5,5,5-trifluoropentan-2-ones [10] with acetic anhydride or aroyl chlorides (Table 1). We have found that compounds **1b**, **e**, **g**, **h** are less reactive than N-3-oxoalkylamides [11,12] towards $PCl_5$ and produce S(−)-4-aryl-4-trifluoromethyl-4H-1,3-oxazines **2a**–**d** (Table 2) only on 8 h boiling in benzene. The reaction is likely to involve the intermediate formation of imidoyl chlorides **A** which undergo intramolecular cyclization.

As previously established [13], thionation of N-3-oxoalkylamides with $P_2S_5$ gives only traces of the corresponding 4H-1,3-thiazines. We have succeeded in developing appropriate conditions to efficiently convert amides **1a**–**h** into S(+)-4-aryl-4-trifluoromethyl-4H-1,3-thiazines **3a**–**h** (Table 3). Boiling reagents for 18–20 h in xylene with a 10-fold excess of $P_2S_5$ affords 75–83% yield of desired products. Interestingly, widely used Lawesson's reagent [14] failed to provide a higher than 15–20% degree of thionation in the reaction concerned.

Formation of thiazines **3** is a multistep process which probably starts with the thionation of carbonyl groups (intermediate B) followed by thermal cyclocondensation (cyclic intermediate C) and finally by hydrogen sulfide elimination. Conversion of amides **1** into oxazines **2** and thiazines **3** does not involve the chiral carbon centre so that the absolute configuration of reagents is retained in target compounds, practically without loss in optical purity (as evidenced by $^{19}F$ NMR spectroscopy using tris[3-(heptafluorobutyryl)-L-camphorato]europium(III) as a chiral lanthanide shift reagent).

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doi:10.1016/j.jfluchem.2009.09.010

**Table 1**
Analytical data of compounds **1**.

| Compound | Ar | R | Yield (%)[a] | Mp (°C)[b] | Ee (%) |
|---|---|---|---|---|---|
| **1a** | Ph | Me | 85 | 127–130 | 75 |
| **1b** | Ph | Ph | 86 | 121–123 | 76 |
| **1c** | Ph | 4-$BrC_6H_4$ | 88 | 216–218 | 76 |
| **1d** | 4-$FC_6H_4$ | Me | 84 | 130–132 | 79 |
| **1e** | 4-$FC_6H_4$ | Ph | 85 | 110–112 | 78 |
| **1f** | 4-$MeC_6H_4$ | Me | 80 | 115–117 | 70 |
| **1g** | 4-$MeC_6H_4$ | 4-$NO_2C_6H_4$ | 87 | 232–234 | 70 |
| **1h** | 4-$MeOC_6H_4$ | Me | 85 | 110–112 | 72 |

[a] Yields of isolated products.
[b] Melting points are uncorrected.

**Table 2**
Analytical data of compounds **2**.

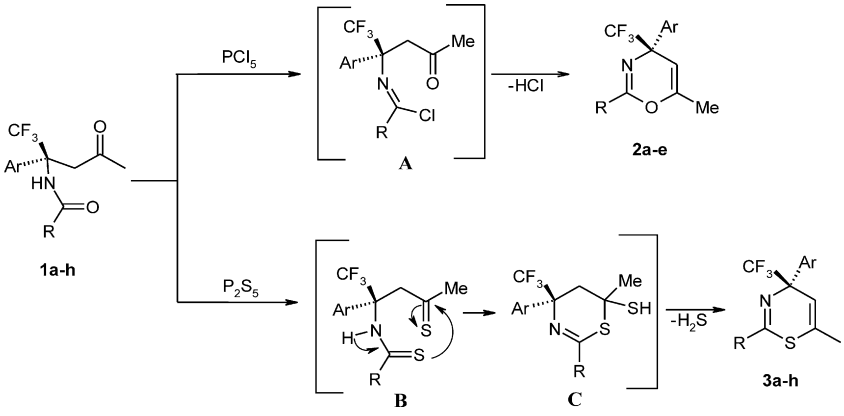
| Compound | Ar | R | Yield (%)[a] | Ee (%) |
|---|---|---|---|---|
| **2a** | Ph | Ph | 77 | 74 |
| **2b** | 4-$FC_6H_4$ | Ph | 73 | 75 |
| **2c** | 4-$MeC_6H_4$ | 4-$NO_2C_6H_4$ | 75 | 68 |
| **2d** | 4-$MeC_6H_4$ | Me | 73 | 70 |
| **2e** | 4-$MeOC_6H_4$ | Me | 70 | 74 |

[a] Yields of isolated products.

