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Thioamides and selenoamides with chirality solely due to hindered rotation about the C–N bond: enantioselective complexation with optically active hosts

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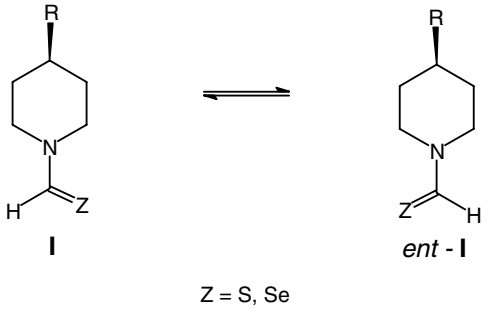
Abstract—Several thioformamides and selenoformamides, with chirality solely due to restricted rotation about the C–N bond, were resolved to enantiomers by inclusion crystallization with optically active diols (TADDOLs). The absolute configuration of the guest molecules was deduced from the X-ray crystal structures of the inclusion complexes. The optical activity of the resolved compounds is manifested by their CD spectra showing relatively strong Cotton effects in the region of thioamide or selenoamide n–π* transition. The optically active thioformamides and selenoformamides are configurationally labile compounds and gradually racemize in solution but are stable in the form of the inclusion complexes. The first-order kinetics of the racemization in solution allowed us to assign the C–N rotation barriers of thioformamides by spectropolarimetric measurements.

1. Introduction

The restricted rotation about the C(O)–N bond in carboxylic amides is a well established phenomenon that has been the subject of numerous experimental and theoretical studies over the past 30 years.[1,2] It is brought about by the partial double bond character between the adjacent carbon and nitrogen, while the corresponding rotation barrier of typical amides usually exceeds 21 kcal/mol.[1] The rotation barrier in thioamides is ca. 5 kcal/mol higher than in the related amides while in selenoamides increases by an additional ca. 1 kcal/mol due to a greater contribution of the bipolar resonance structure that increases double bond character of the C(S)–N and C(Se)–N linkages.[1] The hindered rotation about the C–N bond in amides and their thiocarbonyl or selenocarbonyl analogues results in some intriguing stereochemical and spectroscopic consequences. In the absence of any improper symmetry axis *N*-formyl, *N*-thioformyl and *N*-selenoformyl piperidines such as **I** are chiral and may exist in two enantiomeric forms.



Interconversion between enantiomers occurs by rotation about the C–N bond. In the case of thioamides and selenoamides, the corresponding energy barrier is large enough to permit the potential isolation of stereoisomers at ambient temperature. Thus, we prepared thioamides **1b**–**3b** and selenoamides **1c**–**3c** with chirality solely due to a restricted rotation about the C–N bond and attempted their resolution to enantiomers. The optically active compounds **1b** and **c**–**3b** and **c** would be valuable models for studying chiroptical spectra of the thioamide and selenoamide chromophores. Substitution of the carbonyl oxygen with progressively heavier atoms exerts a substantial effect on the spectroscopic properties of the

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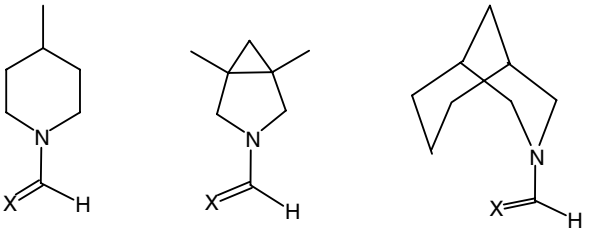
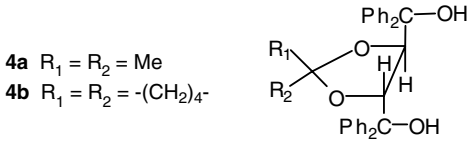
molecules.[3] In particular, it causes a bathochromic shift of UV and CD bands that facilitates the measurements. Whereas thiocarbonyl compounds have been the subject of some chiroptical studies,[4,5] the CD spectra of selenoamides are scarce.[6]



1a X = O
1b X = S
1c X = Se

2a X = O
2b X = S
2c X = Se

3a X = O
3b X = S
3c X = Se



4a $R_1 = R_2 = Me$
4b $R_1 = R_2 = -(CH_2)_4-$

2. Results and discussion

Formamides **1a**–**3a** were obtained by formylation of the corresponding amines with chloral.[7] Thionation of these compounds with Lawesson's reagent[8] in boiling toluene afforded thioformamides **1b**–**3b**. A prolonged heating of **1a**–**3a** with P_4Se_{10}, formed in situ from grey selenium and red phosphorus,[6] in the presence of barium carbonate in boiling xylene gave selenoformamides **1c**–**3c** in excellent yields.

