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[A0043]

An Unexpected Result from a 1,3-Dipolar Cycloaddition: Synthesis of Pyrrolo[1,2,3-*de*]quinoxalines

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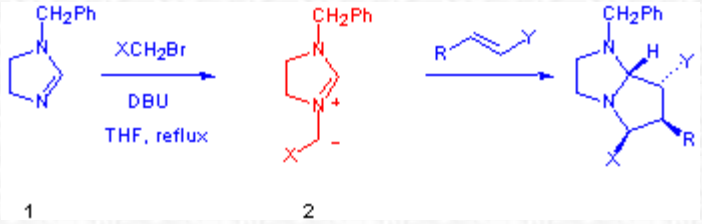
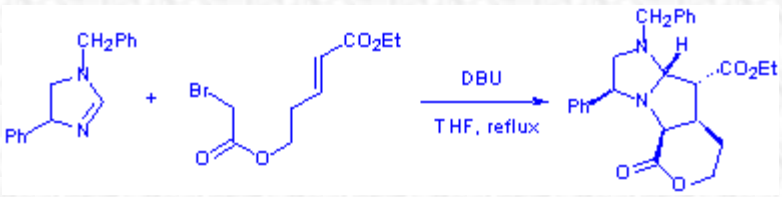
Introduction

As part of a programme to evaluate the imidazolinium ylides **2** in 1,3-dipolar cycloaddition reactions [1], we wished to explore intramolecular cycloaddition. The azomethine ylides **2** are prepared (Scheme 1) by alkylation of imidazolines **1** with an active halide such as an a-halo ester (X = CO_2R) and addition of a base (DBU); in the presence of a dipolarophile, the dipole **2** undergoes regioselective and diasteroselective cycloaddition (e.g. Scheme 1). Thus in one-pot, three of the five bonds of a new pyrrolidine ring are assembled



Scheme 1

We have utilised this protocol in asymmetric synthesis, starting with optically active 1-benzyl-4-phenyl-2-imidazolines and removing the templating atoms from the new pyrrolidine ring [2]. To render this sequence intramolecular, we determined to employ a haloalkyl reagent carrying the dipolarophile, and have succeeded in doing so with an ester tether (Scheme 2) [3].

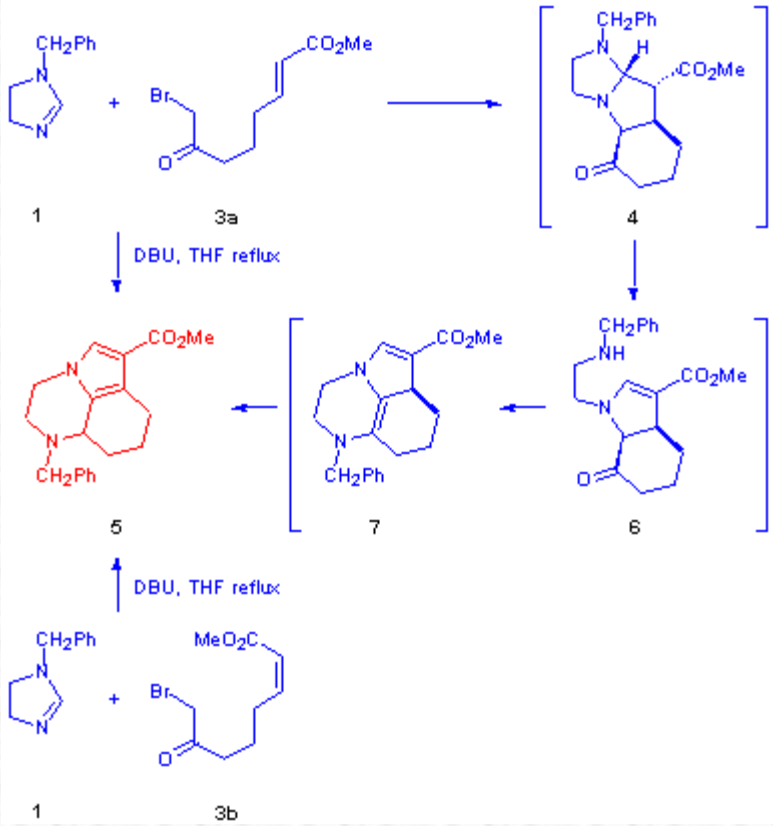


Scheme 2

We report herein that attempts to extend this to an all-carbon tether, using an a-haloketone rather than an a-haloester, lead to unexpected post-cycloaddition events, and eventually to the formation of the novel pyrrolo[1,2,3-*de*]quinoxaline ring system.