**Table 3**
Analytical data of compounds **3**.

| Compound | Ar | R | Yield (%)[a] | Ee (%) |
|---|---|---|---|---|
| **3a** | Ph | Me | 78 | 73 |
| **3b** | Ph | Ph | 83 | 72 |
| **3c** | Ph | 4-$BrC_6H_4$ | 82 | 72 |
| **3d** | 4-$FC_6H_4$ | Me | 80 | 74 |
| **3e** | 4-$FC_6H_4$ | Ph | 77 | 70 |
| **3f** | 4-$MeC_6H_4$ | Me | 83 | 73 |
| **3g** | 4-$MeC_6H_4$ | 4-$NO_2C_6H_4$ | 78 | 69 |
| **3h** | 4-$MeOC_6H_4$ | Me | 75 | 71 |

[a] Yields of isolated products.




To conclude, we have used the easily accessible N-acyl derivatives of optically active 4-amino-4-aryl-5,5,5-trifluoropentan-2-ones to synthesize new chiral trifluoromethyl-substituted 1,3-azines, *viz.*, S-4-aryl-4-trifluoromethyl-4H-1,3-oxa(thia)zines.

## 3. Experimental

IR spectra were recorded on a UR-20 instrument in KBr disks for compounds **1a**–**h** and in $CH_2Cl_2$ solutions for compounds **2a**–**e** and **3a**–**h**. $^1H$, $^{13}C$, and $^{19}F$ NMR spectra were measured in $CDCl_3$ on a Bruker Avance DRX-500 spectrometer at the respective frequencies 500.13, 125.75 and 470.59 MHz using TMS ($^1H$, $^{13}C$) and $CCl_3F$ ($^{19}F$) as internal standards. Compounds were identified by TLC on Silufol-254 plates using a mixture of hexane:ethylacetate as eluent. Elemental analysis was performed in the Analytical Laboratory of the Institute of Organic Chemistry, National Academy of Sciences of Ukraine.

### *3.1. S(−)-N-[1-Aryl-3-oxo-1-(trifluoromethyl)butyl]acetamides (**1a, d, f, h**) and S(−)-N-[1-aryl-3-oxo-1-(trifluoromethyl)butyl]benzamides (**1b, c, e, g**)*

To a solution of 4-amino-4-aryl-5,5,5-trifluoropentan-2-one (0.5 g, 2.16 mmol) in dry toluene (6 ml), acetic anhydride (0.44 g, 4.32 mmol) or the corresponding (un)substituted benzoyl chloride (4.32 mmol) was added to obtain compounds **1a**, **d**, **f**, **h** or **1b**, **c**, **e**, **g**, respectively. The reaction mixture was boiled for 4 h, followed by evaporation of the solvent. The oily residue was recrystallized from hexane.

### *3.2. S(−)-N-[3-Oxo-1-phenyl-1-(trifluoromethyl)butyl]acetamide (**1a**)*

$[\alpha]_D^{20} = -45.98$ ($c = 0.47$; MeOH). IR (KBr) $\upsilon$: 1695, 1755 (C=O), 3315 (N–H). $^1H$ NMR $\delta$: 2.07 (s, 3H), 2.18 (s, 3H), 3.44 (d, 1H, $J = 17.0$ Hz), 3.82 (d, 1H, $J = 17.0$ Hz), 6.58 (s, 1H), 7.37–7.46 (m, $5H_{arom.}$). $^{19}F$ NMR ($CDCl_3$) $\delta$: −75.29. $^{13}C$ NMR $\delta$: 24.14 ($CH_3$), 31.51 ($CH_3$), 43.45 ($CH_2$), 63.07 (q, $J = 27.6$ Hz), 126.02, 127.52 (q, $CF_3$, $J = 286.7$ Hz), 128.64, 128.68, 135.92 ($C_{arom.}$), 170.25 (C=O), 203.89 (C=O). Anal. calculated for $C_{13}H_{14}F_3NO_2$: C, 67.14; H, 5.16; N, 5.13%. Found: C, 67.96; H, 5.24; N, 5.28%.