Only one example of an optically active thioformamide with asymmetry caused by restricted rotation about the partial double bond has been reported. The enantiomeric resolution of the compound bearing a carboxylic acid group was achieved via crystallization of diastereomeric salts.[9] However, the resolution of configurationally labile and non-acidic or non-basic compounds is a challenging task that requires non-classical methods. Host–guest complexation using optically active hosts is now a technique that introduces new possibilities in this field.[10] In particular, inclusion crystallization with chiral diols (*R*,*R*)-**4a** and (*R*,*R*)-**4b** (α,α,α′,α′-tetraphenyl-1, 3-dioxolane-4,5-dimethanols known as TADDOLs), easily accessible from (+)-tartaric acid, is an effective method for the optical resolution of a wide variety of racemic compounds.[11] Recently, we have been able to resolve in this way several *N*-nitrosamines with chirality solely due to the hindered N–N rotation.[12] It also seemed applicable for compounds **1b** and **c**–**3b** and **c**. Thus, we prepared the 1:1 inclusion complexes of these compounds with the host diols by cocrystallization of the equimolar amounts of the components from toluene–hexane at room temperature. Since the inclusion compounds **2c**·**4a** and **2c**·**4b** do not give diffraction quality crystals we prepared benzene solvates of much better quality by crystallization from benzene to hexane.

The X-ray crystal structures of the inclusion complexes **1b**·**4b**, **1c**·**4a**, **2b**·**4a**·C_6H_6, **2c**·**4a**·C_6H_6, **2c**·**4b**·C_6H_6, **3b**·**4a** and **3c**·**4a** (Fig. 1) allowed us to assign the absolute configuration of the guest molecules and to estimate the enantioselectivity of the inclusion crystallization. The X-ray crystallographic analysis of clathrates **2c**·**4a**·C_6H_6

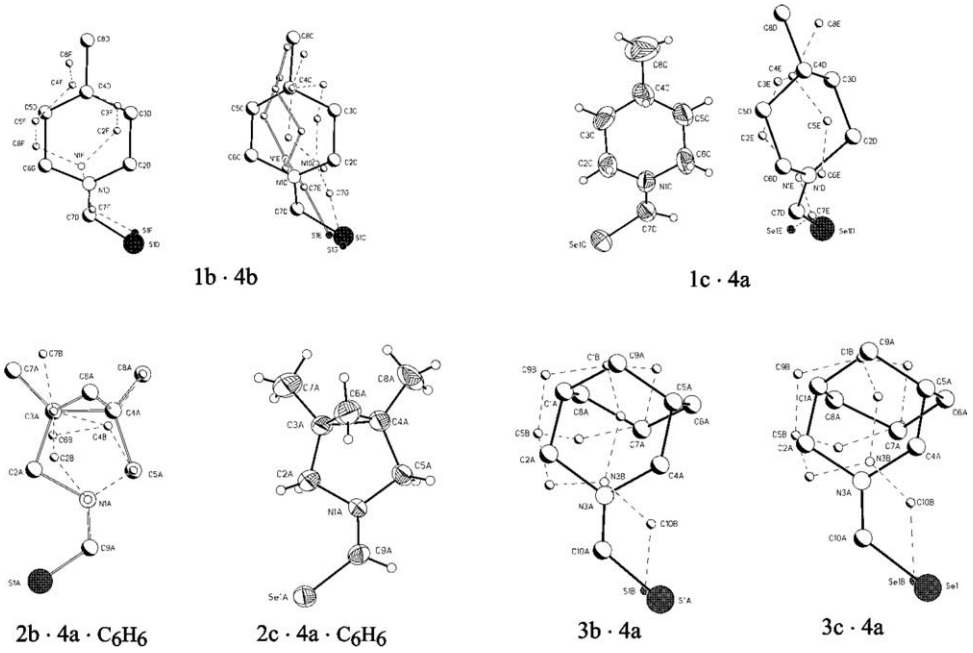


Figure 1. Molecular structures of the guest thio- and selenoamides showing their absolute configuration (the major enantiomer is shown with large circles or thermal ellipsoids; the minor enantiomer is shown with dashed lines and small circles).

