Novel ynamide structural analogues and their synthetic transformations

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Abstract
This Highlight accounts for a recent phenomenon in which a series of novel ynamide structural analogues have emerged and caught the attention of the synthetic community. Preparations and reactions of these de novo ynamide variants are delineated here to demonstrate their accessibility as well as their reactivity. This Highlight should help reveal that these unique *N*-containing alkynes can become highly versatile building blocks in organic syntheses.

Keywords: Ynimides, yne-hydrazides, amidinyl-ynamides, yne-sulfoximines, yne-imines, diaminoacetylenes

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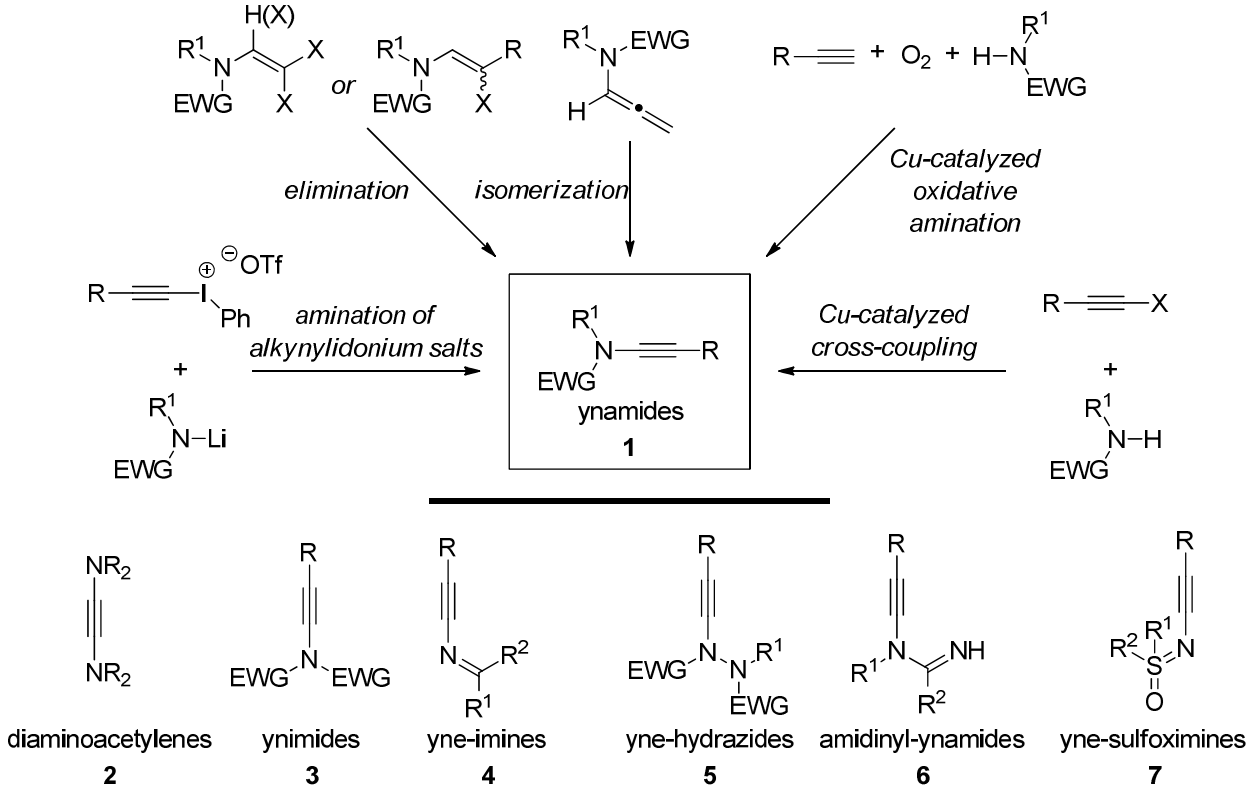
1. Introduction: Ynamide Analogues

Ynamides **1** (Scheme 1), the electron-deficient alternatives of the important but labile ynamines,[1-14] represent one of the most significant and versatile *N*-containing building blocks in organic synthesis.[15-17] Particularly, in the past 15 years, interests in this versatile building block have raised dramatically.[18-21] This boom is closely related to the fact that rapid development of efficient synthesis methods[22-26] has rendered ynamides highly accessible. Very recently, preparations of structural analogues of ynamides have emerged as novel *N*-containing alkyne building blocks.[27-36] These preparations mainly are based on modified methods for ynamide synthesis[22-26] as described in Scheme 1. With the belief that these novel analogues will also become versatile synthons that will be tremendously useful to organic synthesis, especially in the arena of *N*-heterocycle constructions, we highlight herein syntheses and reactions of *de novo* ynamide analogues: diaminoacetylenes **2**, ynimides **3**, yne-imines **4**, yne-hydrazides **5**, amidinyl-ynamides **6**, and yne-sulfoximines **7** (Scheme 1).