### *3.3. S(−)-N-[1-(4-Fluorophenyl)-3-oxo-1-(trifluoromethyl)butyl]acetamide (**1d**)*

$[\alpha]_D^{20} = -9.90$ ($c = 1.01$; MeOH). IR (KBr) $\upsilon$: 1695, 1750 (C=O), 3315 (N–H). $^1H$ NMR $\delta$: 2.09 (s, 3H), 2.19 (s, 3H), 3.41 (d, 1H, $J = 16.8$ Hz), 3.71 (d, 1H, $J = 16.8$ Hz), 6.64 (s, 1H), 7.08 (t, $2H_{arom.}$, $J = 8.7$ Hz), 7.40–7.44 (m, $2H_{arom.}$). $^{19}F$ NMR ($CDCl_3$) $\delta$: −75.59, −114.54. $^{13}C$ NMR $\delta$: 24.03 ($CH_3$), 31.57 ($CH_3$), 43.44 ($CH_2$), 62.94 (q, $J = 27.6$ Hz), 115.55 (d, $J = 21.3$ Hz), 125.12 (q, $CF_3$, $J = 286.7$ Hz), 128.07 (d, $J = 7.5$ Hz), 131.78, 162.6 (d, $J = 247.9$ Hz), 170.35 (C=O), 203.73 (C=O). Anal. calculated for $C_{13}H_{13}F_4NO_2$: C, 53.61; H, 4.50; N, 4.81%. Found: C, 53.98; H, 5.07; N, 4.97%.

### *3.4. S(−)-N-[1-(4-Methylphenyl)-3-oxo-1-(trifluoromethyl)butyl]acetamide (**1f**)*

$[\alpha]_D^{20} = -25.00$ ($c = 1.0$; MeOH). IR (KBr) $\upsilon$: 1715, 1745 (C=O), 3430 (N–H). $^1H$ NMR $\delta$: 2.07 (s, 3H), 2.17 (s, 3H), 2.34 (s, 3H), 3.42 (d, 1H, $J = 16.8$ Hz), 3.81 (d, 1H, $J = 16.8$ Hz), 6.42 (s, 1H), 7.21 (d,

$2H_{arom.}$, $J$ = 8.1 Hz), 7.30 (d, $2H_{arom.}$, $J$ = 8.1 Hz). $^{19}F$ NMR $\delta$: −75.59. $^{13}C$ NMR $\delta$: 20.96 ($CH_3$), 24.14 ($CH_3$), 31.44 ($CH_3$), 43.31 ($CH_2$), 63.08 (q, $J$ = 27.6 Hz), 125.91, 125.27 (q, $CF_3$, $J$ = 286.7 Hz), 129.36, 132.94, 138.56 ($C_{arom.}$), 170.28 (C=O), 203.86 (C=O). Anal. calculated for $C_{14}H_{16}F_3NO_2$: C, 58.53; H, 5.61; N, 4.88%. Found: C, 58.82; H, 5.97; N, 5.06%.

### 3.5. S(−)-N-[1-(4-Methoxyphenyl)-3-oxo-1-(trifluoromethyl)butyl]acetamide (1h)

$[\alpha]_D^{20}$ = −16.12 ($c$ = 0.62; MeOH). IR (KBr) $\upsilon$: 1710, 1721 (C=O), 3365 (N=H). $^1H$ NMR $\delta$: 2.10 (s, 3H), 2.19 (s, 3H), 3.43 (d, 1H, $J$ = 16.5 Hz), 3.83–3.86 (m, 4H), 6.38 (s, 1H), 6.94 (d, $2H_{arom.}$, $J$ = 8.5 Hz), 7.36 (d, $2H_{arom.}$, $J$ = 8.1 Hz). $^{19}F$ NMR $\delta$: −75.81. $^{13}C$ NMR $\delta$: 24.19 ($CH_3$), 31.48 ($CH_3$), 43.26 ($CH_2$), 55.27 ($CH_3O$), 62.91 (q, $J$ = 27.6 Hz), 113.99, 125.28 (q, $CF_3$, $J$ = 286.7 Hz), 127.35, 127.78, 159.65 ($C_{arom.}$), 170.27 (C=O), 203.87 (C=O). Anal. calculated for $C_{14}H_{16}F_3NO_3$: C, 55.44; H, 5.32; N, 4.62%. Found: C, 56.92; H, 5.77; N, 4.81%.

### 3.6. S(−)-N-[3-Oxo-1-phenyl-1-(trifluoromethyl)butyl]benzamide (1b)

$[\alpha]_D^{20}$ = −39.36 ($c$ = 0.65; MeOH). IR (KBr) $\upsilon$: 1695, 1718 (C=O), 3375 (N–H). $^1H$ NMR $\delta$: 2.20 (s, 3H), 3.45 (d, 1H, $J$ = 16.5 Hz), 3.75 (d, 1H, $J$ = 16.5 Hz), 7.38–7.57 (m, $9H_{arom.}$), 7.85–7.87 (m, $2H_{arom.}$). $^{19}F$ NMR $\delta$: −73.55. $^{13}C$ NMR $\delta$: 31.84 ($CH_3$), 44.71 ($CH_2$), 63.87 (q, $J$ = 27.6 Hz), 125.44 (q, $CF_3$, $J$ = 287.9 Hz), 125.88, 127.18, 128.69, 128.78, 128.80, 132.01, 134.37, 136.00 ($C_{arom.}$), 166.88 (C=O), 204.84 (C=O). Anal. calculated for $C_{18}H_{16}F_3NO_2$: C, 64.47; H, 4.81; N, 4.18%. Found: C, 64.63; H, 5.13; N, 4.45%.

