Supporting information

Determination of the Global Material Economy (GME) of Synthesis Sequences – A Green Chemistry Metric to Evaluate the Greenness of Products

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Calculation of GME and GRME for the sequence of Figure S1

The mass of product $\mathbf{P_z}$ for that sequence is

$$m = \frac{x_1}{\nu_{a1}} \nu_p \ M_p \prod_{i=1}^{z} \varepsilon_{1,i} \qquad \text{(S1)}$$

x_1 is the scale of the synthesis (number of moles of **A1**)

ν_{a1} and ν_p are the stoichiometric coefficients of $\mathbf{A_1}$ and $\mathbf{P_z}$ respectively

Mp is the molecular weight of $\mathbf{P_z}$.

$\varepsilon_{1,i}$ is the i th yield of the green sequence

If we divide Eq. 1 by $\frac{x_1}{\nu_{a1}} \sum M$, we obtain a dimensionless term: $GAE \prod_{i=1}^{z} \varepsilon_{1,i}$ (S2)

$\sum M = \nu_{a1} M_{A1} + \nu_{a2} M_{A2} + \sum_{i=1}^{z} \nu_{b1,i} M_{B1,i} + \sum_{j=1}^{m} \nu_{b2,j} M_{B2,j}$ is the summation of the molecular weights of all the reactants with their stoichiometric coefficients.

GAE is the global atom economy.

The total mass used in this sequence is:

$$m_T = x_1 M_A + \sum_{i=1}^{z} \varphi_{1,i} (\varepsilon_{1,i} \ \varepsilon_{1,2} \ldots \varepsilon_{1,i-1}) \frac{x_1}{\nu_{a1}} \nu_{b1,i} M_{B1,i} + x_2 M_{A2} + \sum_{j=1}^{m} \varphi_{2,j} \ (\varepsilon_{2,1} \ \varepsilon_{2,2} \ldots \varepsilon_{2,j-1}) \frac{x_2}{\nu_{a2}} \nu_{b2,j} \ M_{B2,j} + S$$

(S3)

where $\varphi_{1,i} = \dfrac{mol \quad number \quad of \ \ B_{1,i} \ / \nu_{1,i}}{mol \quad number \quad of \ \ P_{1,i-1} \ / \nu_{P1,i-1}}$ (S4)

$$\varphi_{2,j} = \frac{mol \quad number \quad of \ \ B_{2,j} \ / \nu_{b2,j}}{mol \quad number \quad of \ \ P_{2,j-1} \ / \nu_{P2,j-1}} \qquad \text{(S5)}$$

S is the total mass of auxiliaries when processing the total sequence at the scale x_1.

By introducing the ration σ_2, such as $\sigma_2 = \dfrac{x_2 / \nu_{a2}}{x_1 / \nu_{a1}}$ (S6)

the Eq. S3 becomes

$$m_T = x_1\ M_A + \sum_{i=1}^{z} \varphi_{1,i}\ (\varepsilon_{1,i}\ \varepsilon_{1,2}....\varepsilon_{1,i-1}) \frac{x_1}{v_{a1}} v_{b1,i}\ M_{B1,i} + \sigma_2 \left[v_{a2} \frac{x_1}{v_{a1}} M_{A2} + \sum_{j=1}^{m} \varphi_{2,j}\ (\varepsilon_{2,1}\ \varepsilon_{2,2}....\varepsilon_{2,j-1}) \frac{x_1}{v_{a1}} v_{b2,j}\ M_{B2,j} \right] + S$$

(S7)

As previously, we divide the Eq. S7 by $\frac{x_1}{v_{a1}} \sum M$ to obtain a dimensionless term (S8):

$$1 + \sum_{i=1}^{z} \left[\varphi_{1,i}\ (\varepsilon_{1,i}\ \varepsilon_{1,2}....\varepsilon_{1,i-1}) - 1 \right] \frac{v_{b1,i}\ M_{B1,i}}{\sum M} + (\sigma_2 - 1) \frac{v_{a2}\ M_{A2}}{\sum M} + \sum_{j=1}^{m} \left[\sigma_2\ \varphi_{2,j}\ (\varepsilon_{2,1}\ \varepsilon_{2,2}....\varepsilon_{2,j-1}) - 1 \right] \frac{v_{b2,j}\ M_{B2,j}}{\sum M} + \frac{S}{\frac{x_1}{v_{a1}} \sum M}$$

(S8)