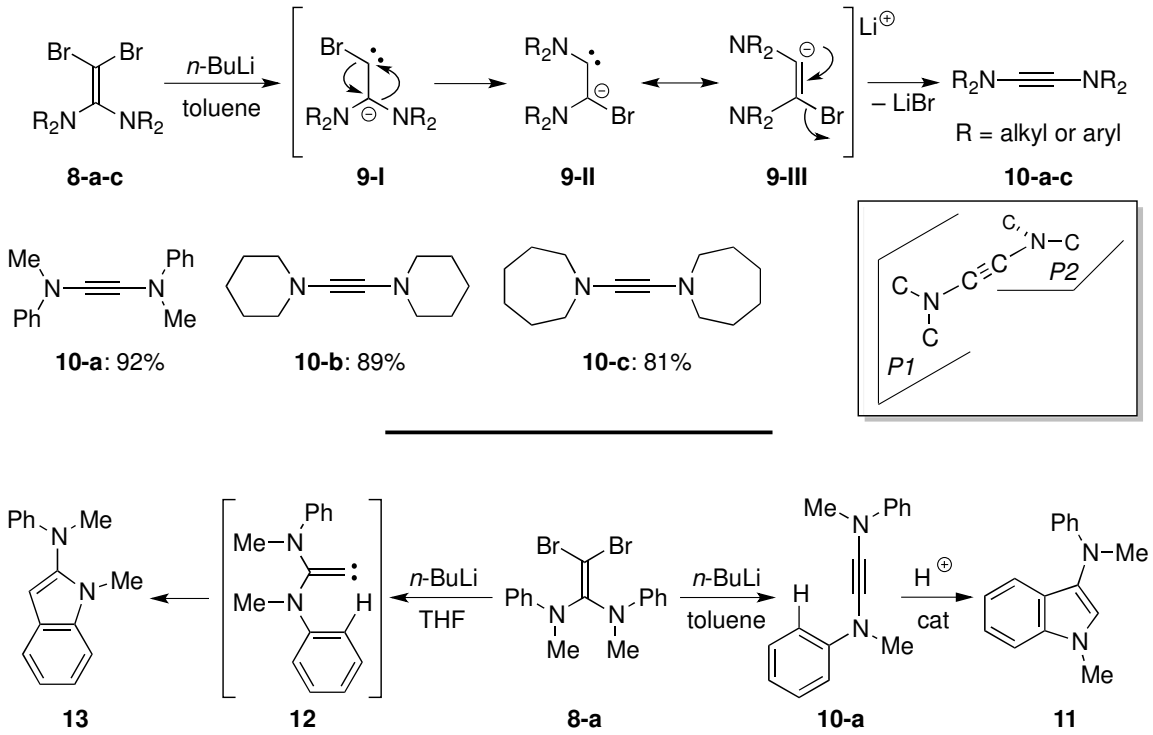


Scheme 1

2. Discussions: Syntheses and Reactions

2.1 Diaminoacetylenes

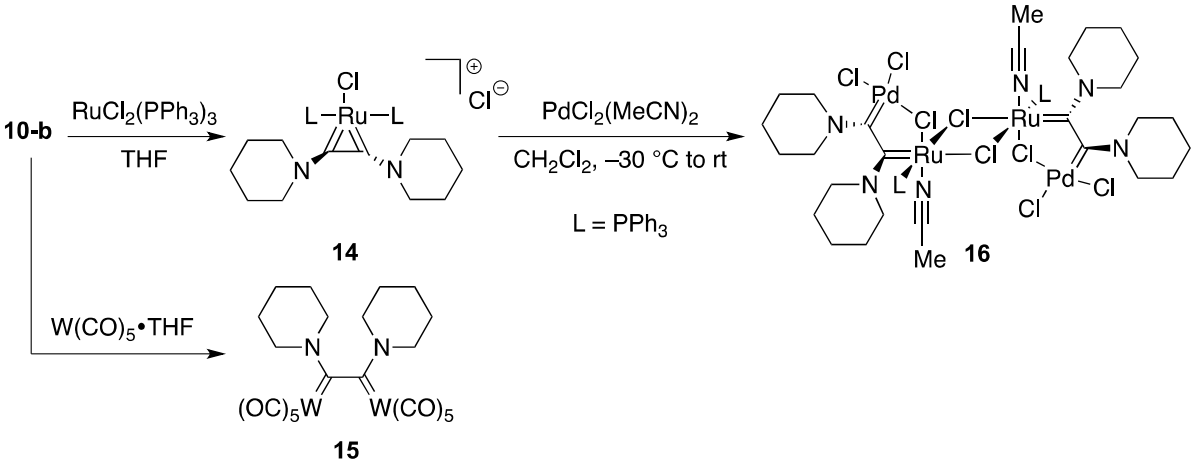
Tamm[27] described a novel approach to access diaminoacetylenes **10** by Fristch-Buttenberg-Wiechell (FBW) rearrangement[37-39] of 1,1-dihalo-2,2-ethenediamines **8** *via* the LiBr-bound carbenoids **9** (Scheme 2). This preparation of diaminoacetylenes **10** led to their X-ray structures for the first time, thereby revealing a virtually perpendicular orientations for the two NC_3 planes (See *P1* and *P2* in box at right in Scheme 2).[27]