### 3.7. S(−)-N-[1-(4-Bromophenyl)-3-oxo-1-(trifluoromethyl)butyl]benzamide (1c)

$[\alpha]_D^{20}$ = −45.68 ($c$ = 0.74; MeOH). IR (KBr) $\upsilon$: 1710, 1730 (C=O), 3370 (N–H). $^1H$ NMR $\delta$: 2.22 (s, 3H), 3.40 (d, 1H, $J$ = 18 Hz), 3.69 (d, 1H, $J$ = 18 Hz), 7.38–7.46 (m, $5H_{arom.}$), 7.60 (s, 1H), 7.62 (d, $2H_{arom.}$, $J$ = 9.0 Hz), 7.71 (d, $2H_{arom.}$, $J$ = 9.0 Hz). $^{19}F$ NMR $\delta$: −73.27. $^{13}C$ NMR $\delta$: 31.93, 44.73, 63.91 (q, $J$ = 27.5 Hz), 125.51 (q, $CF_3$, $J$ = 287.2 Hz), 125.78, 126.79, 128.82, 128.84, 128.88, 132.00, 133.19, 135.82 ($C_{arom.}$), 165.90, 205.13. Anal. calculated for $C_{18}H_{15}BrF_3NO_2$: C, 52.19; H, 3.65; N, 3.38%. Found: C, 52.25; H, 3.62; N, 3.37%.

### 3.8. S(−)-N-[1-(4-Fluorophenyl)-3-oxo-1-(trifluoromethyl)butyl]benzamide (1e)

$[\alpha]_D^{20}$ = −55.56 ($c$ = 0.45; MeOH). IR (KBr) $\upsilon$: 1715, 1735 (C=O), 3365 (N–H). $^1H$ NMR $\delta$: 2.22 (s, 3H), 3.42 (d, 1H, $J$ = 16.5 Hz), 3.67 (d, 1H, $J$ = 16.5 Hz), 7.10 (t, $2H_{arom.}$, $J$ = 8.4 Hz), 7.45–7.56 (m, $6H_{arom.}$), 7.85–7.87 (m, $2H_{arom.}$). $^{19}F$ NMR $\delta$: −73.84, −114.49. $^{13}C$ NMR $\delta$: 31.91 ($CH_3$), 44.74 ($CH_2$), 63.56 (q, $J$ = 27.6 Hz), 115.75 (d, $J$ = 22.6 Hz), 125.34 (q, $CF_3$, $J$ = 286.7 Hz), 127.18, 127.89, 127.95, 128.79, 132.15, 134.12, 162.60 (d, $J$ = 248.9 Hz), 166.93 (C=O), 204.76 (C=O). Anal. calculated for $C_{18}H_{15}F_4NO_2$: C, 61.19; H, 4.28; N, 3.96%. Found: C, 61.97; H, 4.85; N, 4.04%.

### 3.9. S(−)-N-[1-(4-Methylphenyl)-3-oxo-1-(trifluoromethyl)butyl]-4-nitrobenzamide (1g)

$[\alpha]_D^{20}$ = −44.55 ($c$ = 0.10; MeOH). IR (KBr) $\upsilon$: 1705, 1720 (C=O), 3345 (N–H). $^1H$ NMR $\delta$: 2.21 (s, 3H), 2.35 (s, 3H), 3.39 (d, 1H, $J$ = 17.0 Hz), 3.72 (d, 1H, $J$ = 17.0 Hz), 7.22 (d, $2H_{arom.}$, $J$ = 7.0 Hz), 7.36 (d, $2H_{arom.}$, $J$ = 7.0 Hz), 7.50 (s, 1H), 7.60 (d, $2H_{arom.}$, $J$ = 6.5 Hz), 7.72 (d, $2H_{arom.}$, $J$ = 6.5 Hz). $^{19}F$ NMR $\delta$: −73.74. $^{13}C$ NMR $\delta$: 21.02 ($CH_3$), 32.05 ($CH_3$), 44.46 ($CH_2$), 64.02 (q, $J$ = 27.6 Hz), 123.97, 125.32 (q, $CF_3$, $J$ = 287.9 Hz), 125.59, 128.43, 129.67, 132.43, 138.88, 139.91, 149.89 ($C_{arom.}$), 164.83 (C=O), 205.51 (C=O). Anal. calculated for $C_{19}H_{17}F_3N_2O_4$: C, 57.87; H, 4.35; N, 7.10%. Found: C, 58.04; H, 4.85; N, 7.62%.