and **2c·4b·C_6H_6** showed that only one enantiomer of the guest compound was preferentially included and the *E*-configuration (geometric enantiomerism)[13] was assigned to the guest selenoamide molecules. On the other hand, the structures of the remaining complexes revealed that the thioamide and selenoamide molecules are disordered, and that the occupancy factors (or the sum of the occupancy factors) of the enantiomeric molecules differ indicating that one enantiomer of the guest thioamide or selenoamide is preferentially enclathrated in the inclusion crystals. Thus, the (*S*)-configuration (axial chirality) is preferred by **1b** molecules in the complex **1b·4b** and the approximate enantiomeric ratio is 4:1 (see Experimental for details). The crystal structure of **1c·4a** showed that the asymmetric part contains two molecules of the selenoamide and two host molecules. One guest molecule is ordered and assumes an (*R*)-configuration, whereas the second one is disordered with occupancy factors of $R/S = 20{:}80$. Thus, the overall enantiomeric ratio of **1c** in the crystal is $R/S = 3{:}2$ that corresponds to the ee of 20%. The guest molecules are also disordered in the isostructural complexes **3b·4a** and **3c·4a**, which the *E*-enantiomer dominating (78%) in both cases. Analogously, the *E*-configuration was also assigned to the dominating enantiomer (72%) of the guest thioamide in **2b·4a·C_6H_6**. However, a much stronger CD, exhibited by the same complex crystallized without benzene (Table 1), indicates that **2b·4a** contains only one enantiomer of the thiomide guest molecule. It is important to note that due to a configurational lability of the thio- and selenoamides studied in all cases, an asymmetric transformation occurs with yields of resolution exceed 50%.

The optical activity of the guest compounds is manifested by the CD spectra of the complexes in solution (Table 1). Such measurements are possible because the long-wavelength absorption bands of the thioamide and selenoamide chromophores remain outside the absorption range of the host compounds **4a** and **4b**. The lowest energy absorption band in thioamides occurred near 340 nm and unequivocally corresponds to the forbidden n–π* electronic transition.[4,5] An analogous band in selenoamides shifted to considerably longer wavelengths and was observed near 400 nm in non-polar solvents.[6] Obviously, due to similarities in the electronic structure and the nature of electronic transitions, the structurally related thioamides and selenoamides should also exhibit the same n–π* Cotton effect sign.

Table 1. Circular dichroism (CD) data

Compd	Solvent	CD λ, nm ($[\Theta]$)[a]
1b·4b	PhMe	335 (−23), 379 (285)
1c·4a	PhMe	381 (22), 434 (−12)
1c·4a	KBr	370 (2080)[b]
1c·4b	PhMe	377 (−33), 426 (118)
1c·4b	MeCN	368 (−88), 416 (55)
2b·4a	PhMe	370 (8680)
2b·4a·C_6H_6	PhMe	369 (3690)
2b·4b	PhMe	369 (−6950)
2c·4b·C_6H_6	PhMe	417 (59)
3b·4a	PhMe	368 (5760)
3b·4b	PhMe	368 (3180)
3c·4a	PhMe	415 (2310)

[a] Molecular ellipticity in deg cm^2 dmol^{-1}, measured immediately after dissolution of the sample.

[b] Approximate experimental value determined by considering the weight concentration (KBr density 2.75 g cm^{-3}).

Indeed, the comparison of the CD spectra of **3b·4a** and **3c·4a**, shown in Figure 2, shows a close correspondence between the band shape and Cotton effect signs of both classes of compounds. Also, as expected, substitution of selenium for sulfur causes a red shift of the n–π* bands. Owing to conformational rigidity of the bicyclic skeletons of the guest molecules **2b** and **c**, and **3b** and **c** exhibit significantly stronger Cotton effects than the conformationally flexible piperidine derivatives **1b** and **c**. The crystal structures of **1b·4b** and **1c·4a** revealed that the piperidine ring assumes a chair conformation with the methyl substituent occupying an equatorial position. However, the solution CD spectra of these compounds revealed bisignate Cotton effects in the region of the transition (Fig. 3). This can be explained by the small contribution of the axial conformer of the guest compound to the equilibrium in solution, which is responsible for a minor negative Cotton effect at the shorter wavelengths. The existence of such an equilibrium is confirmed by the solvent dependence of the spectrum of **1c·4a**. Furthermore, the solid state CD of **1c·4a**, measured in KBr disk, shows only one positive Cotton effect of relatively strong intensity corresponding to the equatorial conformer observed in X-ray structure.