Scheme 2

With Brønsted acid or Lewis acid serving as catalysts, diaminoacetylene **10-a** would undergo an intramolecular hydroarylation to afford indole **11**. It is noteworthy that with polar solvent such as THF, **8-a** is not subjected to FBW rearrangement. Instead, indole **13** was formed *via* an intramolecular 1,5 C-H insertion of the vinylidene intermediate **12**.[27]

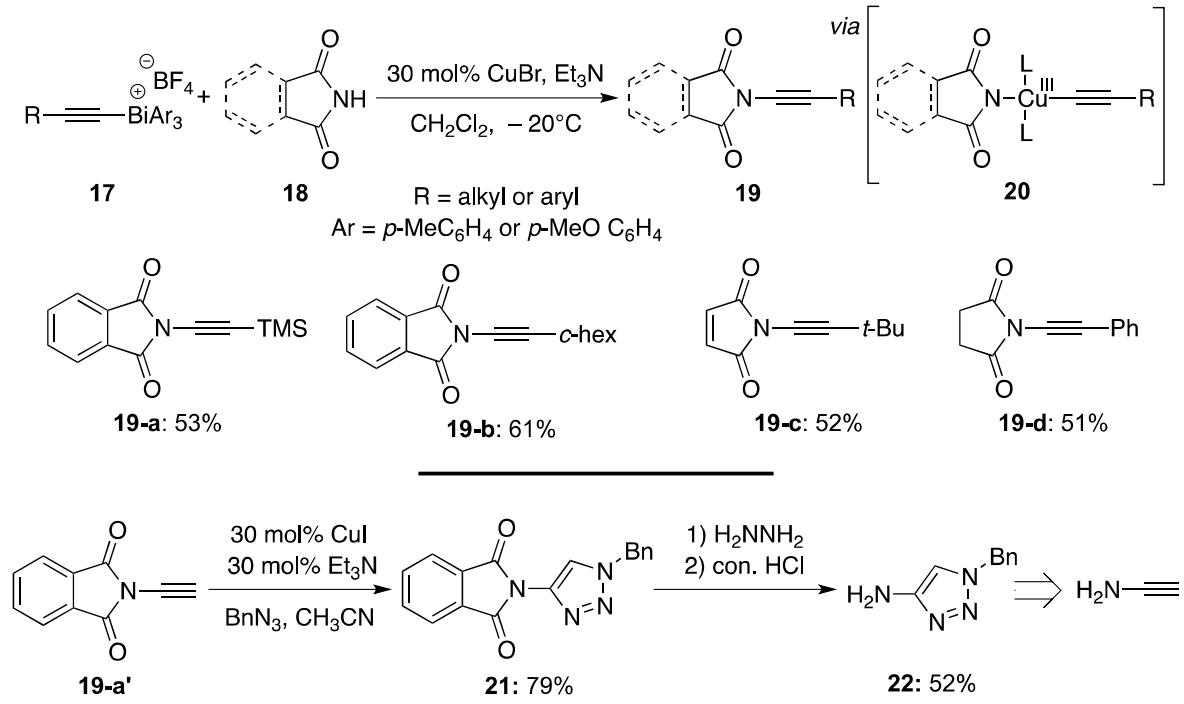
The successful synthesis of 1,2-dipiperidinoacetylene **10-b** enabled studies of coordination chemistry on diaminoacetylenes through preparations of a series of structurally interesting metal complexes such as monometallic complex **14**, homobimetallic complex **15**, and heterobimetallic complex **16** (Scheme 3). [40]



