Tetrahedron: *Asymmetry* xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Tetrahedron: Asymmetry report number XX

The role of hydrazide compounds in asymmetric synthesis

Ghodsi Mohammadi Ziarani *, Vaezeh Fathi Vavsari

Department of Chemistry, School of Science, Alzahra University, Vanak, Tehran, Iran

ARTICLE INFO

Article history:
Received 17 September 2016
Accepted 1 December 2016
Available online xxxx

ABSTRACT

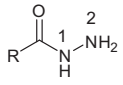
Asymmetric synthesis is one of the important topics in organic synthesis. Hydrazide compounds are valuable substrates in the fields of both chemical reactions and medicinal chemistry due to their chemical reactivity and biological activities, respectively. In this review, the role of hydrazides as substrates and/or chiral catalysts are investigated in the asymmetric organic reactions to gain chiral products.

Contents

1. Introduction

Asymmetric synthesis focuses on the use of chiral auxiliaries, chiral substrates, catalysts, and/or solvents to gain stereoselective reactions.[1] The production of enantiomerically pure organic compounds is one of the most significant topics in modern organic synthesis and pharmaceutical industry research. Consequently, asymmetric synthesis using chiral catalysts and substrates has attracted considerable attention from chemists and great efforts have been developed for the progress of new methodologies in this area.[2]

Hydrazide compounds are valuable compounds in medicinal chemistry.[3–6] For example, isoniazid, or isonicotinylhydrazide, is a famous member of the hydrazide family due to its biological activity which is used as anti-tuberculosis agent.[7] The interest in hydrazides is not only due to its derivatives with good pharmacological activities: in organic synthesis, the hydrazide moiety is used as an active functional group in various chemical reactions, such as Ugi multicomponent reactions,[8] Ugi-azide multicomponent reactions,[9] the synthesis of spiroquinazolinones,[10,11] and the preparation of tetrazoles.[12] Additionally, hydrazides can be used as organocatalysts in chemical syntheses.[13] The use of hydrazides as starting materials is however a challenging issue, due to the regioselectivity between the two competitive amines present in its structure: N^1 and N^2 (Fig. 1). Its reactivity through the N^1 has been explored in cross-coupling reactions and in Michael addition reactions, whereas its reactivity through the N^2 has been almost limited to the synthesis of hydrazones. In this review, we want to investigate the role of hydrazides as reagents and also as chiral catalysts, in the asymmetric synthesis of organic compounds.



Hydrazide

Figure 1. The structure of hydrazide.

2. The role of hydrazides in asymmetric organic syntheses

2.1. Hydrazides as reagents

Alcaine et al. used thiourea organocatalyst **3** in aza-Michael addition reactions of hydrazide **1** to different nitroalkenes **2**

* Corresponding author. Tel./fax: +98 21 88041344.
E-mail addresses: gmziarani@hotmail.com, gmohammadi@alzahra.ac.ir (G. Mohammadi Ziarani).

http://dx.doi.org/10.1016/j.tetasy.2016.12.001
0957-4166/

providing final chiral products **4a–l** with good yields and good enantiomeric ratios (Scheme 1). This developed methodology is an example of catalytic reactivity using hydrazide where the reaction proceeds through the N^2 group.[14] Notably, using a heteroaromatic nitroalkene afforded the highest enantiomeric ratio. In contrast, poorer results were furnished with aliphatic nitroolefins, even with lower temperatures and prolonged reaction times.

Tetrahydro-β-carboline is an important framework in a variety of natural products.[15] Pictet-Spengler cyclization is one of the most significant methods for the synthesis of tetrahydro-β-carboline compounds. A diastereomeric mixture of tetrahydro-β-carboline hydrazides **9a–e** was prepared via the reaction of tryptophan hydrazide **6** with various carbonyl compounds **7–8** via the procedure of Pictet-Spengler in the presence of trifluoroacetic acid. Hydrazide **6** was separately synthesized from tryptophan **5**. The tetrahydro-β-carboline hydrazides **9a–e** were found as mixtures of *cis*- and *trans*-diastereomers in a ratio of 2:1 (Scheme 2).[16]