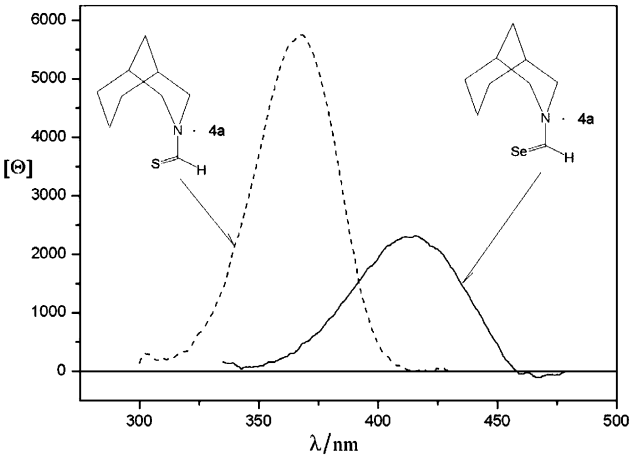


Figure 2. CD spectra of **3b·4a** and **3c·4a** taken in toluene solution.

The measured Cotton effects gradually decreased and finally vanished completely at room temperature (Fig. 4) due to the slow rotation of the thioformyl or selenoformyl group about the C–N bond in solution. The first-order kinetics of racemization can be monitored by spectropolarimetric measurements. The racemization half-life $t_{1/2}$ at 22 °C ranged from 80 min for the thioamide **2b** to 13 h for **3b**, which corresponds to the calculated value from the Eyring equation,[14] with rotation energy barriers $\Delta G^{\ddagger}$ of 95.6, 94.9 and 100.2. ± 0.3 kJ mol^{-1} for **1b**, **2b** and **3b**, respectively. The racemization of the

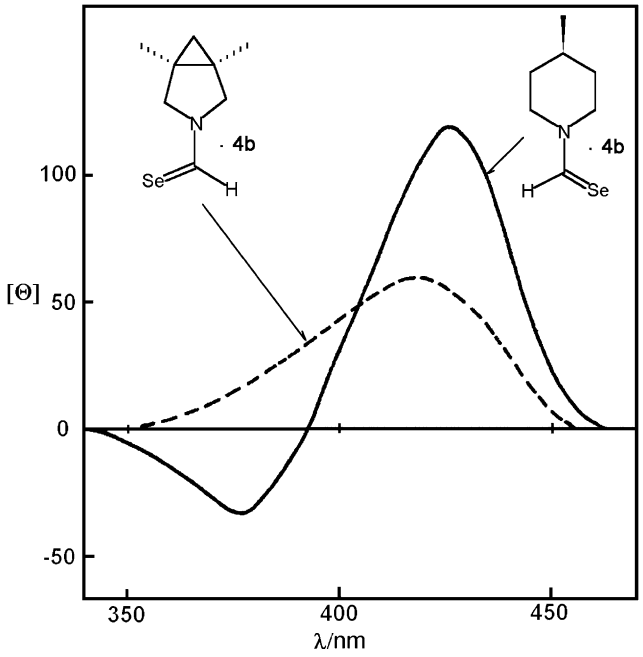


Figure 3. CD spectra of **1c**·**4b** and **2c**·**4b** taken in toluene solution.

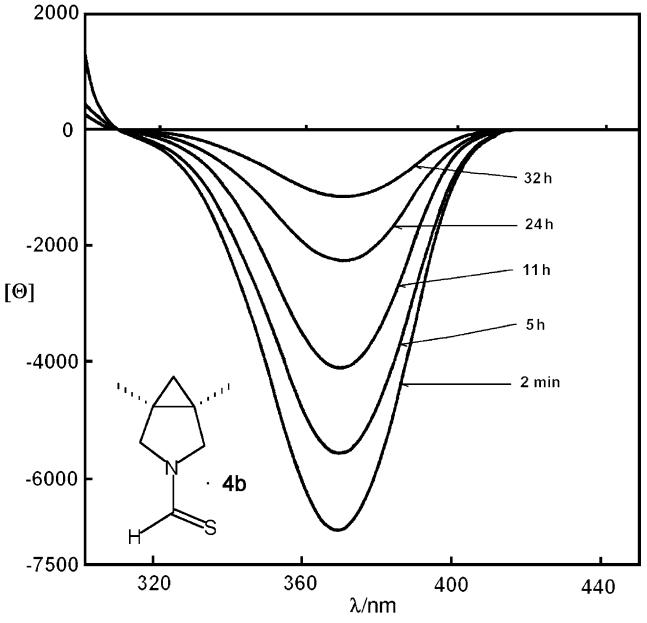


Figure 4. Decay of the CD signal of **2b**·**4b** in toluene solution at 22 °C.

selenoamides is accompanied by the decomposition of these compounds in solution as shown by unusually low CD value for **2c** (Table 1), meaning that their racemization rates obtained from CD measurements are less reliable.