Scheme 3

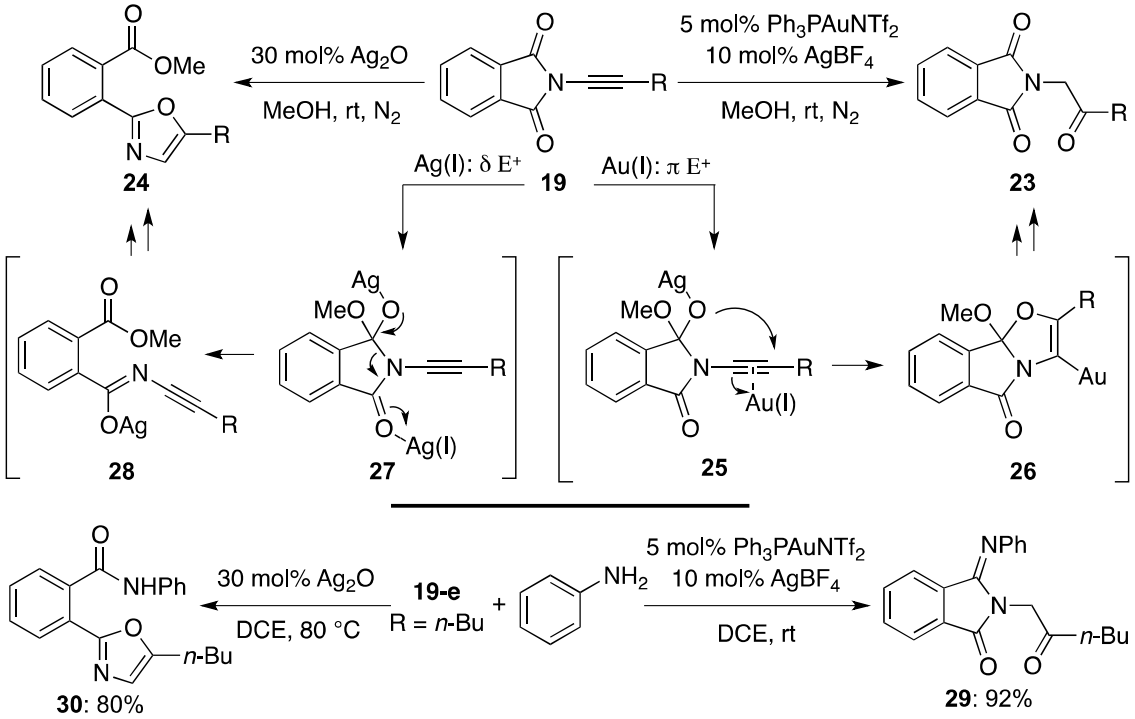
2.2 Ynimides

Sueda[28] reported an efficient synthesis of ynimides **19** *via* a copper catalyzed amidation of alkynyl(trialryl)bismuthonium salts **17**. An application of these *de novo N*-ethynyl phthanlimides was demonstrated through a copper catalyzed [3 + 2] cycloaddition followed by hydrazinolysis, leading to 4-amino-1,2,3-triazole **22**. This transformation represents as an alternative preparation of **22** to the existing [3 + 2] cycloaddition using the highly labile ethynamine.

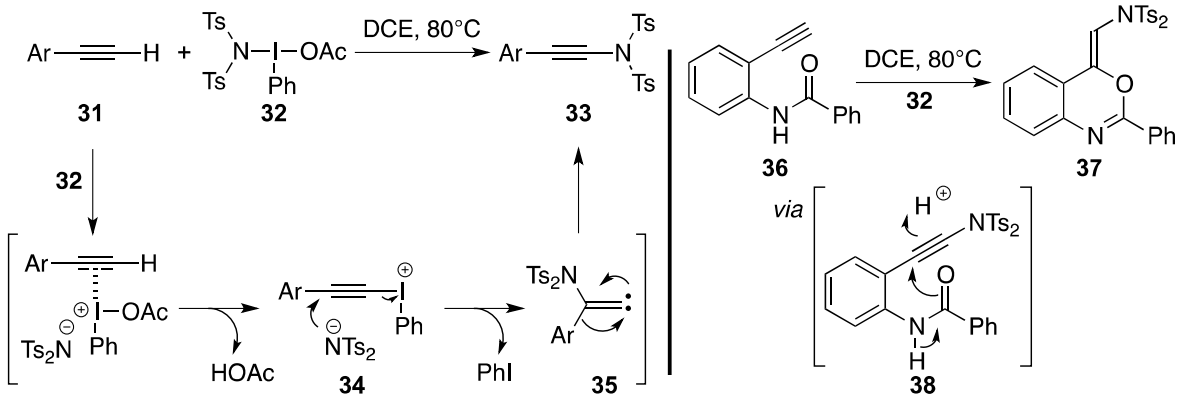


Scheme 4

In addition, with the aid of an Au(I) catalyst, which is a preferred π electrophilic Lewis acid, ynimides **19** reacted with methanol to afford β-ketoimides **23**. On the other hand, with Ag(I) catalyst, oxazoles **24** were formed through an initial coordination of Ag(I) with the carbonyl oxygen (see **27**). Similarly, **19-e** could react with aniline, under Au(I)/Ag(I) or Ag(I) only catalysis, to afford phthalimide **29** and oxazolylbenzamide **30**, respectively (Scheme 5).[29]



