

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 $n-\pi^*$ 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.

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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 **1** are chiral and may exist in two enantiomeric forms.



Z = S, Se

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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