

## A convenient method for the preparation of functionalized *N*-acylsulfenamides from primary amides

Mateusz Musiejuk and Dariusz Witt

Department of Organic Chemistry, Chemical Faculty, Gdansk University of Technology, Gdansk, Poland

### ABSTRACT

We have developed a convenient method for the synthesis of functionalized *N*-acylsulfenamides under mild conditions and in moderate to good yields. The designed method is based on the reaction of (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)-disulfanyl derivatives with nitrogen nucleophiles generated from primary amides or imides and sodium hydride. The developed method allows for the preparation of *N*-acylsulfenamides bearing additional hydroxyl, carboxyl, or amino functionalities.

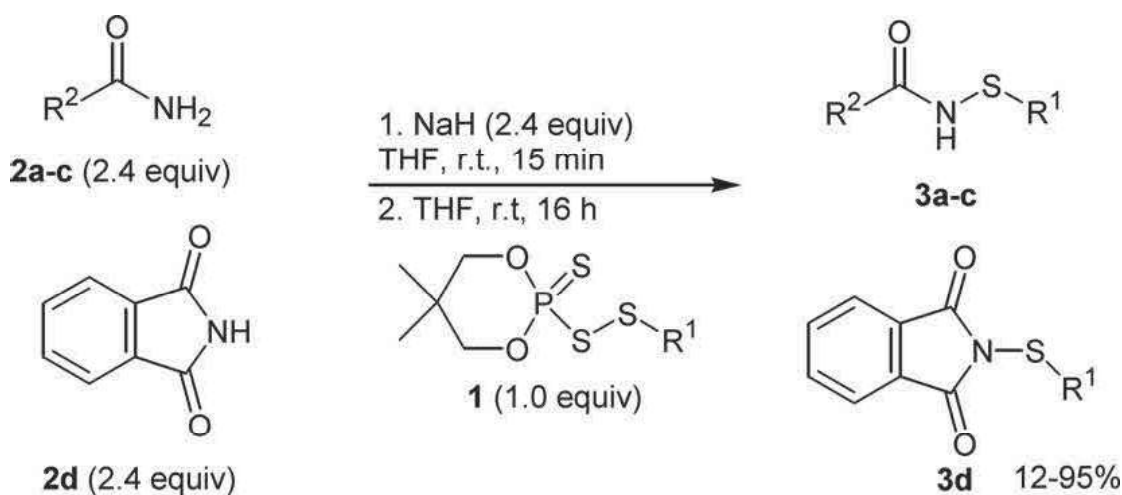
### ARTICLE HISTORY

Received 29 April 2015  
Accepted 26 May 2015

### KEYWORDS

Sulfenamide; thiols; amide; phthalimide; phosphorodithioic acid

### GRAPHICAL ABSTRACT



### Introduction

Sulfenamides are a class of compounds containing a trivalent nitrogen bonded to a divalent sulfur. A number of practical applications have been found for these stable and reactive sulfonylating reagents in industry, including their use as pesticides,<sup>1,2</sup> rubber vulcanization accelerators,<sup>1,3</sup> and prodrugs in medicinal chemistry.<sup>1,4</sup> The interesting chiroptical properties of sulfenamides, based on the S–N bond, have also been studied.<sup>5</sup> Sulfenamides are also useful as synthetic reagents. For instance, *S*-phenyl sulfenamides have been used as a source of aminyl,<sup>6</sup> amidyl,<sup>7</sup> and thioaminyll<sup>8</sup> radicals. Sulfenamides have been also involved in the insertion reactions.<sup>9</sup> Sulfenamides have been produced as intermediates in the synthesis of disulfanes,<sup>10</sup> chiral amines,<sup>11</sup> and amino acids.<sup>12</sup> *S,N*-diaryl sulfenamides have been utilized as a source of electrophilic arylthio units,<sup>13</sup> and methanesulfenamide has been used in the preparation of inversely fused bicyclic  $\beta$ -lactams.<sup>14</sup>

Although sulfenamides are quite useful functionally, their formation is generally limited to rather harsh methods that may not be compatible with other functional groups within the molecule. The synthesis of sulfenamides has been reviewed<sup>15</sup> recently. The most common methods for the synthesis of sulfenamides are based on the reaction of an amine or metal amide with sulfenic acid derivatives,  $\text{RSX}$ , where X may be a halogen, phthalimide, alkoxy group, or sulfur-bearing functionality.<sup>1</sup> Other methods involve the reaction of thiols and amines in the presence of oxidizing reagents<sup>16</sup> or the reaction of disulfides and amines in the presence of silver or mercuric salts.<sup>17</sup> Recently, sulfenamides have been obtained through the reaction of amines with glycosyl thioacetates in the presence of diethyl bromomalonate,<sup>18</sup> 3-phenylsulfenyl-2-(*N*-cyanoimino)thiazolidine,<sup>19</sup> *S*-[2-(3-oxo-1,2-benzisothiazolinyll)-2-mercaptobenzoates,<sup>20</sup> and *N*-(1-alkenylthio)phthalimides,<sup>21</sup> respectively. Sulfenamides can also be prepared by the copper-catalyzed coupling