Scheme 5

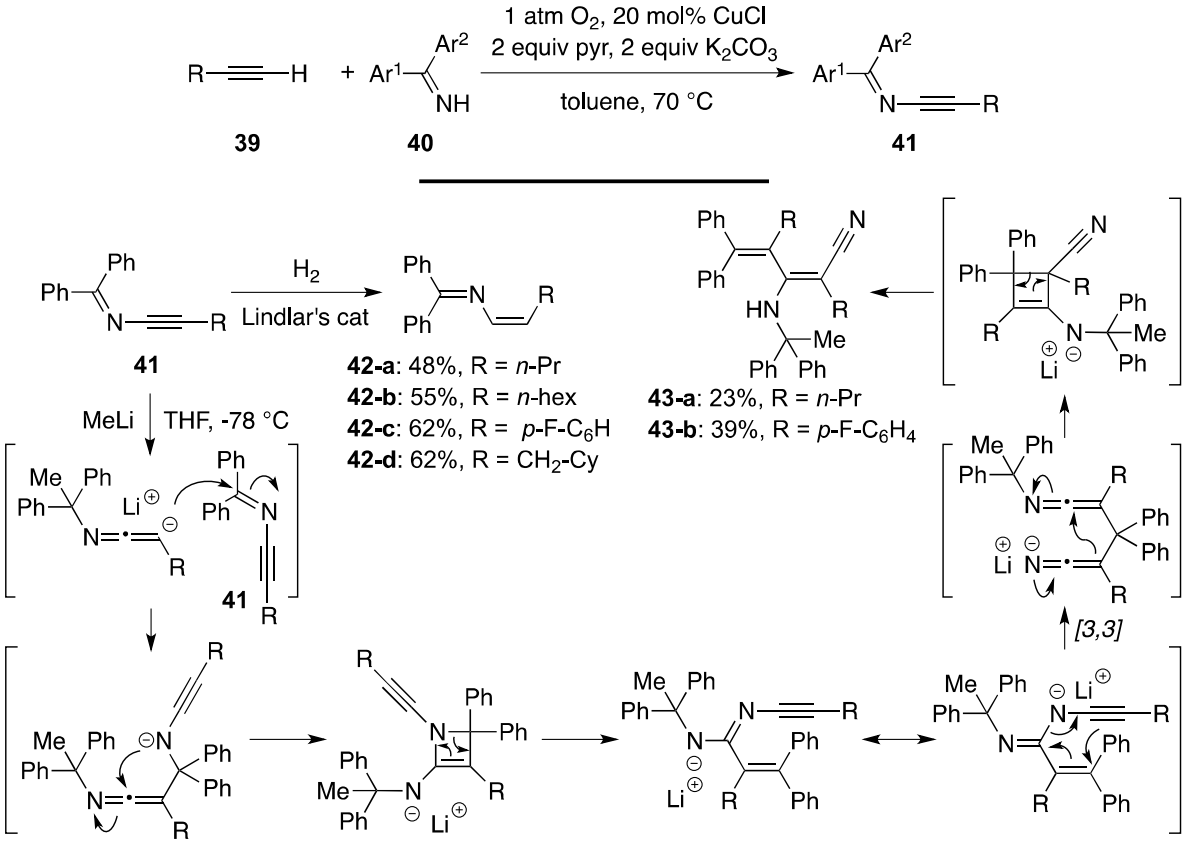


Scheme 6

Muñiz[30] later demonstrated a metal-free amination of aryl substituted terminal alkynes **31** using hypervalent iodine reagent **32** to synthesize ynimides **33**. When treating the aniline derived acetylene **36** with **32**, benzo-1,3-oxazine **37** was obtained likely through the ynimide intermediate **38** (Scheme 6).

2.3 Yne-imines

Evano[31] documented syntheses of yne-iminies **41** through copper catalyzed oxidative cross-couplings of terminal alkynes **39** with diaryl imines **40**. By using Lindlar's catalyst, these *de novo* yne-imines **41** could be reduced to afford *Z*-azadienes **42**. On the other hand, the addition of MeLi induced dimerization of **41** led to the highly substituted azines **43** (Scheme 7).

