In biomimetic chemistry, we take what we have observed in nature and apply its principles to the invention of novel synthetic compounds that can achieve the same goals ... As an analogy, we did not simply make larger versions of birds when we invented airplanes, but we did take the idea of the wing from nature, and then used the aerodynamic principles in our own way to build a jumbo jet.”

-- R. Breslow

1. Biomimetic synthesis of (−) - Alloaristoteline, (−)-Serratoline, and (+)-Aristotelone alkaloids

SCHEME 1:

1 + 2 → 3 → 4

1. (−)-Alloaristoteline

2. (−)-Serratoline

3. (−)-Aristotelone
2. Biomimetic Synthesis of (+)-Brevianamide A and (+)-Brevianamide B alkaloids:

**SCHEME 2:**

- **Step 1:**
  - Reagent and conditions?
  - 2nd chromatographic purification

- **Step 2:**
  - LiOH, H$_2$O/THF
  - r.t., 3 h
  - 94%

- **Step 3:**
  - Reagent and conditions?

- **Step 4:**
  - UCl, DMF
  - 160 °C, 21 h

- **Step 5:**
  - Reagent and conditions?

- **Step 6:**
  - MeOImPO (1 equiv.)
  - CHCl$_3$, r.t., 16 h
  - 67% (d.r. = 2:3)
  - 3rd chromatographic purification
  - d.r. of 17a:17b = 2:3

- **Step 7:**
  - LiOH, H$_2$O
  - r.t., 0.5 h
  - 63% (d.r. = 93:7)
  - 4th chromatographic purification

**Additional Notes:**
- (+)-Brevianamide A: 750 mg
- (+)-Brevianamide B: 60 mg
Biosynthetic Proposals for brevianamides A and B

SCHEME 3:

Previous biosynthetic proposals

New biosynthetic proposal
Cyclopiazonic acid (α-CPA, 27) is a prenylated indole alkaloid present in a number of *Pencillium* species such as *P. griseofulvum*, *P. camemberti* and *P. commune*. These fungi are present in meat, cheese and other dietary products. This alkaloid shows a significant biological activity and is known to be a potent inhibitor of Ca\(^{2+}\)-dependent ATPase (SERCA), which stops calcium reuptake in muscular cells.

Several structurally similar alkaloids have been isolated including iso-α-cyclopiazonic acid 28, α-CPA imine 29 and speradines A-D 30 (Scheme 4). All these alkaloids possess a common 3-acetyltetramic acid unit (highlighted in red in Scheme 4).

**SCHEME 4: α-CPA and Related Natural Products:**

α-CPA alkaloid is biosynthetically derived from L-tryptophan. It is believed that the tetramic acid unit is assembled at an early stage followed by series of alkylations to afford β-cyclopiazonic acid (β-CPA, 31) which is a direct biosynthetic precursor of α-CPA 27. This intermediate β-CPA 31 then undergoes flavin-mediated oxidation followed by cyclisation to afford α-CPA 27 (Scheme 5).
In 2018, Aggarwal et al. reported an bioinspired enantioselective synthesis of cyclopiazonic acid family of alkaloids (Scheme 6).

**SCHEME 6: Enantioselective Synthesis of the Cyclopiazonic Acid Family Using Sulfur Ylides**

![Scheme 6 diagram with chemical structures and reactions](image-url)