Supplementary Material (ESI) for Green Chemistry

One-Pot Synthesis of Dehydrodimethylconidendrin

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Supplementary Information: Green Chemistry Metrics – Table 3

The Original Synthesis:
Anastas, Weber, and Stevenson's approach to arynaphthalene lactones:
3 total steps calculated

E-factor

Steps 1 & 2:

Input	Mass(kg)
3,4-Dimethoxyphenyl propionic acid (SM 1)	1.71
Thionyl chloride (TC)	16.57
3,4-Dimethoxyphenyl propargyl alcohol (SM 2)	1.53
P4-VP ploymer (resin)	3.80
Dichloromethane (DCM)	100.69
Output	
3,4-dimethoxyphenylpropargyl 3,4-dimethoxyphenylpropiolate (DP)	2.2

Waste

$W_{1,2}$= ((1.71 kg SM 1)+(1.53 kg SM2) – 2.2 kg DP) + 16.57 kg TC + 3.80 kg resin + 100.69 kg DCM = 122.1 kg waste from steps 1 & 2

Step 3:

Input	Mass (kg)
3,4-dimethoxyphenylpropargyl 3,4-dimethoxyphenylpropiolate (SM 3)	2.20
Xylenes	15.80
Output	
Desired Product	1.0
Waste	

W_3= (2.2 kg SM 3 – 1 kg Desired Product) + 15.8 kg xylenes = 17 kg waste from step 3

Calculated E-factor:

E-factor = (122.1 kg $W_{1,2}$ + 17 kg W_3) / 1 kg desired product = **139.1**

Atom Economy

AE (%) = (MW Product / Σ MW of Reagents) x 100

Reagent	MW
3,4-Dimethoxyphenyl propionic acid	206.06
3,4-Dimethoxyphenyl propargyl alcohol	192.08
Thionyl Chloride	118.97
Product	
Dehydrodimethyl-conidendrin	380.13

AE (%) = (380.13 / (206.06+192.08+118.97)) x 100 = **73.5 %**

The Improved Synthesis:
Reported in this publication
2 steps total

E-factor

Step 1:

Input	Mass (kg)
3,4-Dimethoxyphenyl propargyl alcohol (SM 1)	1.09
Thionyl Chloride (TC)	0.73
N,N-Dimethylacetamide (DMA)	16.70

Output

3,4-Dimthoxyphenyl propargyl chloride (DP 1)	1.00

Waste

W_1 = ((1.09 kg SM 1) + (0.73 kg TC) – 1.0 kg DP) + 16.70 kg DMA = 17.5 kg waste from step 1

Step 2:

Input	Mass (kg)
3,4-Dimethoxyphenyl propargyl chloride (SM 2)	1.00
3,4-Dimethoxyphenyl acetylene (SM 3)	0.77
Potassium carbonate (Base)	0.67
18-Crown-6 (PTC)	0.26
Carbon dioxide (CO_2)	3.14
Silver Iodide (AgI)	0.11

N,N-Dimethylacetamide (DMA)	12.53

Output

Dehydrodimethyl-conidendrin (DP 2)	1.0

Waste

W_2 = ((1.0 kg SM 2) + (0.77 kg SM 2) – (1.00 kg DP 2)) + 0.67 kg Base + 0.26 kg PTC + 3.14 kg CO_2 + 0.11 kg AgI + 12.53 kg DMA = 17.48 kg waste from step 2

Calculated E-factor

E-factor = (17.50 kg W_1 + 17.48 kg W_2) / 1 kg Desired Product = **34.98**

Atom Economy

AE (%) = (MW Product / Σ MW of Reagents) x 100

Reagent	MW
3,4-Dimethoxyphenyl acetylene	162.07
3,4-Dimethoxyphenyl propargyl alcohol	192.08
Thionyl Chloride	118.97
Carbon dioxide	43.99

Product

Dehydrodimethyl-conidendrin	380.13

AE (%) = (380.13 / (162.07 + 192.08 + 118.97 + 43.99) x 100 = **73.5%**