### 3.10. S(−)-4-Aryl-6-methyl-4-trifluoromethyl-4H-1,3-oxazines (2a–e)

To a solution of amide **1b**, **e**, **f**, **g**, **h** (1 mmol) in dry benzene (10 ml), phosphorus pentachloride (0.23 g, 1.1 mmol) was added and the reaction mixture was boiled for 8 h. After evaporation of the solvent, dichloromethane (15 ml) and a concentrated $K_2CO_3$ solution (15 ml) were added to the residue, followed by stirring for 10 min. The organic layer was separated, washed with water, and dried over $Na_2SO_4$. Filtration and evaporation then afforded analytically pure oily products.

### 3.11. S(−)-2,6-Diphenyl-6-methyl-4-trifluoromethyl-4H-1,3-oxazine (2a)

Oil. $[\alpha]_D^{20}$ = −223.40 ($c$ = 0.47; MeOH). IR ($CH_2Cl_2$) $\upsilon$: 1725 (C=N). $^1H$ NMR $\delta$: 2.06 (s, 3H), 5.38 (s, 1H), 7.28–7.55 (m, $6H_{arom.}$), 7.70 (d, $2H_{arom.}$, $J$ = 7.0 Hz), 8.18 (d, $2H_{arom.}$, $J$ = 7.0 Hz). $^{19}F$ NMR $\delta$: −79.69. $^{13}C$ NMR $\delta$: 18.80 ($CH_3$), 62.09 (q, $C^4$, $J$ = 28.9 Hz), 96.15 ($C^5$), 125.85 (q, $CF_3$, $J$ = 284.1 Hz), 126.72, 127.82, 128.18, 128.30, 128.34, 131.47, 131.64, 140.65 ($C_{arom.}$), 131.43, 153.59. Anal. calculated for $C_{18}H_{14}F_3NO$: C, 68.13; H, 4.45; N, 4.41%. Found: C, 68.85; H, 4.97; N, 4.83%.

### 3.12. S(−)-4-(4-Fluorophenyl)-6-methyl-2-phenyl-4-trifluoromethyl-4H-1,3-oxazine (2b)

Oil. $[\alpha]_D^{20}$ = −136.14 ($c$ = 0.63; MeOH). IR ($CH_2Cl_2$) $\upsilon$: 1725 (C=N). $^1H$ NMR $\delta$: 2.07 (s, 3H), 5.34 (s, 1H), 7.09–7.10 (m, $2H_{arom.}$), 7.50–7.53 (m, $3H_{arom.}$), 7.63–7.64 (m, $2H_{arom.}$), 8.16–8.17 (m, $2H_{arom.}$). $^{19}F$ NMR $\delta$: −80.03, −115.28. $^{13}C$ NMR $\delta$: 18.79 ($CH_3$), 61.68 (q, $C^4$, $J$ = 28.9 Hz), 95.86 ($C^5$), 115.10, 115.27, 125.64, 125.83 (q, $CF_3$, $J$ = 284.4 Hz), 127.81, 128.32, 128.58, 131.31, 131.75 ($C_{arom.}$), 149.28, 153.74, 162.51 (d, $J$ = 247.7 Hz). Anal. calculated for $C_{18}H_{13}F_4NO$: C, 64.48; H, 3.91; N, 4.18%. Found: C, 64.96; H, 4.33; N, 4.47%.

### 3.13. S(−)-6-Methyl-4-(4-methylphenyl)-2-(4-nitrophenyl)-4-trifluoromethyl-4H-1,3-oxazine (2c)

Oil. $[\alpha]_D^{20}$ = −217.10 ($c$ = 0.76; MeOH). IR ($CH_2Cl_2$) $\upsilon$: 1720 (C=N). $^1H$ NMR $\delta$: 2.08 (s, 3H), 2.38 (s, 3H), 5.40 (s, 1H), 7.24 (d, $2H_{arom.}$, $J$ = 8.5 Hz), 8.18 (d, $2H_{arom.}$, $J$ = 8.5 Hz), 8.31–8.32 (m, $4H_{arom.}$). $^{19}F$ NMR $\delta$: −79.71. $^{13}C$ NMR $\delta$: 18.80 ($CH_3$), 62.09 (q, $C^4$, $J$ = 28.9 Hz), 96.15 ($C^5$), 125.85 (q, $CF_3$, $J$ = 284.1 Hz), 126.72, 127.82, 128.18, 128.30, 128.34, 131.47, 131.64, 140.65 ($C_{arom.}$), 131.43, 153.59. Anal. calculated for $C_{19}H_{15}F_3N_2O_3$: C, 60.64; H, 4.02; N, 7.44%. Found: C, 61.18; H, 4.55; N, 7.53%.