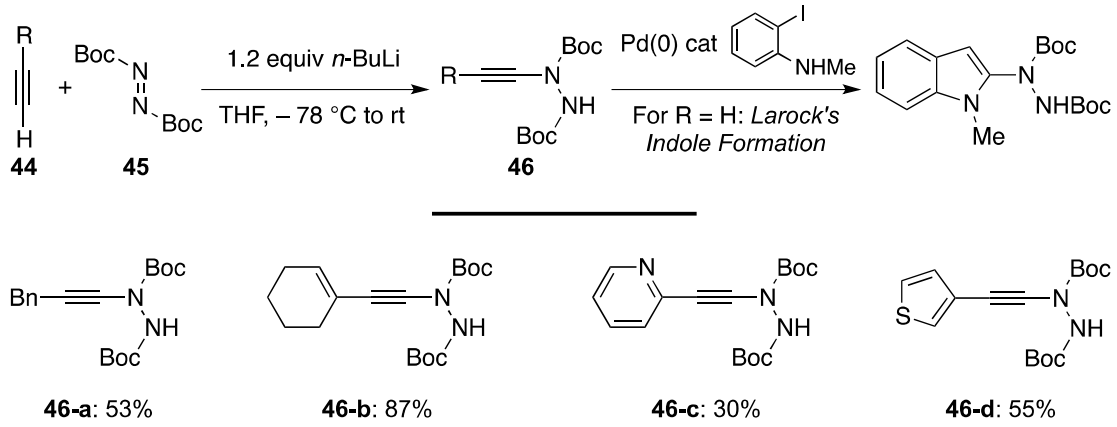


Scheme 7

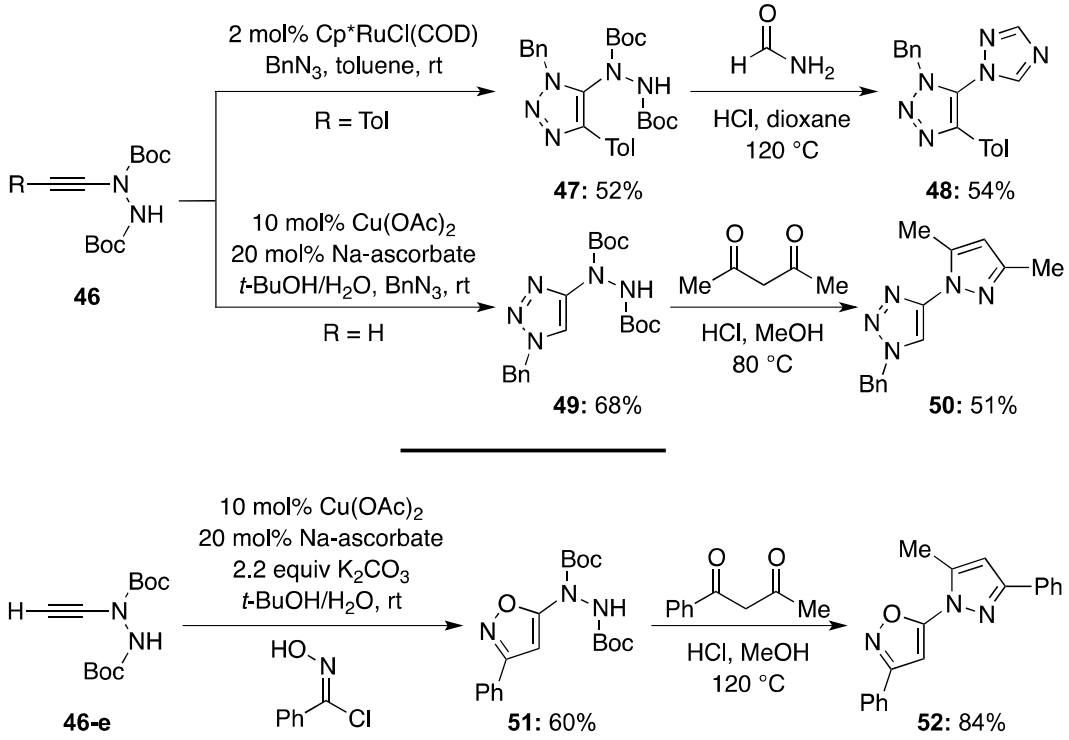
2.4 Yne-hydrazides

Batey[32] reported a concise synthesis of yne-hydrazides **46** through a straightforward addition of lithiated acetylenes **44** to diazodicarboxylates **45** (Scheme 8). These novel yne-hydrazides were shown as useful building blocks in a series of interesting transformations. In addition to a Larock-type indole formation (Scheme 8),[41] Batey showcased syntheses of structurally unique heterocycles such as **48**, **50**, and **52** through a sequence of [3 + 2] cycloaddition followed by

condensation under acidic conditions (Scheme 9). It is noteworthy of the complete regioselectivity switch in the [3 + 2] cycloaddition step between using Cp*RuCl(COD) and $Cu(OAc)_2$ (see **47** versus **49**),[42] albeit the former used an internal yne-hydrazide, while the latter employed a terminal yne-hydrazide.



