Flow Photo-Oxidative Dearomative Cyclization Enables Unified Asymmetric Synthesis of Trichodermamides A–F

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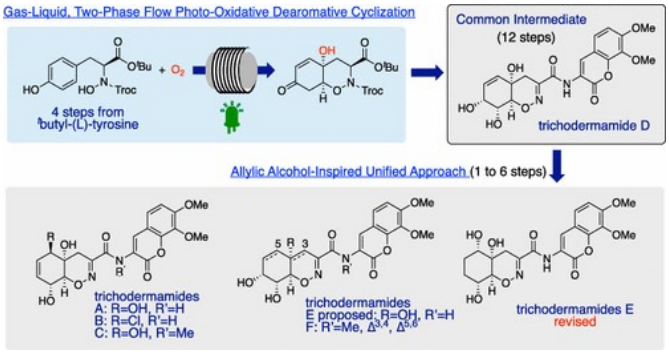


new gas—liquid two-phase continuous flow photo-oxidation process

(L)-tyrosine butyl

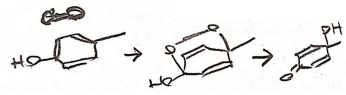
4 steps

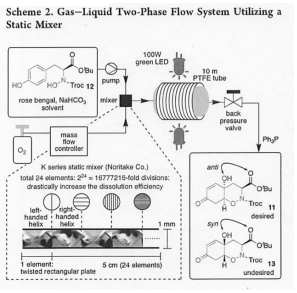
Table 1. Optimization of the Photo-Oxidative Dearomative Cyclization of Tyrosine-Derived Hydroxylamine

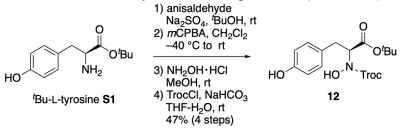
entry	flow rate (mL/min) O_2	flow rate (mL/min) solution	solvent (0.1 M)	[recovered SM] (%)	11:13	Productivity of 11 (mg/h)
1[a]	1.3	0.04	^{t}BuOH-H_2O 1:1	56 [3]	1.7:1	38
2[a]	1.3	0.04	MeCN-H_2O-THF 9:6:2	60 [10]	1.9:1	42
3	7.0	0.5	MeCN-H_2O-THF 9:6:2	63	1.9:1	547
4[b]	7.0	0.5	MeCN-H_2O-THF 9:6:2	32 [55]	1.9:1	279
5	7.0	0.5	TFE-H_2O 1:1	64 [7]	2.0:1	569
6	7.0	0.4	TFE-H_2O 1:1	75	2.1:1	542
7[a]	7.0	0.4	TFE-H_2O 1:1	73	2.2:1	534

[a]A 5 m tube and T-shaped mixer were used. [b]A T-shaped mixer was used. [c]5 mol % of rose bengal was used.

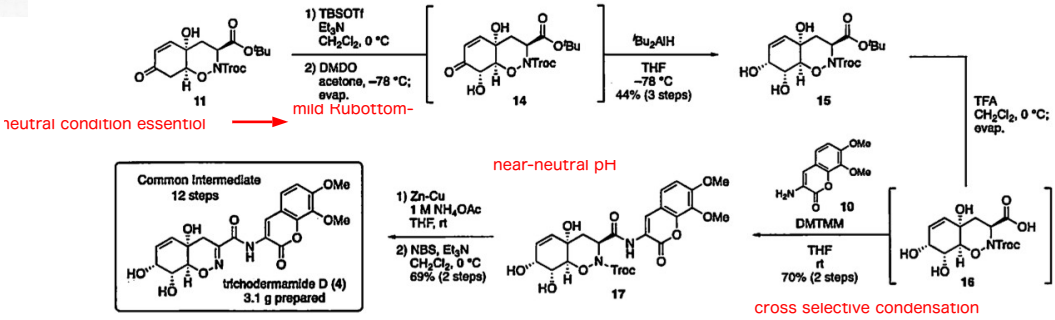
low yield in a batch process, probably due to low irradiation







Scheme 3. Asymmetric Synthesis of Trichodermamide D, a Common Intermediate for a Series of Trichodermamides