### 3.14. S(−)-2,6-Dimethyl-4-(4-methylphenyl)-4-trifluoromethyl-4H-1,3-oxazine (2d)

Oil. $[\alpha]_D^{20}$ = −30.61 ($c$ = 9.8; MeOH). IR ($CH_2Cl_2$) $\upsilon$: 1725 (C=N). $^1H$ NMR $\delta$: 1.86 (s, 3H), 2.13 (s, 3H), 2.34 (s, 3H), 5.19 (s, 1H), 7.19 (d, $2H_{arom.}$, $J$ = 8.1 Hz), 7.48 (d, $2H_{arom.}$, $J$ = 8.1 Hz). $^{19}F$ NMR $\delta$: −78.20. $^{13}C$ NMR $\delta$: 18.67 ($CH_3$), 20.94 ($CH_3$), 55.28 ($CH_3$), 61.45 (q, $C^4$, $J$ = 28.9 Hz), 95.77 ($C^5$), 124.54 (q, $CF_3$, $J$ = 284.1 Hz), 125.67, 126.50, 129.04, 129.41 ($C_{arom.}$), 148.64, 156.22. Anal. calculated for $C_{14}H_{14}F_3NO$: C, 62.45; H, 5.24; N, 5.20%. Found: C, 62.98; H, 5.87; N, 5.67%.

*3.15. S(−)-2,6-Dimethyl-4-(4-methoxyphenyl)-4-trifluoromethyl-4H-1,3-oxazine (**2e**)*

Oil. $[\alpha]_D^{20}$ = −48.60 (*c* = 0.72; MeOH). IR ($CH_2Cl_2$) υ: 1725 (C=N). $^1$H NMR δ: 1.88 (s, 3H), 2.14 (s, 3H), 3.80 (s, 3H), 5.19 (s, 1H), 6.91 (d, 2H$_{arom.}$, *J* = 8.7 Hz), 7.48 (d, 2H$_{arom.}$, *J* = 8.7 Hz). $^{19}$F NMR δ: −79.83. $^{13}$C NMR δ: 18.66 ($CH_3$), 20.91 ($CH_3$), 55.28 ($CH_3$), 61.44 (q, $C^4$, *J* = 28.9 Hz), 95.76 ($C^5$), 113.69, 124.53 (q, $CF_3$, *J* = 284.1 Hz), 127.90, 132.37, 148.62 ($C_{arom.}$), 156.40, 159.36. Anal. calculated for $C_{14}H_{14}F_3NO_2$: C, 58.95; H, 4.95; N, 4.91%. Found: C, 61.18; H, 4.55; N, 4.98%.

*3.16. S(+)-4-Aryl-6-methyl-4-trifluoromethyl-4H-1,3-thiazines (**3a–h**)*

To a solution of amide **1a–h** (1 mmol) in dry xylene (15 ml), phosphorus pentasulfide (0.22 g, 10 mmol) was added and the reaction mixture was boiled with vigorous stirring for 18–20 h. After cooling, the organic layer was decanted and the solvent was evaporated to give analytically pure oily products.

*3.17. S(+)-2,6-Dimethyl-4-phenyl-4-trifluoromethyl-4H-1,3-thiazine (**3a**)*

Oil. $[\alpha]_D^{20}$ = +20.62 (*c* = 0.97; MeOH). IR ($CH_2Cl_2$) υ: 1690 (C=N). $^1$H NMR δ: 2.12 (s, 3H), 2.55 (s, 3H), 6.01 (s, 1H), 7.33–7.46 (m, 5H$_{arom.}$). $^{19}$F NMR δ: −77.88. $^{13}$C NMR δ: 21.87 ($CH_3$), 26.70 ($CH_3$), 69.58 (q, $C^4$, *J* = 28.8 Hz), 113.26 ($C^5$), 124.73 (q, $CF_3$, *J* = 284.1 Hz), 127.81, 127.53, 128.24, 128.97 ($C_{arom.}$), 131.43, 136.8. Anal. calculated for $C_{13}H_{12}F_3NS$: C, 57.55; H, 4.46; N, 5.16; S, 11.82%. Found: C, 58.02; H, 4.97; N, 5.34; S, 11.98%.

