Aza-Oxy-Carbanion Relay via Non-Brook Rearrangement: Efficient Synthesis of Furo[3,2-c] pyridinones
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Double Isocyanide Cyclization: A Synthetic Strategy for Two-Carbon-Tethered Pyrrole/Oxazole Pairs

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Short Literature Presentation
January 24, 2011
Aza-Oxy-Carbanion Relay via Non-Brook Rearrangement: Efficient Synthesis of Furo[3,2-c] pyridinones
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On the basis of the former Northeast University, combining with the former Changchun University and Changbai Normal College, the chemistry department of natural science college of NENU was founded in Oct. 1948. It was renamed the Chemistry Department of NENU in 1950. As one of the earlier departments of science established in our university, the Chemistry Department merged with the Analysis & Testing Center to form the Faculty of Chemistry of NENU.

29 professors
24 associate professors,
15 doctoral supervisors
32 teachers with doctoral degrees
34 people engaging in the doctoral program
Anionic Relay Chemistry

an anionic functional group resulting from one organic reaction is transferred to a different location within the same carbon framework and available for secondary reactions.
Initial Idea and Optimization

1. **NaOH/EtOH reflux**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   - $\text{Ph}$
   $+ \text{PhNH}$
   $\rightarrow$
   $\text{PhN}$
   $\text{O}$
   $\text{Ph}$
   $\text{O}$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $77\%$

2. **t-BuOK/t-BuOH**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   $+ \text{PhH}$
   $\rightarrow$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $81\%$

3. **NaH/DMSO reflux**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   $+ \text{PhH}$
   $\rightarrow$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $85\%$

4. **NaH/THF reflux**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   $+ \text{PhH}$
   $\rightarrow$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $70\%$

5. **NaH/DMF 80°C**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   $+ \text{PhH}$
   $\rightarrow$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $35\%$

6. **NaH/DMF 80°C**
   - $\text{O}$
   - $\text{NHPh}$
   - $\text{O}$
   - $\text{H}$
   $+ \text{PhH}$
   $\rightarrow$
   $\text{Ph}$
   $\text{N}$
   $\text{O}$
   $\text{Ph}$
   $\text{Ph}$
   $\text{O}$
   $77\%$
Control Reaction to Probe Mechanism

The bicyclic product is formed when an additional electrophile is NOT present.
Proposed Mechanism

1. **Base** treatment of the starting material leads to an aza-Michael addition.
2. Following the aza-Michael addition, the cyclopropane ring undergoes opening and cyclization.
3. The resulting intermediate then undergoes electrophile trapping, yielding the final product.

The mechanism involves a series of chemical transformations, including addition, ring opening, and substitution.
Substrate Scope

aryl groups can be electron-rich or poor

aldehydes include electron rich aryl, electron poor aryl, or heteroaryls

3 new bonds in one-pot
C-O
C-C
C-N

79-91%
10 examples

Ar = Ph 88%
4-ClPh 85%
2-furyl 81%
Double Isocyanide Cyclization: A Synthetic Strategy for Two-Carbon-Tethered Pyrrole/Oxazole Pairs
Previous Work

**R' = (CH2)2**
**EWG = COR**


**R' = Et**
**EWG = CONHR**


**R' = (CH2)2**
**EWG = CN**

C2-Tethered Heterocyclic Natural Products

Siphonazole

Cyclooroidin

Paprotrain
Initial Reaction

\[ \text{Initial Reaction} \]

\[ \text{p-ClPh} \]

\[ \text{DBU (0.5 eqv)} \]

\[ \text{MeCN} \]

\[ 80°C \]

\[ 84\% \]

\[ \text{2 eqv.} \]

\[ \text{CN} \text{CO}_2\text{Et} \]

\[ \text{DBU (0.5 eqv)} \]

\[ \text{MeCN} \]

\[ 80°C \]

\[ 50-89\% \]

\[ 12 \text{ examples} \]

\[ \text{electron rich, electron deficient, aromatic and heteroaromatic groups tolerated} \]
Bicyclic Aminal Product

Single Isocyanide Cyclization

61%
Isolation of Intermediate Product

Re-subjecting to modified reaction conditions leads to product.
Proposed Mechanism

1. **Double Michael Addition [5+1]**
   - $\text{R} - \text{CN} - \text{CO}_2\text{Et}$

2. **Alkylthio Elimination**
   - $\text{R} - \text{EtO}_2\text{C} - \text{O}$

3. **Loss of thiirane 1,2 addition**
   - $\text{CN} - \text{CO}_2\text{Et}$

4. **Isocyanide cyclization formation of pyrrole**
   - $\text{CN} - \text{CO}_2\text{Et}$

5. **Deprotonation to form thiol**
   - $\text{CN} - \text{CO}_2\text{Et}$

6. **Deprotonation to form enolate**
   - $\text{CN} - \text{CO}_2\text{Et}$

7. **Isocyanide cyclization formation of oxazole**
   - $\text{CN} - \text{CO}_2\text{Et}$
5 New Bonds Formed
4 C-C
1 C-O
2 heterocycles
One-Pot

2 eqv.
CN\text{CO}_2\text{Et}

DBU (0.5 eqv)
MeCN
80°C

50-89%
12 examples