3. Conclusion

In summary, host–guest inclusion complexation using optically active hosts was found to be a reliable and effective method of optical resolution of configurationally labile compounds. Such resolutions were facilitated by the asymmetric transformation of thio- and selenoamides that lead to yields exceeding 50%. Since the configuration of the host compounds is firmly established, the absolute configuration of the guest molecules can be easily deduced from the X-ray crystal structures of the inclusion complexes.

The optical activity of the guest compounds can be detected by the CD spectra in solution, without their liberation from inclusion complexes. The clathrates are stable in the crystal form, but in solution liberated guest compounds racemize due to a slow rotation about the C–N bond as shown by the gradual decrease of the n–π* Cotton effect in the CD spectra.

4. Experimental

4.1. General

^{1}H, ^{13}C and ^{77}Se NMR spectra were obtained with a Varian Unity Plus spectrometer at 500, 125 and 95.4 MHz, respectively. The deuteriated solvents were used as an internal lock for ^{1}H and ^{13}C NMR. The ^{77}Se NMR spectra were recorded using diphenyl diselenide as the external standard. Chemical shifts are reported relative to dimethyl selenide (δ 0.0 ppm) by assuming that the signal of the standard is at δ 461.0 ppm.[15] FT-IR absorptions were taken with a Bruker IFS66 spectrometer. CD spectra were recorded on a JASCO J-715 dichrograph. The solid state CD spectrum was taken in freshly prepared KBr disk. A mixture of 3 mg of the sample and 200 mg of dried KBr was ground and formed into a disk 0.5 mm thick and with radius of 15 mm. The disk was rotated around the optical axis and the CD recordings were made for several positions in order to check the reproducibility of the spectrum.

4.2. *N*-Thioformyl-4-methylpiperidine 1b

Anhydrous chloral (13.0 g, 88 mmol) was dropped into a solution of 4-methylpiperidine (8.0 g, 81 mmol) in chloroform (30 mL) with vigorous stirring and cooling (10 °C). The reaction mixture was left standing at rt for 5 h, then refluxed for 0.5 h and after cooling washed with dilute HCl, aqueous $NaHCO_3$ and dried over $MgSO_4$. After removal of the solvent, the residue was distilled at a reduced pressure; yield 8.3 g (80%) of amide **1a**; bp 95–100 °C/12 mmHg; ^{1}H NMR ($CDCl_3$) δ 7.99 (s, 1H), 4.34 (dd, $J = 11.0$ and 2.1 Hz, 1H), 3.56 (dd, $J = 13.1$ and 2.1 Hz, 1H), 3.04 (td, $J = 12.7$ and 2.9 Hz, 1H), 2.60 (td, $J = 12.8$ and 2.9 Hz, 1H), 1.66 (m, 3H), 1.07 (m, 2H), 0.95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 160.2, 45.6, 39.8, 34.1, 32.7, 30.7, 21.2.

The above amide (4.0 g, 32 mmol) and Lawesson's reagent (6.4 g, 16 mmol) were refluxed in toluene (35 mL) for 1 h. After removal of toluene the residue was chromatographed on silica gel (elution with benzene) obtaining 3.8 g (84%) of the product as an orange oil; IR (film) 1507, 1455, 1228, 1142 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.21 (s, 1H), 5.16 (dt, $J = 13.2$ and 1.9 Hz, 1H), 3.78 (dt, $J = 12.7$ and 2.0 Hz, 1H), 3.42 (dt,

$J = 13.2$ and 2.4 Hz, 1H), 2.86 (dt, $J = 12.7$ and 2.4 Hz, 1H), 1.74 (m, 3H), 1.20 (m, 2H), 0.95 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 184.8, 54.9, 44.2, 33.9, 32.1, 29.9, 20.6. Complex with **4b**: mp 111–112 °C. Anal. Calcd for $C_{33}H_{32}O_4{\cdot}C_7H_{13}NS$ (634): C, 75.80; H, 6.84; N, 2.21; S, 5.06. Found: C, 75.50; H, 7.12; N, 2.17; S, 4.90.