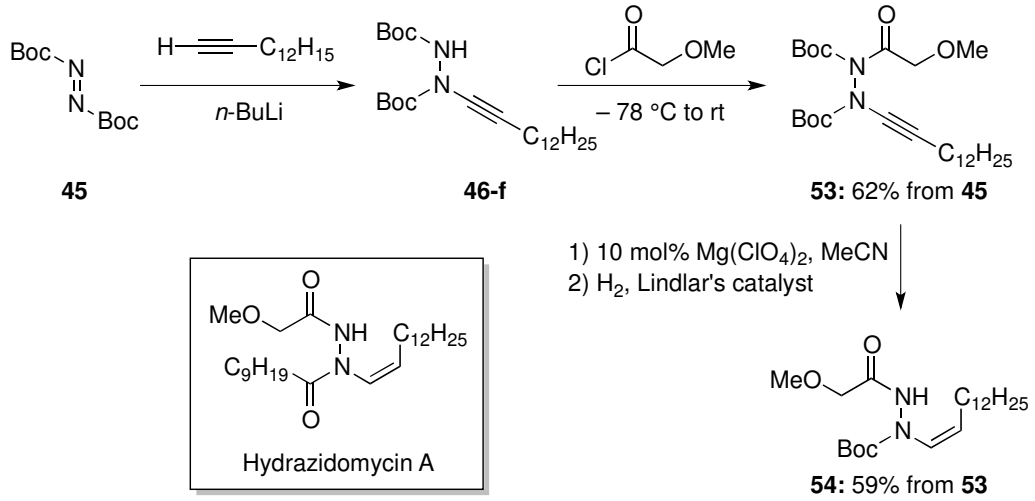
Scheme 8



Scheme 9

Recently, Batey[33] utilized yne-hydrazide **46-f** to synthesize *Z*-ene-hydrazide **54,** which

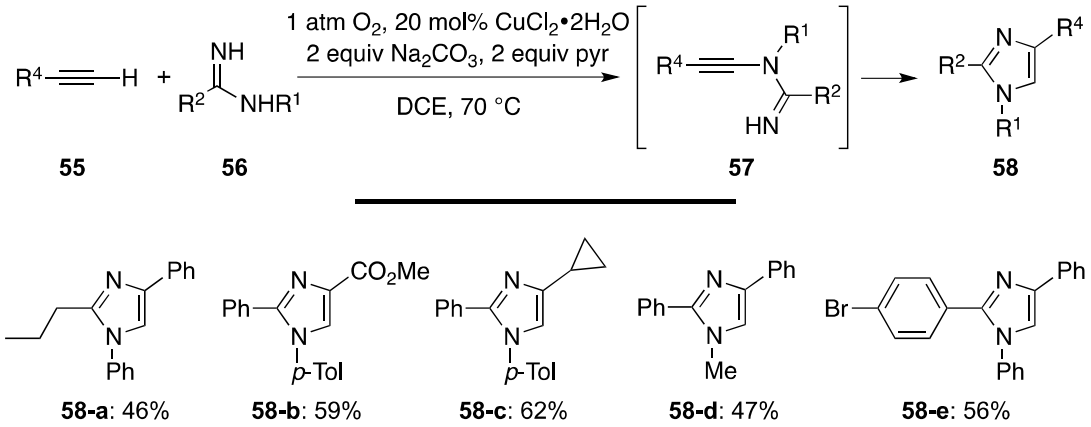
represent an analogue of biologically active natural product hydrazidomycin A[43] (Scheme 10). The key Lindlar's hydrogenation approach is similar to that of Hsung's *Z*-enamides syntheses from ynamides.[44]



Scheme 10

2.5 Amidinyl-ynamides

Neuville[34] reported syntheses of 1,2,4-trisubstituted imidazoles **58** from terminal alkynes **55** and amidines **56**. Amidinly-ynamides **57** are believed to be the intermediates resulting from a copper catalyzed oxidative amination of **55** with **56** (Scheme 11).