*3.18. S(+)-2,4-Diphenyl-6-methyl-4-trifluoromethyl-4H-1,3-thiazine (**3b**)*

Oil. $[\alpha]_D^{20}$ = +23.48 (*c* = 0.75; MeOH). IR ($CH_2Cl_2$) υ: 1695 (C=N). $^1$H NMR δ: 2.24 (s, 3H), 6.15 (s, 1H), 7.32–7.34 (m, 3H$_{arom.}$), 7.47–7.60 (m, 5H$_{arom.}$), 8.02 (d, 2H$_{arom.}$, *J* = 7.0 Hz). $^{19}$F NMR δ: −78.63. $^{13}$C NMR δ: δ 21.98 ($CH_3$), 70.13 (q, $C^4$, *J* = 27.6 Hz), 114.87 ($C^5$), 124.98 (q, $CF_3$, *J* = 282.9 Hz), 127.99, 128.22, 128.32, 128.93, 129.01, 129.11, 132.11, 133.07($C_{arom.}$), 134.91, 136.62. Anal. calculated for $C_{18}H_{14}F_3NS$: C, 64.85; H, 4.23; N, 4.20; S 9.62%. Found: C, 64.98; H, 4.83; N, 4.66; S, 9.77%.

*3.19. S(+)-2-(4-Bromphenyl)-6-methyl-4-phenyl-4-trifluoromethyl-4H-1,3-thiazine (**3c**)*

Oil. $[\alpha]_D^{20}$ = +40.93 (*c* = 0.50; MeOH). IR ($CH_2Cl_2$) υ: 1690 (C=N). $^1$H NMR δ: 2.22 (s, 3H), 6.17 (s, 1H), 7.32–7.34 (m, 3H$_{arom.}$), 7.50–7.51 (m, 2H$_{arom.}$), 7.62 (d, 2H$_{arom.}$, *J* = 8.0 Hz), 7.93 (d, 2H$_{arom.}$, *J* = 8.0 Hz). $^{19}$F NMR δ: −78.47. $^{13}$C NMR δ: 22.16 ($CH_3$), 69.71 (q, $C^4$, *J* = 27.6 Hz), 114.25 ($C^5$), 127.50 (q, $CF_3$, *J* = 284.2 Hz), 126.63, 127.98, 128.78, 129.20, 131.05, 131.93, 132.28, 135.33 ($C_{arom.}$), 137.36, 160.54. Anal. calculated for $C_{18}H_{13}BrF_3NS$: C, 52.44; H, 3.18; N, 3.40; S, 7.78%. Found: C, 52.87; H, 4.97; N, 3.58; S, 7.97%.

*3.20. S(+)-2,6-Dimethyl-4-(4-fluorophenyl)-4-trifluoromethyl-4H-1,3-thiazine (**3d**)*

Oil. $[\alpha]_D^{20}$ = +10.03 (*c* = 0.50; MeOH). IR ($CH_2Cl_2$) υ: 1690 (C=N). $^1$H NMR δ: 2.18 (s, 3H), 2.73 (s, 3H), 5.98 (s, 1H), 7.00–7.10 (m, 2H$_{arom.}$), 7.43–7.51 (m, 2H$_{arom.}$). $^{19}$F NMR δ: −76.75 (3F), −112.19 (1F). $^{13}$C NMR δ: 21.68 ($CH_3$), 26.26 ($CH_3$), 68.50 (q, $C^4$, *J* = 28.9 Hz), 113.63 ($C^5$), 115.72 (d, *J* = 21.4 Hz), 126.72 (q, $CF_3$, *J* = 284.2 Hz), 128.92, 129.80, 129.87($C_{arom.}$), 130.79, 131.32, 163.12 (d, $C_{arom.}$, *J* = 250.2 Hz). Anal. calculated for $C_{13}H_{11}F_4NS$: C, 53.97; H, 3.83; N, 4.84; S 11.08%. Found: C, 54.12; H, 4.03; N, 4.93; S, 11.23%.

*3.21. S(+)-4-(4-Fluorophenyl)-6-methyl-2-phenyl-4-trifluoromethyl-4H-1,3-thiazine (**3e**)*

Oil. $[\alpha]_D^{20}$ = +34.03 (*c* = 0.89; MeOH). IR ($CH_2Cl_2$) υ: 1690 (C=N). $^1$H NMR δ: 2.28 (s, 3H), 6.16 (s, 1H), 7.04–7.11 (m, 2H$_{arom.}$), 7.54–7.62 (m, 5H$_{arom.}$), 8.05 (d, 2H$_{arom.}$, *J* = 8.0 Hz). $^{19}$F NMR δ: −78.34 (3F), −113.73 (1F). $^{13}$C NMR δ: 22.01 ($CH_3$), 69.65 (q, $C^4$, *J* = 27.6 Hz), 114.57 ($C^5$), 115.24 (d, *J* = 21.4 Hz), 123.91 (q, $CF_3$, *J* = 282.9 Hz), 128.25, 129.04, 129.92, 132.40, 132.60, 133.10 ($C_{arom.}$), 134.60, 134.88, 162.94 (d, *J* = 248.9 Hz). Anal. calculated for $C_{18}H_{13}F_4NS$: C, 61.53; H, 3.73; N, 3.99; S, 9.13%. Found: C, 61.94; H, 4.14; N, 4.17; S, 9.54%.