4.3. *N*-Selenoformyl-4-methylpiperidine 1c

Amide **1a** (1.0 g, 7.9 mmol), powdered selenium (0.6 g, 19 mmol), red phosphorus (0.6 g, 19 mmol) and $BaCO_3$ (1.0 g, 5.1 mmol) were refluxed in xylene (30 mL) for 24 h. After cooling, the reaction mixture was filtered and the precipitate washed with benzene. Evaporation of the solvents at a reduced pressure afforded 1.1 g (74%) of the product as a yellow oil, solidifying upon refrigeration; IR (film) 1516, 1454, 1228 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.59 (s, 1H), 5.29 (dt, $J = 13.1$ and 2.0 Hz, 1H), 3.81 (dt, $J = 12.9$ and 2.0 Hz, 1H), 3.38 (td, $J = 12.8$ and 2.6 Hz, 1H), 2.89 (td, $J = 12.8$ and 2.8 Hz, 1H), 1.79 (m, 3H), 1.29 (m, 2H), 0.99 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 186.9, 57.8, 47.9, 33.8, 32.1, 29.8, 20.5; ^{77}Se NMR ($CDCl_3$) δ 498.0.

Complex with **4b**: mp 110–112 °C. Anal. Calcd for $C_{33}H_{32}O_4{\cdot}C_7H_{13}NSe$ (681): C, 70.58; H, 6.37; N, 2.06. Found: C, 70.30; H, 6.31; N, 2.01.

4.4. *N*-Thioformyl-1,5-dimethyl-3-azabicyclo[3.1.0]hexane 2b

Formamide **2a** was obtained by formylation of 1,5-dimethyl-3-azabicyclo[3.1.0]hexane[16] in a similar manner to that of compound **1a**; bp 100–106 °C/12 mmHg; ^{1}H NMR ($CDCl_3$) δ 8.03 (s, 1H), 3.82 (d, $J = 11.5$ Hz, 1H), 3.52 (d, $J = 10.1$ Hz, 1H), 3.30 (d, $J = 10.1$ Hz, 1H), 2.94 (d, $J = 11.5$ Hz, 1H), 1.11 (s, 3H), 1.10 (s, 3H), 0.36 (d, $J = 5.1$ Hz, 1H), 0.23 (d, $J = 4.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 160.8, 53.8, 50.4, 24.1, 19.4, 14.3.

Thioamide **2b** was obtained from formamide **2a** in a similar manner to that of compound **1b**; mp 49–50 °C; IR (KBr) 1503, 1218, 971 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 4.30 (d, $J = 13.3$ Hz, 1H), 3.80 (d, $J = 11.3$ Hz, 1H), 3.66 (d, $J = 11.3$ Hz, 1H), 3.27 (d, $J = 13.3$ Hz, 1H), 1.22 (s, 3H), 1.19 (s, 3H), 0.47 (d, $J = 5.3$ Hz, 1H), 0.40 (d, $J = 5.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 184.6, 60.8, 55.7, 24.4, 20.5, 13.9. Anal. Calcd for $C_8H_{13}NS$ (155): C, 61.89; H, 8.44; N, 9.02; S, 20.65. Found: C, 61.93; H, 8.50; N, 8.93; S, 20.37.

4.5. *N*-Selenoformyl-1,5-dimethyl-3-azabicyclo[3.1.0]-hexane 2c

Compound **2c** was obtained from formamide **2a** in a similar manner to that of compound **1c** as an orange oil; IR (film) 1503 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.58 (s, 1H), 4.30 (d, $J = 13.6$ Hz, 1H), 3.68 (d, $J = 11.7$ Hz, 1H), 3.48 (d, $J = 11.7$ Hz, 1H), 3.21 (d, $J = 13.6$ Hz, 1H), 1.22 (s, 3H), 1.17 (s, 3H), 0.47 (d, $J = 5.4$ Hz, 1H), 0.40 (d, $J = 5.3$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 186.3, 62.9, 58.7, 24.6, 20.5, 13.9; ^{77}Se NMR ($CDCl_3$) δ 592.6.

4.6. *N*-Thioformyl-3-azabicyclo[3.3.1]nonane 3b

Formamide **3a** was obtained by formylation 3-azabicyclo[3.3.1]nonane[17] in a similar manner to that of compound **1a** as a colourless oil; ^{1}H NMR ($CDCl_3$) δ 7.97 (s, 1H), 4.33 (d, $J = 13.2$ Hz, 1H), 3.57 (d, $J = 12.7$ Hz, 1H), 3.37 (d, $J = 12.7$ Hz, 1H), 2.86 (d, $J = 13.2$ Hz, 1H), 1.90 (bs, 2H), 1.80–1.58 (m, 7H), 1.43 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 162.3, 52.1, 46.0, 33.8, 31.1, 30.6, 28.1, 27.4, 20.2.

