Pergamon

Tetrahedron Letters 43 (2002) 3347–3350

TETRAHEDRON
LETTERS

Vinyl vicinal tricarbonyl esters as trielectrophiles. Reactions with diamines and related trinucleophiles

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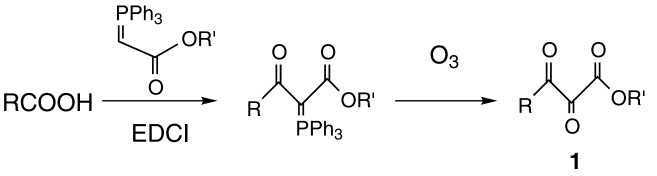
Received 4 March 2002; accepted 13 March 2002

Abstract—The scope of the reactions of vinyl vicinal tricarbonyl esters with trinucleophiles has been extended in forming dipyrroles and novel polycyclic heterocyclic systems. In particular, diamines and analogs have been studied as polynucleophiles. © 2002 Elsevier Science Ltd. All rights reserved.

In recent years we have studied the chemistry of vicinal tricarbonyl (VTC) esters of type **1** which are readily prepared from carboxylic acids by the general procedure shown below.[1]

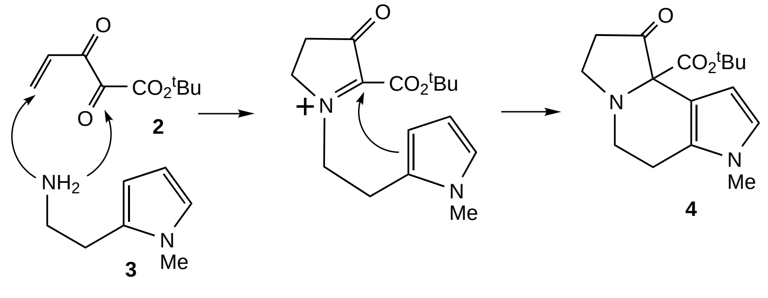
A powerful electrophile, the central carbonyl in **1** readily adds water, alcohols, thiols, amines or other nucleophiles, and this chemistry, along with rearrangement reactions, has been reported in the early literature.[2]



In previous studies on the utility of this reactive electrophilic system in synthesis we focused our attention on tricarbonyls substituted by a second electrophilic residue, such as an olefin, acetylene, or ester carbonyl.[3] Our goal was to make use of the resulting di- and trielectrophilic aggregate for reactions with polynucleophiles to generate cyclic systems, not readily accessible by conventional methods.

A reagent showing promise as a building block in this regard is the vinyl vicinal tricarbonyl **2**.[3a] We have described studies on the reactions of this vinyl VTC entity with primary amines where the amino reactant incorporates a pyrrole, an enol ether or other activated olefin, an indole or amide among other residues which provide trinucleophilic capability.[4,5] An example of this type of reaction is shown in the use of the aminoethyl pyrrole **3** to form **4**.[4]

In the present work, we focus on a group of diamines and related systems which may add to the vinyl VTC system to yield building blocks of interest in the generation of bioactive products. The vinyl VTC esters used in this study were prepared from β-halopropionic acid by methods which we have previously reported.[1]



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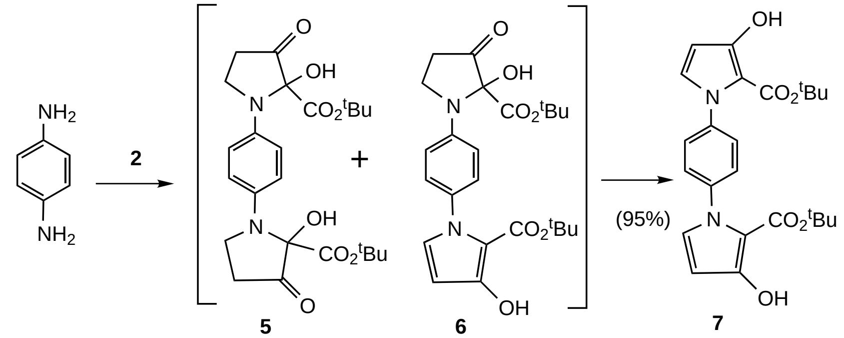
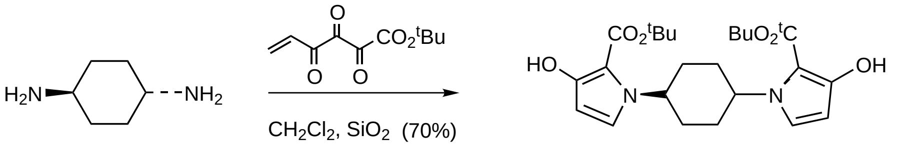
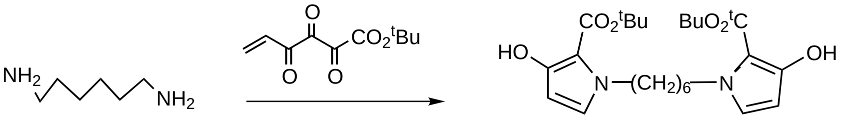


