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Lithiation of *N*,*N*,*N*′,*N*′-tetraisopropylpyridine-2,6-dicarboxamide: synthesis, characterization and single crystal X-ray studies of chalcogen (Se/Te) derivatives of *N*,*N*,*N*′,*N*′-tetraisopropylpyridine-2,6-dicarboxamide

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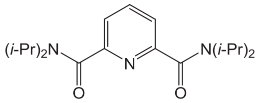
ABSTRACT

The lithiation of *N*,*N*,*N*′,*N*′-tetraisopropylpyridine-2,6-dicarboxamide (**1**) and its application in the synthesis of chalcogen (Se/Te) derivatives was investigated. It was found that the selectivity of the reaction changed with the change in the amount of *n*-BuLi used. The lithiation of **1** with 6.1 equiv of *n*-BuLi followed by subsequent reactions with selenium/tellurium and iodomethane exclusively afforded the monosubstituted chalcogen derivative (**2a**/**2b**) in excellent yield. However, the use of 2.1 or 4.2 equiv of *n*-BuLi gave two additional products along with **2a**/**2b**. One of the isolated products corresponded to the double lithiation of **1** and the other to the *ortho* lithiation followed by nucleophilic addition of *n*-BuLi to the one of the two carbonyl moieties. The prepared compounds have been characterized by single crystal X-ray crystallography, NMR (^{1}H, ^{13}C, ^{77}Se and ^{125}Te), IR, UV–Visible and Mass spectroscopy. Crystal structure of *N*,*N*,*N*′,*N*′-tetraisopropyl-3,5-bis(methyltelluryl)pyridine-2,6-dicarboxamide (**3b**) reveals a strong intramolecular C•O···Te secondary and intermolecular Te···π pyridyl interactions.

1. Introduction

Organoselenium and -tellurium compounds exhibiting Se/Te···heteroatom (N/O/halogen atoms) secondary interaction have shown immense potential as biological active agents,[1,2] chiral reagents for asymmetric synthesis[3] and precursor to semiconducting materials.[4–6] The presence of these secondary interactions often lead to the isolation of many hypervalent organochalcogen[7,8] and trichalcogen compounds.[9] Recently, we have reported the synthesis of internally chelated chalcogen derivatives of 2-pyridylcarboxamides through the lithiation of *N*,*N*-diisopropylpyridine-2-carboxamide.[10] While the lithiation of phenyl-[11,12] and pyridylcarboxamides[12–14] has been well investigated, the corresponding chemistry of dicarboxamides is unexplored. To the best of our knowledge, there is no report on the lithiation of *N*,*N*,*N*′,*N*′-tetraisopropylpyridine-2,6-dicarboxamide (**1**). The present work is an attempt to investigate the lithiation of **1** with the emphasis on the synthesis of the corresponding chalcogen derivatives. The crystal structures of some of the representative compounds have been determined by single crystal X-ray diffraction analysis in order to elucidate the Se/Te···heteroatom secondary interactions in these molecules.



(1)

2. Results and discussion

2.1. Synthesis of chalcogen derivatives of 1

The reaction of **1** with 2.1 equiv of *n*-BuLi in dry THF followed by treatment with selenium gave the corresponding selenolate anion, which on quenching with iodomethane afforded **2a** in 64% yield. Two more products, **3a** and **4a** were also obtained from the reaction in a 5% and 10% yield, respectively (Scheme 1). The use of tellurium

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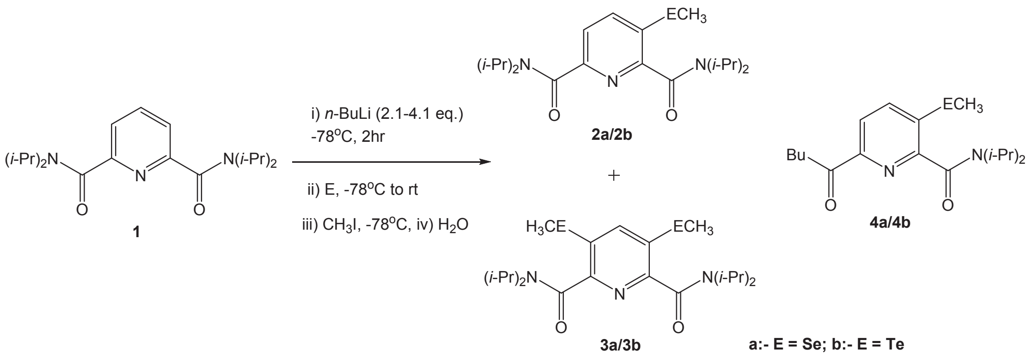


