Total Synthesis of the Akuammiline Alkaloid Picrinine

Questions:
1. Propose a mechanism for the oxidation of ketone 4 to enone 5.
2. Propose a mechanism for the formation of epoxide 6 from enone 5 and aldehyde 8 from enone 7.
3. Suggest a sequence of reaction for the formation of tricycle 11 starting from aldehyde 8. Give the intermediates and conditions.
4. In the formation of 12, triphosgene is used to protect the product. How many equivalents of triphosgene have to be used and what is its reaction with pyridine?
5. What are the names of the reactions in the steps 12→13a and 14→15?
6. Propose a mechanism for the formation of 14 from 13a.
7. (If time: Suggest a synthesis of the vinyl iodide in the first step, starting from but-2-yn-1-ol using Bu₃SnH. How could you synthesize the isomer (with Bu₃SnH)?)

Source:
Solutions:

1. Oxidation of ketone with IBX


2. Epoxidation with NaBO₃

Hydrostannylation

3. Reaction sequence

Submitted by Sam
4. 0.33 equiv. of triphosgene are used in an ideal case.

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\begin{align*}
\text{Cl}_2\text{C}(\text{O})\text{O}\cdot\text{O} &\rightarrow \text{Cl}_2\text{C}(\text{O})\text{O}^\text{-} & \rightarrow \text{Cl}_2\text{C}(\text{O})\text{Cl} + \text{Cl}\text{O} \text{N} \text{Cl} + \text{Cl}^- \\
\rightarrow & \text{Cl}_2\text{C}(\text{O})\text{Cl} + \text{N} \text{H} \text{O} & \rightarrow 2 \text{Cl}_2\text{C}(\text{O})\text{Cl} 
\end{align*}
\]

5. Fischer Indole Synthesis, Pinnick Oxidation

6. Diol cleavage

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\begin{align*}
\text{R}_\text{O} &\rightarrow \text{NaOH, H}_2\text{O} & \text{R} \text{OH} &\rightarrow \text{NaO}_4 & \text{R} \text{OH} &\rightarrow \text{HO}\text{O} \text{O} \\
\rightarrow & \text{R} \text{H} \text{O} &\rightarrow \text{HO} \text{O} \text{O} 
\end{align*}
\]

7. Precursor Synthesis

\[
\begin{align*}
\text{Bu}_3\text{SnH}, \text{AIBN}, \Delta T &\rightarrow \text{I}_2, \text{CCl}_4 & \text{TsCl, Et}_3\text{N, DMAP, CH}_2\text{Cl}_2 \\
\text{Bu}_3\text{SnH}, \text{Pd(PPH}_3)_4\text{, benzene} &\rightarrow \text{I}_2, \text{CCl}_4 & \text{TsCl, Et}_3\text{N, DMAP, CH}_2\text{Cl}_2
\end{align*}
\]