Unified, Biosynthesis-Inspired, Completely Stereocontrolled Total Synthesis of All Highest-Order [n + 1] Oligocyclotryptamine AlkaloidsClick to copy article link

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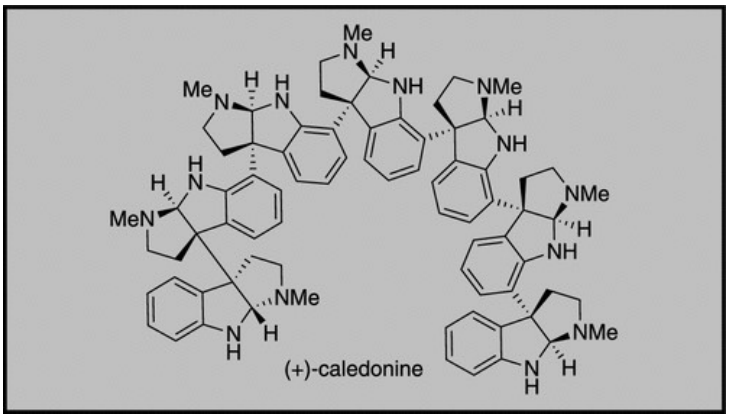
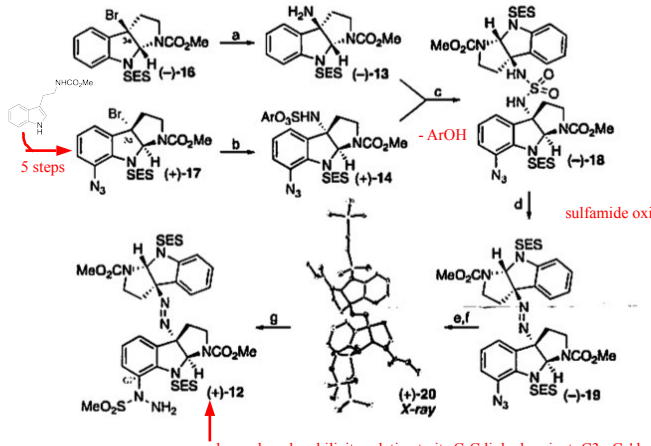
J. Am. Chem. Soc. 2024, 146, 33, 23574–23581




**D. Synthesis of heterodimeric headcap (+)-12[a]**




[a] Reagents and conditions: (a) 2,6-difluorophenyl sulfamate, AgOTf, DTBMP, $CH_2Cl_2$, 23 °C; pyridine, MeCN, $H_2O$, 70 °C, 86% over two steps; (b) 2,6-difluorophenyl sulfamate, AgOTf, DTBMP, 1,2-DCE, 70 °C, 80%; (c) DMAP, THF, 84%; (d) 1,3-dichloro-5,5-dimethylhydantoin, MeOH, DBU, 95%; (e) dithiothreitol, $NEt_3$, MeOH, $CH_2Cl_2$, 23 °C; (f) $MeSO_2Cl$, pyridine, 23 °C, 93% over 2 steps; (g) NaH, THF, 0 → 23 °C, then $Ph_2P(O)ONH_2$, 23 °C, 88%; Ar = 2,6-difluorobenzene. In the ORTEP representation of diazene dimer (+)-20, thermal ellipsoids are drawn at 30% probability and hydrogen atoms are omitted for clarity.

17 is less reactive than 16

Teoc group was unstable

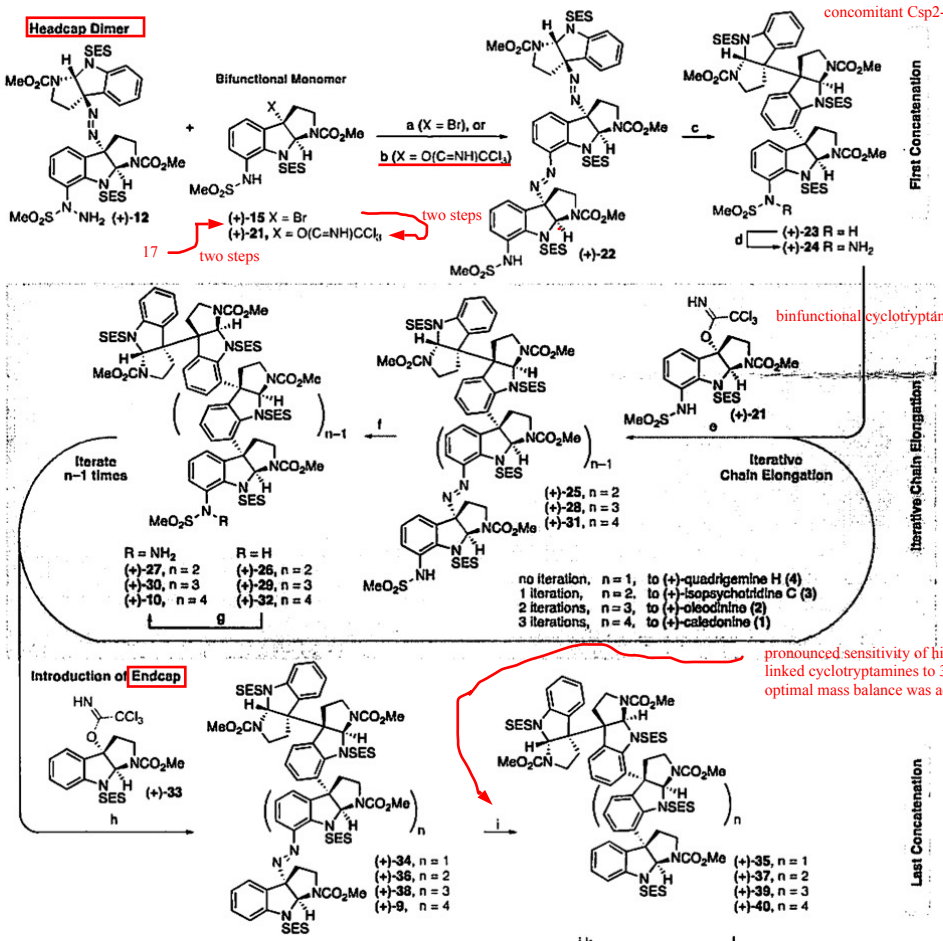
enhanced nucleophilicity relative to its C-C linked variant: C3a-Ca' bond formation was strategically delayed until after the first concatenation

