

# SYNLETT Spotlight 475

## Acid Hydrazides

Compiled by Twinkle Keshari



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

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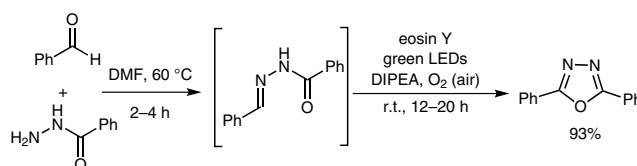
### Introduction

Acid hydrazides are organic derivatives of hydrazine. Transformations using these species to synthesize heterocycles have been research objectives for over a century.<sup>1</sup> Because of their wide utility, acid hydrazides have always been attractive precursors for the synthesis of heterocycles. They have been used for the synthesis of five- and six-membered heterocycles incorporating two or more heteroatoms in the ring, such as indoles, pyrazoles, oxadiazoles, and triazoles which display a wide spectrum of bi-

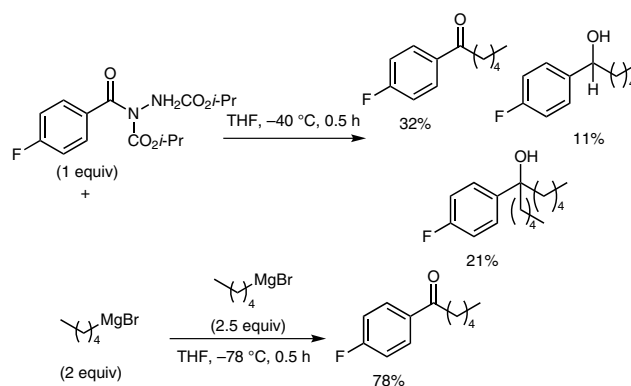
ological activities.<sup>2</sup> Hydrazone analogues<sup>3</sup> also possess useful biological activities.<sup>4</sup> Isonicotinic acid hydrazide has been used in medical practice.<sup>5</sup> In organic synthesis, acid hydrazides have similarities with Weinreb amides, as plenty of sites are available for forming a stable metal chelate. Thus, they are used as effective acyl donors for the synthesis of ketones<sup>6</sup> and amides.<sup>7</sup> Acid hydrazides can be easily prepared by the combination of hydrazine with various acyl derivatives, including esters, cyclic anhydrides, and acyl halides.

### Abstracts

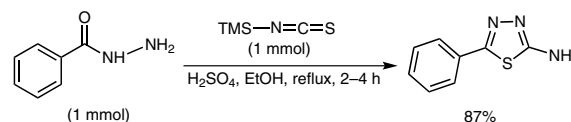
(A) Yadav and co-workers have reported a transition-metal-free, visible-light-mediated synthesis of symmetrical and unsymmetrical 2,5-disubstituted 1,3,4-oxadiazoles directly from aldehydes and acid hydrazides. The method involves oxidative cyclization of the intermediate acylhydrazones using eosin Y as an organophotoredox catalyst.<sup>8</sup>



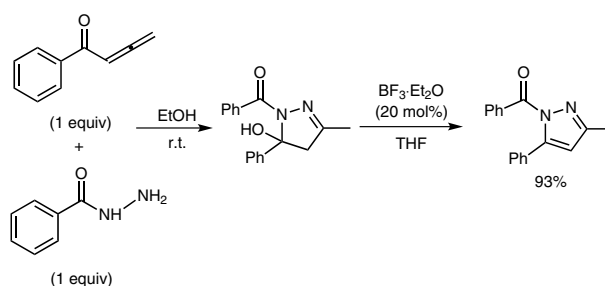
(B) Caddick and co-workers have reported the synthesis of valuable diaryl and aryl alkyl ketones using acyl hydrazides as an acyl donors. Using 2.0 equivalents of Grignard reagent at  $-40\text{ }^{\circ}\text{C}$  resulted in a mixture of products, whereas 2.5 equivalents of Grignard reagent at  $-40\text{ }^{\circ}\text{C}$  and a decreased temperature of  $-78\text{ }^{\circ}\text{C}$  gave the corresponding product in 78% yield. Thus, a mild and efficient protocol for ketone formation has been developed, which tolerates sensitive functional groups.<sup>6</sup>



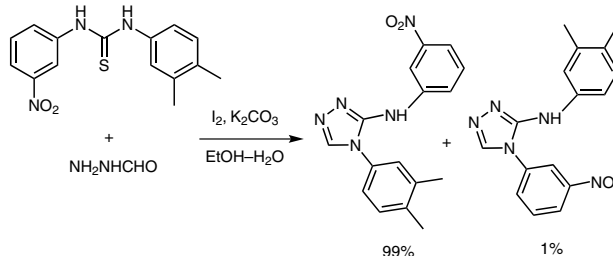
(C) 2-Amino-1,3,4-thiadiazoles have been efficiently synthesized utilizing TMSNCS and acid hydrazides as starting materials. The method involves in situ generation of thiosemicarbazides, which undergo acid-catalyzed cyclodehydration to give 2-amino-5-aryl-1,3,4-thiadiazoles.<sup>9</sup>



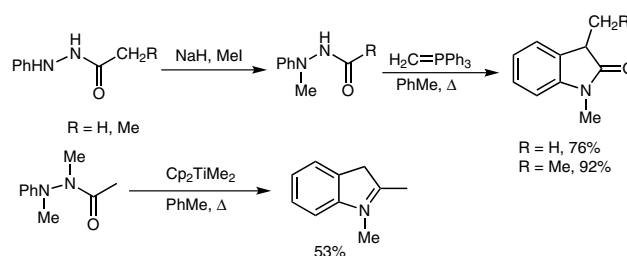
(D) Guo, Fan, and co-workers have reported a highly regioselective synthesis of 1-acyl-5-hydroxypyrazolines through the condensation of 1,2-allenic ketones. These were further transformed into 1-acyl pyrazoles.<sup>10</sup>



(E) An efficient method for the regioselective one-pot synthesis of 3-amino-1,2,4-triazoles from thioureas using molecular iodine was developed. The acyl hydrazide attacks the more basic nitrogen atom of the in situ generated unsymmetrical carbodiimide intermediate to give an acylureidrazone which then undergoes an intramolecular cyclodehydration to afford the product.<sup>11</sup>



(F) A Wittig reaction involving the alkylation of an acyl hydrazides with a phosphorane and the Petasis reagent leads to the formation of indoles. In the absence of the Petasis reagent, due to its basic character, the phosphorane deprotonates the acid hydrazide to give the enolate of the hydrazide which undergoes Brunner synthesis to form an indolin-2-one product along with the indole.<sup>12</sup>



## References

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