*3.22. S(+)-2,6-Dimethyl-4-(4-methylphenyl)-4-trifluoromethyl-4H-1,3-thiazine (**3f**)*

Oil. $[\alpha]_D^{20}$ = +28.76 (*c* = 1.0; MeOH). IR ($CH_2Cl_2$) υ: 1695 (C=N). $^1$H NMR δ: 2.15 (s, 3H), 2.33 (s, 3H), 2.67 (s, 3H), 5.99 (s, 1H), 7.19 (d, 2H$_{arom.}$, *J* = 7.8 Hz), 7.34 (d, 2H$_{arom.}$, *J* = 7.8 Hz). $^{19}$F NMR δ: −77.06. $^{13}$C NMR δ: 21.19 ($CH_3$), 21.70 ($CH_3$), 26.37 ($CH_3$), 68.78 (q, $C^4$, *J* = 27.6 Hz), 113.88 ($C^5$), 123.23, 126.51 (q, $CF_3$, *J* = 284.2 Hz), 127.58, 129.31, 132.79($C_{arom.}$), 130.83, 131.11. Anal. calculated for $C_{14}H_{14}F_3NS$: C, 58.93; H, 4.95; N, 4.91; S, 11.24%. Found: C, 59.17; H, 5.43; N, 4.98; S, 11.76%.

*3.23. S(+)-6-Methyl-4-(4-methylphenyl)-2-(4-nitrophenyl)-4-trifluoromethyl-4H-1,3-thiazine (**3g**)*

Oil. $[\alpha]_D^{20}$ = +34.40 (*c* = 1.0; MeOH). IR ($CH_2Cl_2$) υ: 1690 (C=N). $^1$H NMR δ: 2.20 (s, 3H), 2.31 (s, 3H), 6.13 (s, 1H), 7.11 (d, 2H$_{arom.}$, *J* = 7.8 Hz), 7.34 (d, 2H$_{arom.}$, *J* = 7.8 Hz), 7.61 (d, 2H$_{arom.}$, *J* = 8.7 Hz), 7.89 (d, 2H$_{arom.}$, *J* = 8.7 Hz). $^{19}$F NMR δ: −78.61. $^{13}$C NMR δ: 21.15 ($CH_3$), 22.14 ($CH_3$), 70.38 (q, $C^4$, *J* = 27.6 Hz), 114.29 ($C^5$), 126.73 (q, $CF_3$, *J* = 284.2 Hz), 127.80, 128.65, 129.11, 131.84, 132.08, 134.32, 134.68, 135.51, 138.57, 159.86 ($C_{arom.}$). Anal. calculated for $C_{19}H_{15}F_3N_2O_2S$: C, 58.16; H, 3.85; N, 7.14; S, 8.17%. Found: C, 58.73; H, 4.02; N, 7.56; S, 8.75%.

*3.24. S(+)-2,6-Dimethyl-4-(4-methoxyphenyl)-4-trifluoromethyl-4H-1,3-thiazine (**3h**)*

Oil. $[\alpha]_D^{20}$ = +14.86 (*c* = 0.95; MeOH). IR ($CH_2Cl_2$) υ: 1695 (C=N). $^1$H NMR δ: 2.19 (s, 3H), 2.91 (s, 3H), 3.81 (s, 3H), 5.98 (s, 1H), 6.98 (d, 2H$_{arom.}$, *J* = 8.7 Hz), 7.43 (d, 2H$_{arom.}$, *J* = 8.7 Hz). $^{19}$F NMR δ: −76.79. $^{13}$C NMR δ: 21.60 ($CCH_3$), 29.72 ($CH_3$), 55.45 ($CH_3O$), 68.58 (q, $C^4$, *J* = 27.6 Hz), 114.26 ($C^5$), 126.38 (q, $CF_3$, *J* = 284.2 Hz), 126.92, 128.94, 129.10, 132.15, 143.70, 160.40 ($C_{arom.}$). Anal. calculated for $C_{14}H_{14}F_3NOS$: C, 55.80; H, 4.68; N, 4.65; S, 10.65%. Found: C, 55.99; H, 4.97; N, 4.77; S, 10.92%.

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