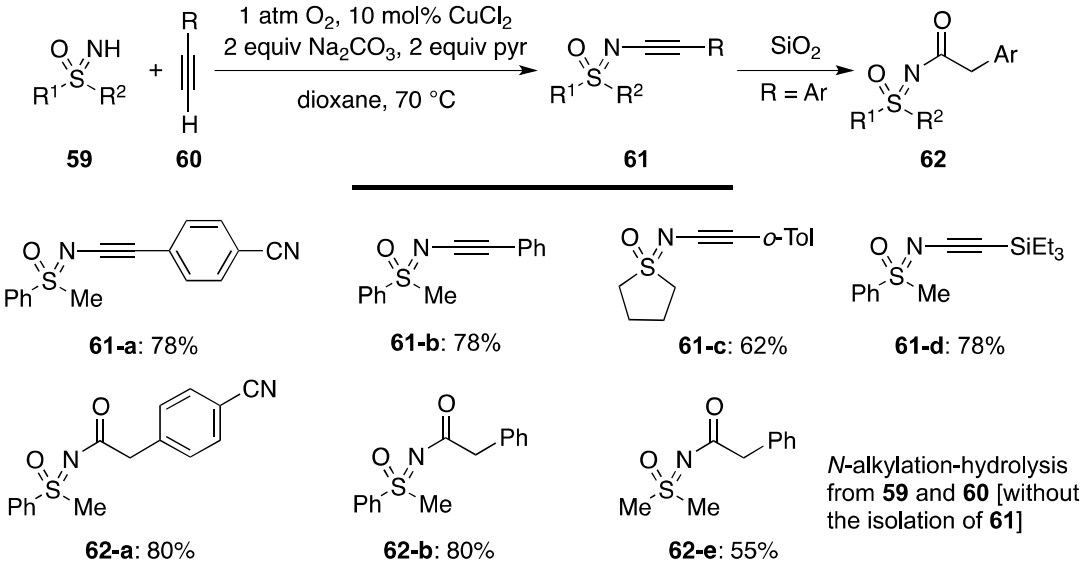


Scheme 11

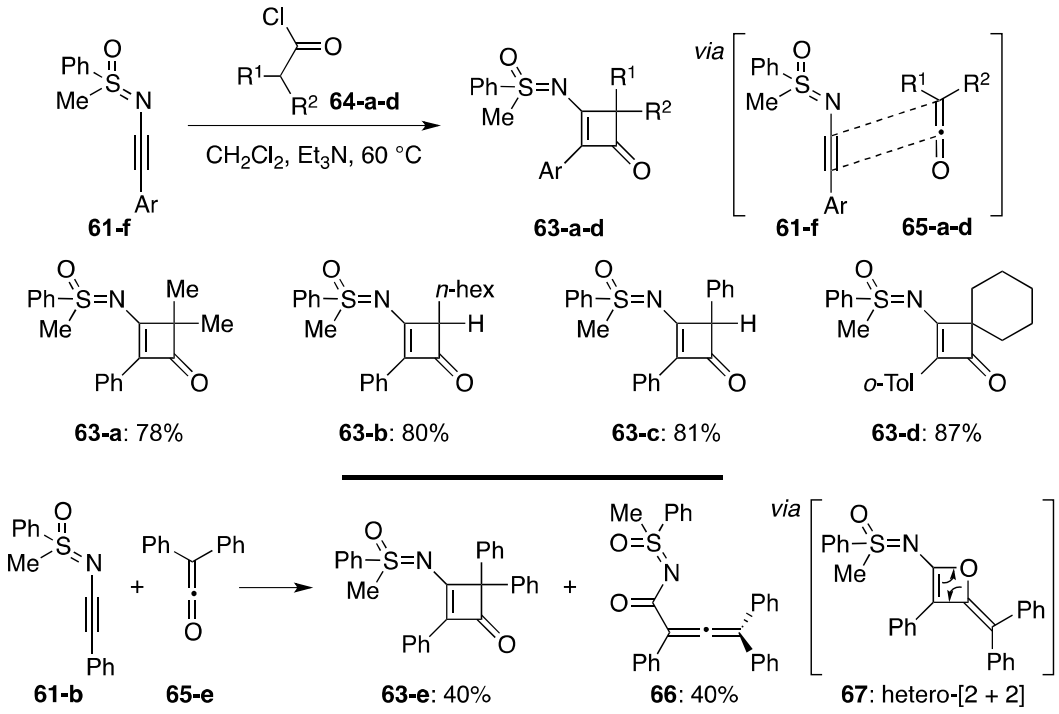
2.6 Yne-sulfoximines

Bolm[35] described the first preparations of yne-sulfoximines **61** through a copper catalyzed oxidative cross-coupling of sulfoximines **59** with terminal alkynes **60**. These yne-sulfoximines

61 could be transformed to *N*-acyl sulfoximines **62** *via* simple hydrolysis upon silica gel column chromatography (Scheme 12).



Scheme 12



Scheme 13

Recognizing the excellent potential of yne-sulfoximines **61** as new synthetic building blocks, Bolm's group also explored their usage in thermal [2 + 2] cycloaddition reactions.[36] They found that yne-sulfoximines **61** could react with ketenes **65** to form the sulfoximine derived cyclobutenones **63** *via* a [2 + 2] cycloaddition pathway. When using diphenyl ketene **65-e**, allenyl amide **66** was also isolated in addition to the expected cyclobutenone **63-e**. The formation of **66** is likely a result of pericyclic ring opening of the oxetene intermediate **67**,[45-54] which could be envisioned through a hetero-[2 + 2] pathway (Scheme 13).

3. Conclusions

This Highlight presents a recent phenomenon in developing syntheses and reactions of novel structural analogues of ynamides. While their syntheses and reactivities are similar to those of ynamides in many aspects, their unique motifs have rendered them special merits in terms of reactivities. These *N*-containing alkynes should become new versatile building blocks in organic synthesis.

Acknowledgements

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