

Spontaneous generation of chirality and chiroptical spectra of *N*-nitroso-2,4-diaryl-3-azabicyclo[3.3.1]nonanes

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ABSTRACT

The crystal structures of several bicyclic *N*-nitrosamines indicate that they crystallize in the chiral (Sohncke) space group $P2_12_12_1$ as conglomerates. This allows the resolution of these compounds by manual picking of the enantiomorphous crystals. The optical activity of the single crystals was confirmed by their CD spectra taken in KBr disks. The absolute configurations of the title nitrosamines were assigned by crystallographic measurements and by a comparison of their CD spectra with those of a reference compound resolved by classical methods. The observed Cotton effect signs, corresponding to the $n-\pi^*$ transition, were correlated with the helicity of the inherently chiral nitrosamine chromophore.

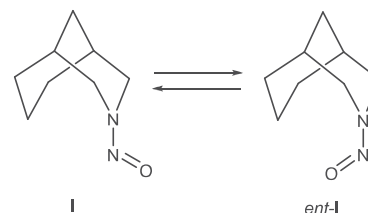
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1. Introduction

N-Nitrosamines have been extensively investigated over the last three decades because of their strong carcinogenic and mutagenic properties.¹ They have also found synthetic applications as intermediates for the preparation of various *N,N*-bonded functionalities.² The restricted rotation about the N–N bond brought about by the polar resonance structure $>N^+=N-O^-$ leads to many unusual stereochemical features in these compounds. A weak long-wavelength absorption makes the *N*-nitrosamino chromophore an attractive model for spectroscopic studies.^{2a,3} Their chiroptical properties have been the subject of many investigations in the last few years.⁴

The rigid 3-azabicyclo[3.3.1]nonane system upon *N*-substitution with a nitroso group loses its symmetry and becomes chiral. The conversion between the two enantiomers occurs by the rotation of the nitroso group (Scheme 1).

The title *N*-nitrosamines **1b–3b** owe their chirality solely to the restricted rotation about the N–N bond. In contrast, compounds **4a,b** and **6a,b** are chiral due to the desymmetrization of the bicyclic skeleton by methyl substitution at C-1. Our X-ray crystallographic studies and a literature survey revealed that the *N*-nitrosamines **1b–4b** crystallize in the chiral space group $P2_12_12_1$.^{5,6} Usually this means that the racemic mixture forms a conglomerate; that is, a mechanical mixture of homochiral crystals wherein each single crystal is comprised of only one enantiomer.⁷ Thus, the spontaneous generation of chirality occurs during the crystallization. This is a relatively rare and unpredictable



Scheme 1.

phenomenon that deserves considerable attention due to it being one of the simplest and least expensive methods for the preparation of enantiomerically pure compounds. It may also have important implications for the prebiotic origin of chirality⁸ or so-called ‘absolute’ asymmetric synthesis.⁹

Herein, we report the solid state CD spectra taken in KBr disks and correlate the observed Cotton effect signs with molecular chirality. In addition, we have resolved the chiral amine **6a** into its enantiomers and converted them into nitrosamines **6b**. This allowed us to study their solid state and solution CD spectra in relation to those of **1b–4b**. Due to the close relationship between the nitrosamine and nitramine chromophores,¹⁰ nitrosamine **6b** was oxidized into *N*-nitramine **6c** whose chiroptical spectra were examined in order to gain further insight into the nature of the optical activity of the title compounds.

2. Results and discussion

2,4-Diaryl-3-azabicyclo[3.3.1]nonan-9-ones **1a–5a** were prepared by a Mannich condensation of substituted benzaldehydes

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