

# SYNLETT Spotlight 91

## Phenyl Isothiocyanate: A Very Useful Reagent in Heterocyclic Synthesis

Compiled by Geoffroy Sommen



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Geoffroy Sommen was born in 1976 in Thionville, France. He studied chemistry at the University of Metz (1999-2003) where he obtained his PhD under the tutelage of Professor Gilbert Kirsch in 2003. His area of interest concerned the development of new ways to synthesize sulfur- and selenium-containing compounds by using ketene-S,S and N,S-acetals as starting materials. He is currently at the University of Florida in the Center for Heterocyclic Compounds where he works as a research assistant on benzotriazole chemistry under the direction of Professor A. R. Katritzky.

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### Introduction

Naturally occurring isothiocyanates are limited in number. There is, however, a large number of synthetic isothiocyanates which constitute an important class of compounds. Thus, it is apparent that the chemistry of and from isothiocyanates has burgeoned over the years,<sup>1</sup> and it continues to be a blossoming field. The attraction of isothiocyanates as synthons is due to their ready availability. The most important isothiocyanate which is easily synthesized from aniline and carbon disulfide is phenyl

isothiocyanate. Several heterocycles, such as thiophenes, pyrroles, pyrimidines<sup>2</sup> or imidazoles,<sup>3</sup> can be constructed from this starting material.

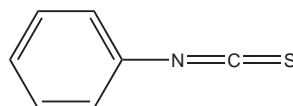
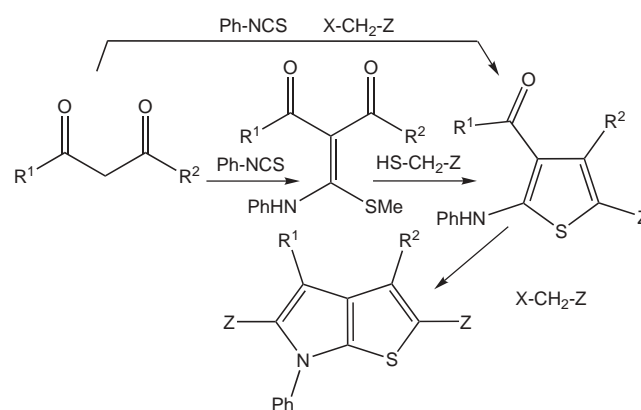


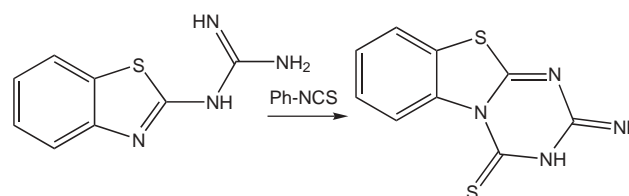
Figure 1

### Abstracts

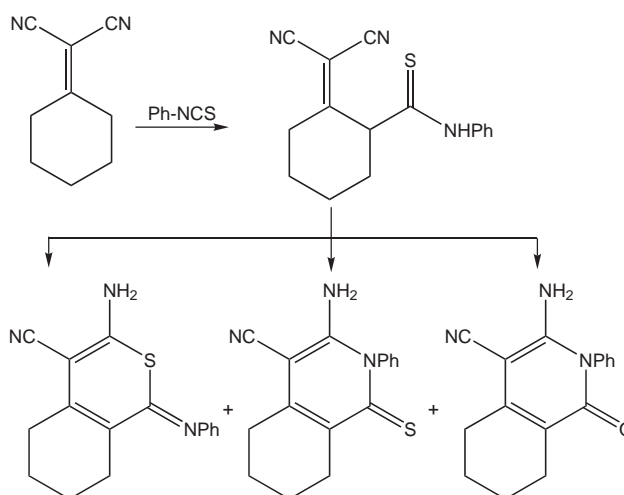
(A) Phenyl isothiocyanate can be condensed with a 1,3-dicarbonyl compound (or its equivalent) in basic media, followed by the addition of an activated methylene compound to synthesize 5-phenylamino-thiophenes.<sup>4</sup> Another equivalent of an activated methylene compound can react with the amine to build the pyrrole fused ring.<sup>5</sup>



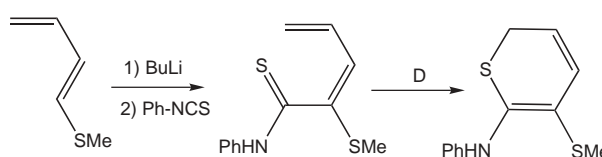
(B) When benzothiazolyl-2-guanidine reacts with phenyl isothiocyanate, instead of the expected addition products, 2-imino-3,4-dihydro-2*H*-benz[1,3]thiazolo[3,2-*a*]-1,3,5-triazin-4-ones are obtained.<sup>6</sup> The thioureas are formed as intermediates in the first step and then undergo ring closure to the triazinthiones with elimination of aniline.



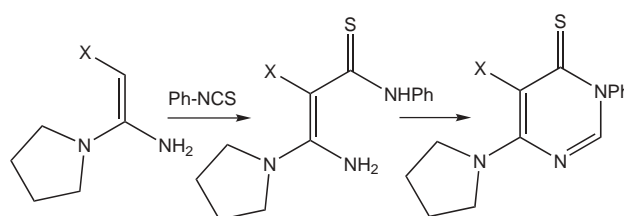
(C) Cyclohexylidenemalononitrile was allowed to react with phenyl isothiocyanate under phase-transfer catalysis to give the following bicyclic fused compounds: 3-amino-4-cyano-1-phenylimino-5,6,7,8-tetrahydroisothiachromene, 3-amino-4-cyano-2-phenyl-1-thioxo-5,6,7,8-tetrahydroisochromene and 3-amino-4-cyano-2-phenyl-5,6,7,8-tetrahydroisochromene-1-one.<sup>7</sup>



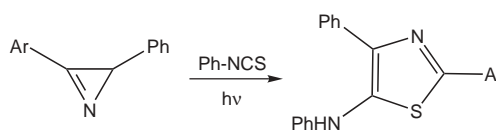
(D) 1-Methylsulfonyl-1,3-butadiene is metalated by *n*-BuLi followed by the addition of phenyl isothiocyanate to give an intermediate thioamide. The latter undergoes electrocyclic cyclization to provide imino-thiopyran.<sup>8</sup>



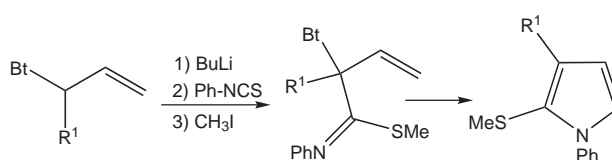
(E) The reaction of ketene-*N,N*-acetals and phenyl isothiocyanate at room temperature in acetonitrile afforded a thioamide intermediate. The propenamide was converted into 6-thioxopyrimidine upon treatment with excess DMF-DMA in toluene.<sup>9</sup>



(F) Photocondensation of the unstable azirene with phenyl isothiocyanate leads to the 2,4-diarylthiazole.<sup>10</sup>



(G) 1-Allylbenzotriazole was functionalized by the sequential addition of *n*-BuLi and quenching of the resulting anion with phenyl isothiocyanate followed by an S-methylation. Cyclization readily occurred with a Lewis acid in dry methylene chloride to give the corresponding 2-methylsulfonylpyrrole.<sup>11</sup>



## References

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