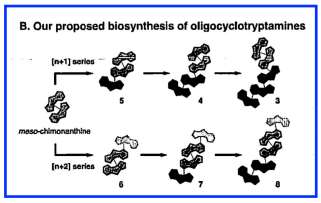
**Scheme 2. Total Synthesis of (+)-Quadrigemine H (4), (+)-Isopsychotridine C (3), (+)-Oleoidine (2), and (+)-Caledonine (1)[a]**

diazene-directed fragment assembly

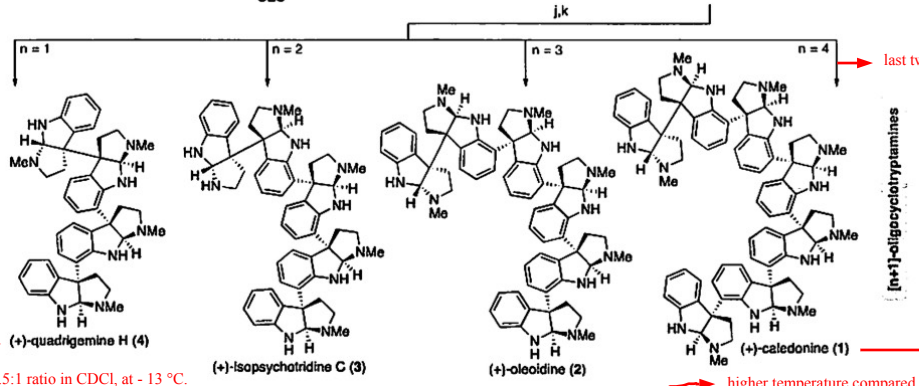
photoextrusion of dinitrogen

concomitant Csp2-Csp3 and Csp3-Csp3 diazene photolysis




pronounced sensitivity of higher order C-C linked cyclotryptamines to 300 nm light: optimal mass balance was achieved by stopping




last two steps = cleavage of seven N-S bonds and the

exists as two contormers in a 1.5:1 ratio in CDCl, at - 13 °C.

displays extreme atopisomerism

higher temperature compared to the diazene dimer nucleophile

[a]Reagents and conditions: (a) AgOTf, DTBMP, 1,2-DCE, 60 °C, 54% (b) $CF_3SO_3H$, 1,2-DCE, 60 °C, 77%; (c) hv (300 nm), thin film, 25 °C, 45%; (d) NaH, THF, 0 → 23 °C, then $Ph_2P(O)ONH_2$, 23 °C, 90%; (e) $CF_3SO_3H$, 1,2-DCE, 75 °C, 59% for (+)-25, 62% for (+)-26, 58% for (+)-27; (f) hv (300 nm), thin film, 25 °C, 55% for (+)-28, 48% for (+)-29, 47% for (+)-30. (g) NaH, THF, 0 → 23 °C, then $Ph_2P(O)ONH_2$, 23 °C, 86% for (+)-31, 89% for (+)-32, 83% for (+)-4; (h) $CF_3SO_3H$, $CH_2Cl_2$, 23 °C, 79% for (+)-34, 87% for (+)-35, 75% for (+)-36, 62% for (+)-9; (i) hv (300 nm), thin film, 5 °C, 59% for (+)-37, 61% for (+)-38, 51% for (+)-39, 56% for (+)-40; (j) TASF, DMF, 45 °C; (k) $EtNMe_2$·AlH3, quinuclidine, PhMe, 70 °C, 76% over two steps for (+)-4, 65% over two steps for (+)-3, 49% over two steps for (+)-2, 51% over two steps for (+)-1.

critical: alane-quinuclidine complex eliminates persitent byproducts from partial reduction