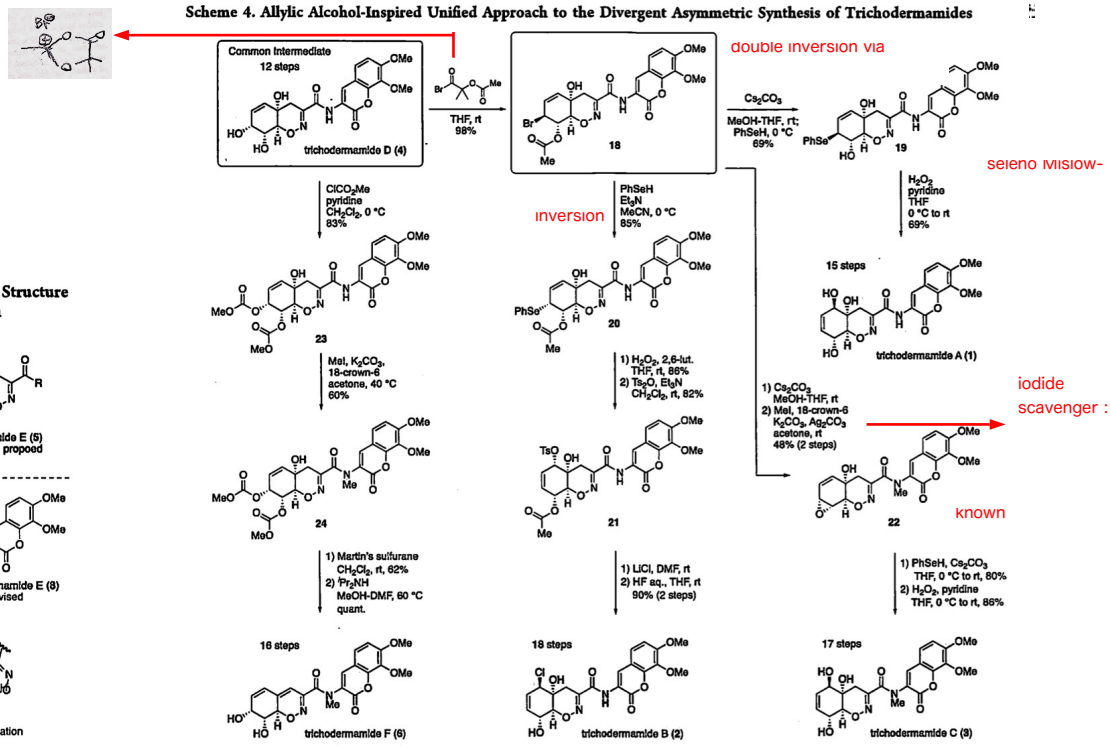
neutral condition essential

mild Rubottom-

near-neutral pH

cross selective condensation

Scheme 4. Allylic Alcohol-Inspired Unified Approach to the Divergent Asymmetric Synthesis of Trichodermamides



double inversion via

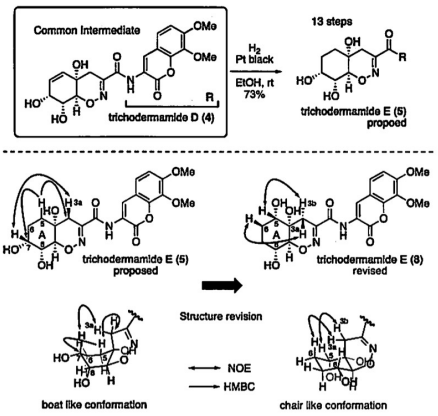
seleno Mislow-

inversion

iodide scavenger :

known

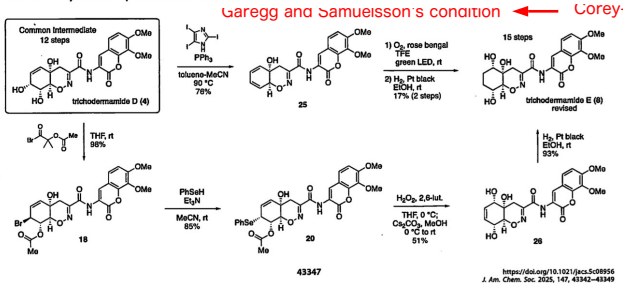
Scheme 5. Asymmetric Synthesis of the Proposed Structure of Trichodermamide E and Its Structure Revision



Scheme 6. Asymmetric Synthesis of the Revised Structure of Trichodermamide E

Garegg and Samuelsson's condition

Corey-Winter olefination and Hanessian olefination unsuccess



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