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ORIGINAL RESEARCH

Synthesis and structural characterization of novel 2-benzimidazolylthioureas: adducts of natural isothiocyanates and 2-amino-1-methylbenzimidazole

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Abstract Adducts of natural allyl, phenethyl, and benzyl isothiocyanates and 2-amino-1-methylbenzimidazole were synthesized. After optimization of the reaction conditions, the target 2-benzimidazolylthioureas were obtained in reasonable yields. The detailed molecular and crystal structures of these compounds were characterized by spectroscopic and X-ray methods. Spectral analysis demonstrated that *N*-(1-methylbenzimidazolyl)-*N′*-allylthiourea, *N*-(1-methylbenzimidazolyl)-*N′*-benzylthiourea, and *N*-(1-methylbenzimidazolyl)-*N′*-phenethylthiourea exist in solution in an unprecedented three tautomeric forms, whose structures were corroborated unambiguously.

Keywords Thioureas · Isothiocyanates · 2-Aminobenzimidazole · Tautomerism

Introduction

Isothiocyanates (ITCs) are reactive electrophilic agents [1] capable of modifying proteins and other biologically important molecules. Whereas, 2-amino-1-methylbenzimidazole **1** (MABI) is an interesting compound because the structure of the benzimidazole unit is a constituent of various important molecules like vitamin B12 [2]. The reaction between heterocycles containing an exocyclic amino group and ITCs yields unsymmetrical thioureas, which are significant biologically active products [3], modern catalysts in organic synthesis, [4], selective neutral receptors for inorganic anion recognition [5–7], as well as valuable building blocks [8] for self-assembled diverse hydrogen-bonded networks in the solid state and in solution. Therefore, it is crucial to determine the exact molecular and supramolecular structure of unsymmetrical thioureas if we are to design them rationally and to understand their activity and selectivity in the reactions they catalyze.

Until now, only one report has been published of the reaction between **1** and phenylisothiocyanate (PITC). On the basis of X-ray crystallographic data and NMR spectra, Morkovnik [9] claimed that the thus obtained *N*-(1-methylbenzimidazolyl)-*N′*-phenylthiourea adopts only one 1,3-dihydrobenzimidazolinylidene tautomeric form in crystals and in solution. Quantum-chemical calculations (DFT, B3LYP/6-31G**) have confirmed that this sole tautomer has the lowest energy.

In this work, we present an optimized procedure for the conversion of natural ITC to 2-benzimidazolylthioureas **2a–c** (Scheme 1), as well as the results of a study of the structure of their isomers in solution and in crystals. DFT calculations were conducted to rationalize the unusual existence of **2** in three tautomeric forms in solution.

Experimental section

Methods

All reagents (AITC, BITC, PEITC, and **1**) and solvents were purchased from the Aldrich Chemical Company. Solvents were purified and dried using standard procedures.

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