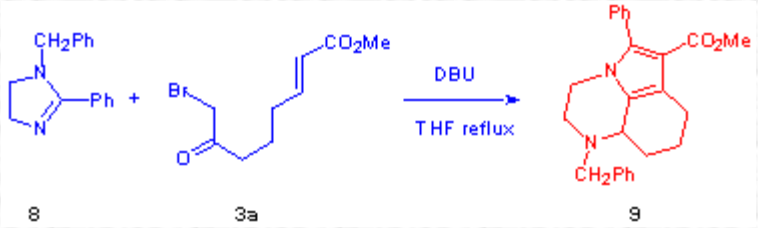
Results and Discussion

Thus, when methyl *E*-8-bromo-7-oxooct-2-enoate **3a** was heated with 1-benzyl-2-imidazoline **1** in THF at reflux, and DBU was added dropwise over 4 hours, the expected cycloadduct **4** was not isolated, but instead a product characterised as the pyrrolo[1,2,3-*de*]quinoxaline **5** was formed (30%) (Scheme 3). The formation of this unexpected novel heterotricycle can be rationalised as shown in Scheme 3, *via* initial dipolar cycloaddition and eliminative ring-opening of the primary cycloadduct **4** to give the enamino-ester **6**; the liberated secondary amine then attacks the ketone carbonyl group [4] to form in the first instance an enamine such as **7**, although we cannot be sure of the regiochemistry. In any event, tautomeric shifts of proton then result in formation of the aromatic pyrrole sub-structure and formation of **5**. Pyrroloquinoxaline **5** was also the isolated product (20%) when the diastereosomeric dienophile methyl *Z*-8-bromo-7-oxooct-2-enoate **3b** was used in the reaction.



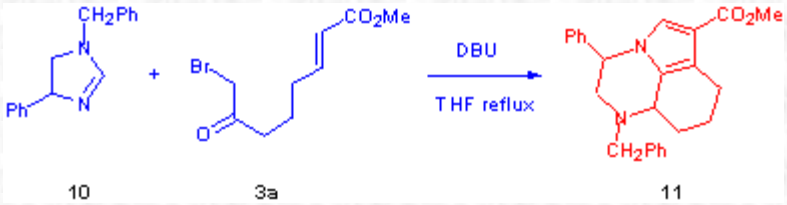
Scheme 3

Other examples of this ring-opening and recyclisation were observed: using 1-benzyl-2-phenyl-2-imidazoline **8** with bromoketone **3a** afforded tricycle **9** (32%) (Scheme 4);



Scheme 4

and using 1-benzyl-4-phenyl-2-imidazoline **10** as heterocyclic starting material also with **3a**, to give 6-benzyl-1-methoxycarbonyl-4-phenyl-4,5,6a,7-tetrahydro-6*H*-pyrrolo[1,2,3-*de*]quinoxaline **11** (30%) (Scheme 5).



Scheme 5

Tricycle **11** was isolated as a crystalline solid that was subjected to X-ray crystallographic examination [5]. This confirmed the structure of the ring system (Figure 1) with the bridgehead hydrogen atom and the 4-phenyl substituent on the same face of the molecule. We are presently exploring the scope of this cycloaddition-rearrangement.

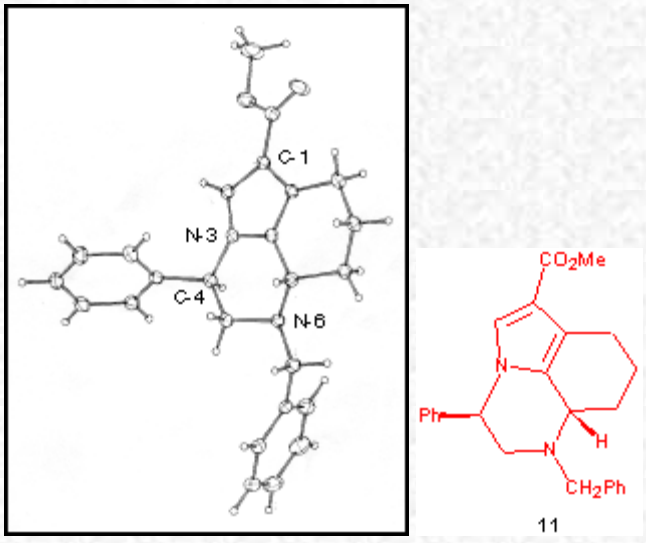


Figure 1: X-Ray crystal structure of 6-benzyl-1-methoxycarbonyl-4-phenyl-4,5,6a,7-tetrahydro-6*H*-pyrrolo[1,2,3-*de*]quinoxaline **11**

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References

[1] Jones, R. C. F.; Howard, K. J.; Nichols, J. R.; Snaith, J. S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2061-2072, and references therein.

[2] Jones, R. C. F.; Howard, K. J.; Snaith, J. S. *Tetrahedron Lett.* **1996**, *37*, 1707-1710; Jones, R. C. F.; Howard, K. J.; Snaith, J. S. *Tetrahedron Lett.* **1996**, *37*, 1711-1714.

[3] Jones, R. C. F.; Howard, K. J.; Snaith, J. S. *Tetrahedron Lett.* **1997**, *38*, 1647-1650.

[4] *Cf.* Reference 1 for a related recyclization to afford a lactam.

[5] We thank Dr Simon C Coles for this determination.