Thioamide **3b** was obtained from formamide **3a** in a similar manner to that of compound **1b**; mp 129–131 °C; IR (KBr) 1510, 1241, 1104 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.19 (s, 1H), 5.18 (d, $J = 14.2$ Hz, 1H), 3.81 (d, $J = 12.7$ Hz, 1H), 3.73 (d, $J = 13.2$ Hz, 1H), 3.01 (dd, $J = 13.7$ and 2.9 Hz, 1H), 2.10 (s, 1H), 2.01 (s, 1H), 1.90–1.60 (m, 7H), 1.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 187.5, 61.8, 51.2, 33.5, 31.4, 30.7, 29.2, 28.6, 20.0. Anal. Calcd for $C_9H_{15}NS$ (169): C, 63.90; H, 8.86; N, 8.28; S, 18.93. Found: C, 63.86; H, 8.99; N, 8.22; S, 18.84.

4.7. *N*-Selenoformyl-3-azabicyclo[3.3.1]nonane 3c

Compound **3c** was obtained from formamide **3a** in a similar manner to that of compound **1c**; mp 143–144 °C; IR (KBr) 1507, 1436, 1235 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 10.59 (s, 1H), 5.30 (d, $J = 14.2$ Hz, 1H), 3.83 (d, $J = 13.2$ Hz, 1H), 3.61 (d, $J = 12.7$ Hz, 1H), 3.00 (d, $J = 14.2$ Hz, 1H), 2.15 (s, 1H), 2.02 (s, 1H), 1.90–1.60 (m, 7H), 1.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 189.9, 64.4, 54.6, 33.2, 31.3, 30.6, 29.3, 28.8, 19.9; ^{77}Se NMR ($CDCl_3$) δ 535.1. Anal. Calcd for $C_9H_{15}NSe$ (216): C, 50.00; H, 6.94; N, 6.48. Found: C, 50.42; H, 7.10; N, 6.43.

4.8. Preparation of the crystalline inclusion compounds

A solution of the suitable host compounds **4a** and **b** with the respective racemic thioamides **1b**–**3b** or selenoamides **1c**–**3c** in a small amount of toluene–hexane (1:2) was kept at room temperature for 4 h. The crystals, which formed, were collected by suction, washed with hexane and dried. Host–guest stoichiometry was determined by ^{1}H NMR integration.

4.9. X-ray structure analysis

Diffraction data were collected using a Kuma CCD diffractometer with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods with the program SHELXS-97.[18] Full matrix least-squares refinement was carried out with SHELXL-97.[19]

Crystal data for $C_{33}H_{32}O_4{\cdot}C_7H_{13}NS$ (**1b**·**4b**): triclinic, $P1$, $a = 9.4983(6)$, $b = 9.7270(7)$, $c = 18.8808(12)$ Å, $\alpha = 98.495(5)$, $\beta = 93.921(5)$, $\gamma = 90.892(5)°$, $V = 1720.6(2)$ Å^3, $Z = 2$, $D_{calcd} = 1.287$ g cm^{-3}, $T = 100(2)$ K, $R_1 = 0.0635$, $wR2 = 0.0806$ for 5823 reflections with $I > 2\sigma(I)$.

The guest molecules occupied two symmetry independent sites in the unit cell, and in both sites were disordered. The first site was occupied by a molecule in two orientations with the occupancy ratio 74:26. The molecule in the major orientation had an (*S*)-configuration, whereas the one in the minor orientation had the opposite configuration. The second site was occupied by the guest molecule in three orientations with occupancy factors estimated as 50:35:15. The guest molecules in the two major orientations had an (*S*)-configuration, whereas the molecule in minor orientation had an (*R*)-configuration. Thus, the guest enantiomer ratio in this inclusion compound as estimated from the X-ray analysis is ca. $R/S = 1{:}4$.