5 **6** **7**



8 **9**

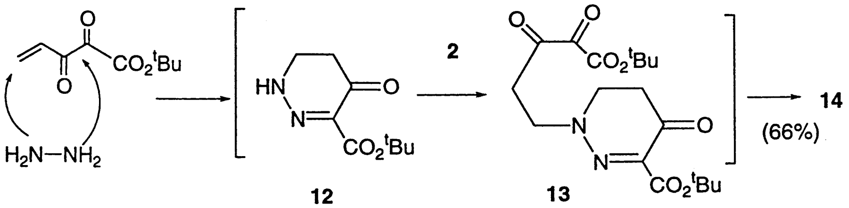


10 **11**

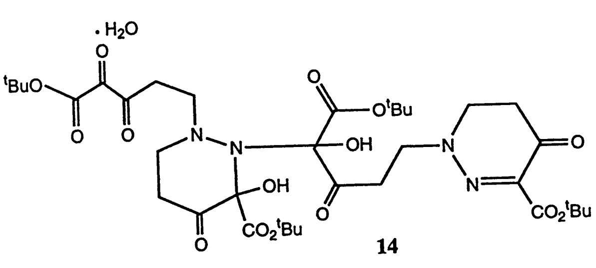
In the first phase of the current work, we examined readily available diamines such as 1,2-phenylenediamine and ethlyenediamine. Although these polynucleophiles underwent ready addition to **2**, multiple products resulted and the reactions appeared to be unsuited for use in this protocol. On the other hand, when the amino groups were separated by a suitable spacer, the additions took place with specificity. Thus, 1,4-diaminobenzene underwent bis-coupling with two equivalents of the vinyl VTC (**2**), forming the bis-pyrrolidinone **5** which could be further converted under acidic conditions to the mixed pyrrolidinone-pyrrole **6**, and ultimately, to the bipyrrole **7** (95%). The structurally related 1,4-*trans*-diaminocyclohexane **8** underwent the same type of reaction to form the bipyrrole **9**. Linear alkyl diamines such as 1,6-diaminohexane **10** behaved in the same way to yield the alkyl bipyrrole **11**.

The reaction of **2** with hydrazine led to a product incorporating the reactants in a 2:1 ratio of **2** to hydrazine. HRMS analysis showed a molecular ion peak of 801 corresponding to a dimer of **13**. Based on ^{1}H NMR and ^{13}C NMR, we have assigned the structure **14** to this dimer.

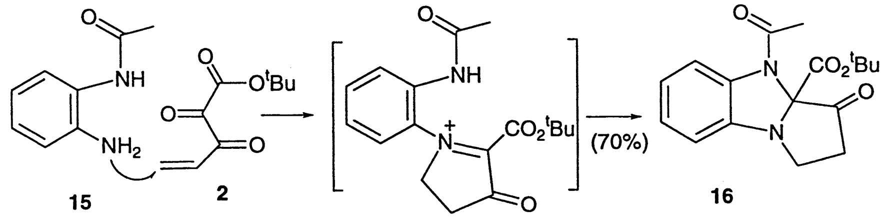
The monoacylated 1,2-phenylenediamine **15** reacted smoothly with vinyl VTC to give the bicyclic derivative **16**. Here, the formation of **16** appears to involve a first stage attack of the aryl primary amine followed by intramolecular addition of the amide NH to the incipient iminium ion. In similar fashion, the reaction of the