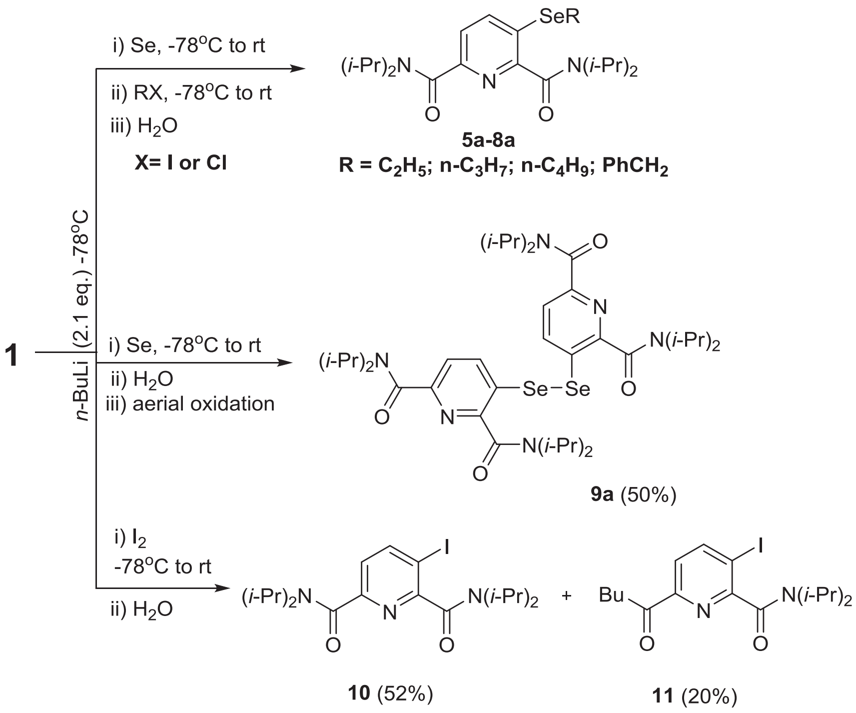
Scheme 1. Lithiation of **1** with 2.1 equiv of *n*-BuLi.

instead of selenium in the later reaction afforded **2b**, **3b**, and **4b** in 47%, 6% and 20% yield, respectively (Scheme 1). The compound **3a**/**3b** results from the double lithiation of **1** at the positions that are *ortho* to the two carboxamides moieties. The formation of **4a** and **4b** suggests *ortho* lithiation followed by nucleophilic addition of *n*-BuLi to the one of the two carbonyl moieties of **1**, which is surprising as *N*,*N*-diisopropylcarboxamides are known to resist the nucleophilic addition of *n*-BuLi.[15,16]

The reactions involving electrophiles other than iodomethane proceeded without the formation of any by-product. The treatment of the selenolate anion, with iodoethane, bromopropane, iodobutane and (chloromethyl)benzene afforded **5a**, **6a**, **7a**, and **8a**, respectively in moderate (54–58%) yields (Scheme 2, Table 1, entries 1–4). In another variation, the selenolate anion was directly hydrolyzed and subjected to aerial oxidation to afford the corresponding diselenide, **9a**, in 48% yield (Scheme 2). Since the products corresponding to **3a** and **4a** were not isolated from the later reactions, it can be inferred that the nature of the electrophile plays a detrimental role in the formation of the by-products. This was confirmed when we investigated the reaction with iodine as the electrophile. The treatment of **1** with 2.1 equiv of *n*-BuLi and subsequent trapping with iodine gave **10** and **11** in 52% and 20% yield, respectively (Scheme 2).

Next, the role of the amount of *n*-BuLi on the selectivity of the reactions depicted in Scheme 1 was examined. Our thought was that an increase in the amount of *n*-BuLi would lead to increase in the proportion of **3a**/**3b** and **4a**/**4b**. This to some extent was the case when 4.1 equiv of *n*-BuLi was used. There was 10% increase in the yield of **4a** and a corresponding decrease in the yield of **2a** (Table 1, entry 6). This suggested nucleophilic addition of *n*-BuLi on the carbonyl moiety of **2a**. However, the reaction of **1** with 6.1 equiv of *n*-BuLi gave result that was contrary to the expectation. **2a**/**2b** was the sole product obtained and there was no indication of the formation of **3a**/**3b** or **4a**/**4b** (Table 1, entries 7 and 8). Similarly, the monosubstituted product, **10**, was the only product obtained when iodine was used as the electrophile (Table 1, entry 9). In case of the reactions where no by-products were formed (Table 1, entries 3 and 5), a substantial improvement in the yield of the product was noticed (Table 1, entries 10 and 11).

In light of the above results, it appears that a pure organolithium species $(RLi)_x$ exists in equilibrium with a lithium hetero-aggregate, $[(RLi)_x\ (n\text{-BuLi})_{6-x}]$, (Scheme 3). At a lower *n*-BuLi concentration,



Scheme 2. Synthesis of selenium and iodo derivative of **1**.