Crystal data for $C_{31}H_{30}O_4{\cdot}C_7H_{13}NSe$ (**1c·4a**): monoclinic, $P2_1$, $a = 9.6016(3)$, $b = 9.5406(4)$, $c = 36.9810(9)$ Å, $\beta = 96.546(2)°$, $V = 3365.56(19)$ Å^3, $Z = 4$, $D_{calcd} = 1.296$ g cm^{-3}, $T = 130(2)$ K, $R_1 = 0.0414$, $wR2 = 0.0547$ for 7664 reflections with $I > 2\sigma(I)$. The guest molecules occupied two symmetry independent sites in the unit cell and in one site they were disordered. The disordered site was occupied by the molecule in two orientations with the occupancy ratio 80:20. The molecule in the major orientation has the *S* configuration whereas the one in the minor orientation had the opposite configuration. The second site was occupied by the guest molecule in an (*R*)-configuration. Thus, the guest enantiomer ratio in this inclusion compound as determined from X-ray analysis is $R/S = 3{:}2$.

Crystal data for $C_{31}H_{30}O_4{\cdot}C_8H_{13}NS{\cdot}C_6H_6$ (**2b·4a·C$_6$H$_6$**): triclinic, $P1$, $a = 9.4015(19)$, $b = 9.7245(18)$, $c = 11.868(2)$ Å, $\alpha = 65.512(18)$, $\beta = 82.227(16)$, $\gamma = 78.833(16)°$, $V = 966.9(3)$ Å^3, $Z = 1$, $D_{calcd} = 1.202$ g cm^{-3}, $T = 170(2)$ K, $R_1 = 0.0464$, $wR2 = 0.0569$ for 3364 reflections with $I > 2\sigma(I)$. The thioformyl guest molecule was disordered and adopted two orientations. The major orientation (72%) was occupied by the *E* form, whereas the molecule in the minor orientation (28%) had the *Z*-configuration.

Crystal data for $C_{31}H_{30}O_4{\cdot}C_8H_{13}NSe{\cdot}C_6H_6$ (**2c·4a·C$_6$H$_6$**): triclinic, $P1$, $a = 9.4054(7)$, $b = 9.6902(8)$, $c = 11.8676(8)$ Å, $\alpha = 65.971(7)$, $\beta = 81.925(6)$, $\gamma = 78.549(6)°$, $V = 966.07(13)$ Å^3, $Z = 1$, $D_{calcd} = 1.284$ g cm^{-3}, $T = 130(2)$ K, $R_1 = 0.0478$, $wR2 = 0.0571$ for 3629 reflections with $I > 2\sigma(I)$. The selenoformyl guest molecule assuming the *E*-configuration is ordered.

Crystal data for $C_{33}H_{32}O_4{\cdot}C_8H_{13}NSe{\cdot}C_6H_6$ (**2c·4b·C$_6$H$_6$**): triclinic, $P1$, $a = 9.292(1)$, $b = 9.805(1)$, $c = 12.011(1)$ Å, $\alpha = 68.48(1)$, $\beta = 81.98(1)$, $\gamma = 79.19(1)°$, $V = 996.95(17)$ Å^3, $Z = 1$, $D_{calcd} = 1.287$ g cm^{-3}, $T = 130(2)$ K, $R_1 = 0.0333$, $wR2 = 0.0377$ for 3677 reflections with $I > 2\sigma(I)$.

The selenoformyl guest molecule in the *E* conformation is ordered.

Crystal data for $C_{31}H_{30}O_4{\cdot}C_9H_{15}NS$ (**3b·4a**): orthorhombic, $P2_12_12_1$, $a = 9.5736(4)$, $b = 10.3397(5)$, $c = 34.1111(12)$ Å, $V = 3376.6(2)$ Å^3, $Z = 4$, $D_{calcd} = 1.251$ g cm^{-3}, $T = 130(2)$ K, $R_1 = 0.0397$, $wR2 = 0.0499$ for 4788 reflections with $I > 2\sigma(I)$. The thioformyl guest molecule is disordered and adopts two orientations. The major orientation (77%) is occupied by the *E* form whereas the molecule in the minor orientation (23%) has the *Z*-configuration.

Crystal data for $C_{31}H_{30}O_4{\cdot}C_9H_{15}NSe$ (**3c·4a**): orthorhombic, $P2_12_12_1$, $a = 9.5746(3)$, $b = 10.4566(4)$, $c = 34.0863(10)$ Å, $V = 3412.6(2)$ Å^3, $Z = 4$, $D_{calcd} = 1.329$ g cm^{-3}, $T = 130(2)$ K, $R_1 = 0.0320$, $wR2 = 0.0402$ for 5032 reflections with $I > 2\sigma(I)$. The selenoformyl guest molecule was disordered and adopts two orientations. The major orientation (78%) was occupied by the *E*-form whereas the molecule in the minor orientation (22%) had the *Z*-configuration.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 279506-279511. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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