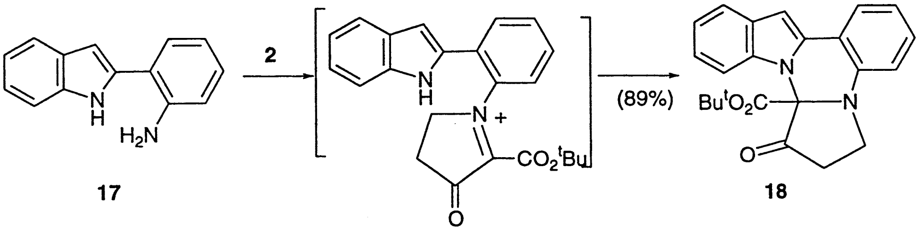


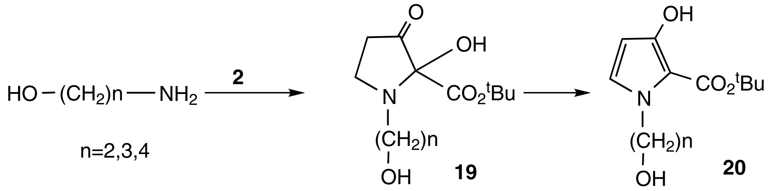
12 **13**

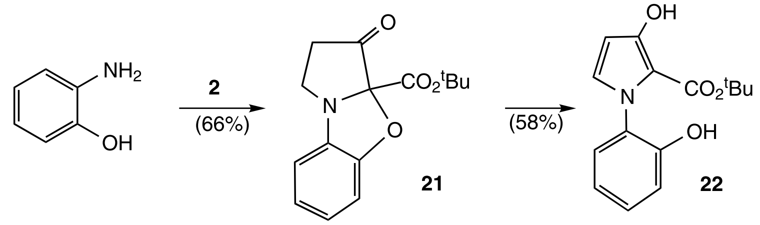


14





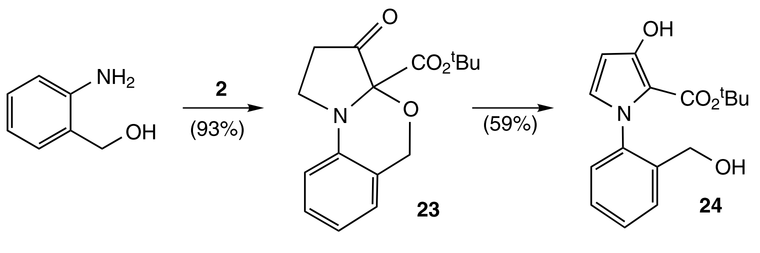


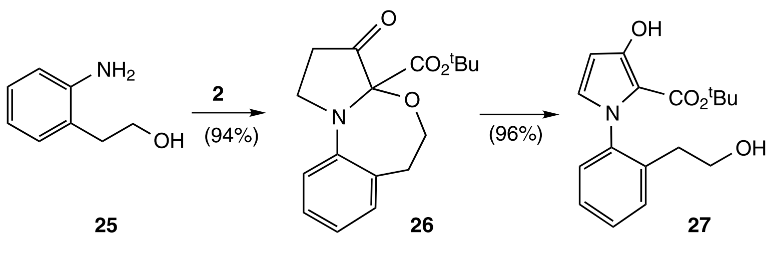


indoloamine **17** with **2**, yielded **18** after workup on silica gel.

Consistent with earlier studies on the reaction of **2** with 4-amino-1-butanol,[6] ethanolamine and propanolamine added to **2** to form *N*-hydroxyalkyl pyrroles **20** through intermediates **19**. Tricyclic systems from alcohol–iminium addition could not be isolated. If the amine group of the amino alcohol is aromatic, the tricyclic intermediates are more stable. With 2-aminophenol, the product **21**, isolated in good yield, could be converted to the pyrrole **22** under acidic conditions or thermally. In the case of 2-aminobenzyl alcohol, the product **23** is quite stable and is converted to pyrrole **24** only under extended reflux with silica gel. The reaction of **2** with amino alcohol **25** yielded **26** which could be converted to pyrrole **27** under moderately acidic conditions.

In summary, using diamines and related systems as polynucleophiles, we have demonstrated the versatility of the vinyl VTC reagent as a polyelectrophilic building block in synthesis.





Acknowledgements

This work was supported by grants from the NIH and NSF. We thank Dr. Walter McMurray of the Yale Center for Cancer Research for expert help in determining the HRMS spectra of all new compounds.

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