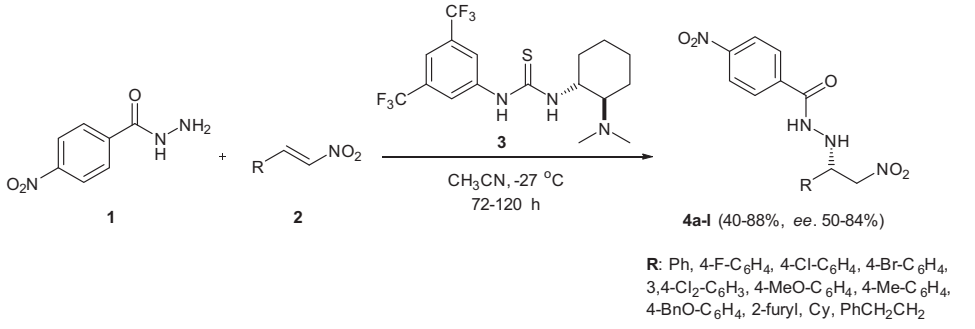
The asymmetric α-amination of α-aroyloxyaldehyde derivatives **10** was performed through an *N*-heterocyclic carbene (NHC)-catalyzed redox reaction with *N*-aryl-*N*-aroyldiazenes **11** to form a wide range of α-hydrazino esters **13a–o** with high enantioselectivity (up to 99% ee). These synthetically useful hydrazide products **13a–o** can readily be converted into chiral *N*-aryl amino esters **14a–j** through an N—N bond cleavage in the presence of samarium(II) iodide without any observed erosion in enantioselectivity (Scheme 3).[17] *N*-Heterocyclic carbene (NHC)-redox catalysis, promoted through addition of an NHC to an aldehyde bearing an R-reducible functional group, allows access to a range of catalytic intermediates including acyl azoliums, azoliumenolates, and homoenolates. However, there are only limited reports of its use in amination processes. This methodology allows simple aldehydes to be functionalized in two steps via the R-aroyloxyaldehyde into synthetically useful enantioenriched R-hydrazino esters.

The conversion of *Z*-phenylalanine hydrazide **15** to the corresponding 2-amino-1,3,4-oxadiazole **16** was accomplished using cyanogen bromide which followed by spontaneous cyclization of the cyanohydrazide intermediate (Scheme 4).[18]

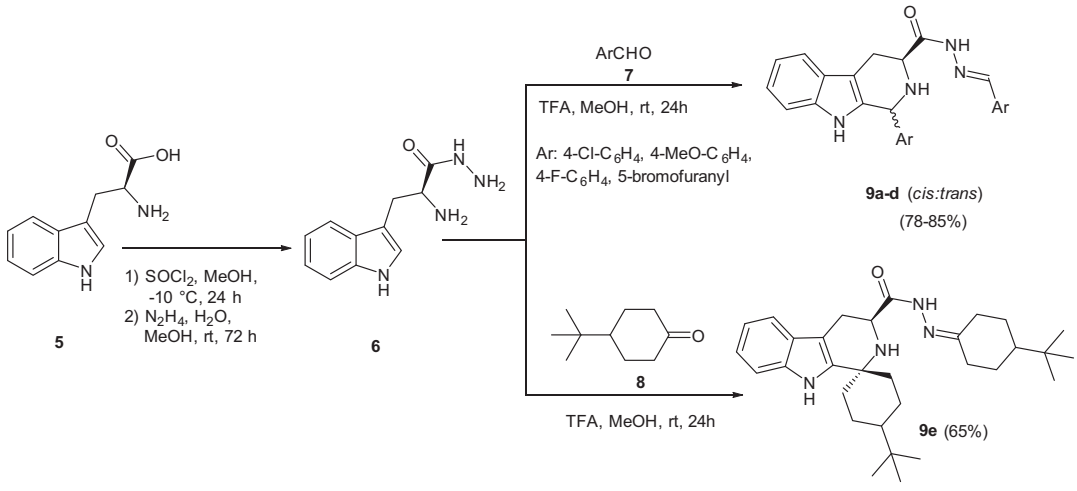
Hydrazide **18** was prepared from the reaction of phenylalanine (*Z*-Phe-OH) **17** with methylhydrazine, which was then reacted with different aldehydes to obtain hydrazones **19** in good yields. To reduce the C—N double bond of these hydrazones, a quantitative and smooth reduction was achieved. Finally, the desired azadipeptide nitriles **21** were prepared through treatment of N^1-methyl-N^2-alkylhydrazides **20a–c** with cyanogen bromide (Scheme 5).[19]

Lebrun et al. applied an efficient procedure for the enantioselective production of 5-arylmethylpyrrolidin-2-ones **28a–e** and 2-arylmethylpyrrolidines **29a–e**. The key step in this reaction was the stereoselective hydrogenation of the corresponding arylmethylenehydrazides **26a–e**. These highly conjugated compounds were readily prepared from the reaction of a chiral succinimide **24** with arylmethyl Grignard reagents. Removal of the chiral auxiliary from compound **27a–e** and subsequent reduction completed the synthesis of the target compounds (Scheme 6).[20]

The enantioselective total synthesis of (+)-Negamycin **33** (Scheme 7) and (−)-3-Epinegamycin **38** (Scheme 8) was achieved from isoxazolidine derivatives **30** and **34**, respectively. For the synthesis of (+)-Negamycin **33**, the related isoxazolidine derivative **30** was converted into the ethyl carbonate **31** which without isolation



Scheme 1. Synthesis of β-nitrohydrazides through aza-Michael addition.



Scheme 2. Synthesis of tetrahydro-β-carbolinehydrazides through Pictet-Spengler reaction.

Please cite this article in press as: Mohammadi Ziarani, G.; Fathi Vavsari, V. *Tetrahedron: Asymmetry* (2016), http://dx.doi.org/10.1016/j.tetasy.2016.12.001