Therefore $$GME = \frac{GAE \prod_{i=1}^{z} \varepsilon_{1,i}}{1 + a_2 + \sum_{i=1}^{z} b_{1,i} + \sum_{j=1}^{m} b_{2,j} + s} \qquad \text{(S9)}$$

where $$a_2 = (\sigma_2 - 1) \frac{v_{a2} M_{A2}}{\sum M} \qquad \text{(S10)}$$

$$b_{1,i} = \left[\varphi_{1,i} (\varepsilon_{1,1} \varepsilon_{1,2} ... \varepsilon_{1,i-1}) - 1 \right] \frac{v_{b1,i} M_{B1,i}}{\sum M} \qquad \text{(S11)}$$

$$b_{2,j} = \left[\sigma_2 \varphi_{2,j} \left(\varepsilon_{2,1} .... \varepsilon_{2,j-1} \right) - 1 \right] \frac{v_{b2,j} M_{B2,j}}{\sum M} \qquad \text{(S12)}$$

$$s = \frac{S}{\frac{x_1}{v_{a1}} \sum M} \qquad \text{(S13)}$$

GRME is obtained by omitting in Eq. S9 the term corresponding to the auxiliaries so that

$$GRME = \frac{GAE \prod_{i=1}^{z} \varepsilon_{1,i}}{1 + a_2 + \sum_{i=1}^{z} b_{1,i} + \sum_{j=1}^{m} b_{2,j}} \qquad \text{(S14)}$$

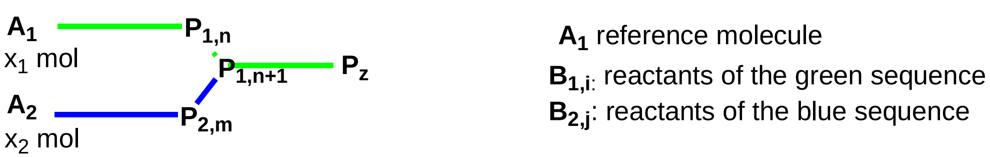


Figure S1 Convergent synthesis with one point of convergence. By convention **A1** is the reference molecule so that the main branch starting from **A1** is green. The other branch is blue.

Calculation of GME and GRME for the sequence of Figure S2

Using the same method, we can give the expressions of GME and GRME for the sequence of Figure 2

The mass of product $\mathbf{P_z}$ for that sequence is given by Eq. S1. If we divide Eq. S1 by $\frac{x_1}{\nu_{a1}}\sum M$ where

$$\sum M = \nu_{a1} M_{A1} + \nu_{a2} M_{A2} + \nu_{a3} M_{A3} + \sum_{i=1}^{z} \nu_{b1,i} M_{B1,i} + \sum_{j=1}^{m} \nu_{b2,j} M_{B2,j} + \sum_{k=1}^{r} \nu_{b3,k} M_{B3,k}$$

we obtain the dimensionless term of Eq. S2.

The total mass of reactants used in the sequence is:

$$m_T = x_1 M_A + \sum_{i=1}^{z} \varphi_{1,i} (\varepsilon_{1,i}.\varepsilon_{1,i-1}) \frac{x_1}{\nu_{a1}} \nu_{b1,i} M_{B1,i} + x_2 M_{A2} + \sum_{j=1}^{m} \varphi_{2,j} (\varepsilon_{2,1}..\varepsilon_{2,j-1}) \frac{x_2}{\nu_{a2}} \nu_{b2,j} M_{B2,j} + x_3 M_{A3} + \sum_{k=1}^{r} \varphi_{3,k} (\varepsilon_{3,1}...\varepsilon_{3,k-1}) \frac{x_3}{\nu_{a2}} \nu_{b3,k} M_{B3,k} + S$$

(S15)

where $\varphi_{1,i}$ and $\varphi_{2,j}$ are given by Eq. S4 and S5

$$\varphi_{3,k} = \frac{mol \quad number \quad of \quad B_{3,k} / \nu_{b3,k}}{mol \quad number \quad of \quad P_{3,k-1} / \nu_{P3,k-1}} \qquad \text{(S16)}$$

S is the total mass of auxiliaries when processing the total sequence at the scale x_1.

We introduce the ratio σ_2 and σ_3; they are respectively defined by Eq. S6 and S17:

$$\sigma_3 = \frac{x_3 / \nu_{a3}}{x_1 / \nu_{a1}} \qquad \text{(S17)}$$

The Eq. S15 becomes

$$m_T = x_1 M_A + \sum_{i=1}^{z} \varphi_{1,i} (\varepsilon_{1,i}..\varepsilon_{1,i-1}) \frac{x_1}{\nu_{a1}} \nu_{b1,i} M_{B1,i} + \sigma_2 \left[\nu_{a2} \frac{x_1}{\nu_{a1}} M_{A2} + \sum_{j=1}^{m} \varphi_{2,j} (\varepsilon_{2,1}..\varepsilon_{2,j-1}) \frac{x_1}{\nu_{a1}} \nu_{b2,j} M_{B2,j} \right] + \sigma_3 \left[\nu_{a3} \frac{x_1}{\nu_{a1}} M_{A3} + \sum_{k=1}^{r} \varphi_{3,k} (\varepsilon_{3,1}..\varepsilon_{3,j-1}) \frac{x_1}{\nu_{a1}} \nu_{b3,k} M_{B3,k} \right] + S$$

(S18)

As previously, we divide the Eq. S18 by $\frac{x_1}{\nu_{a1}}\sum M$ to obtain a dimensionless term (S19):

$$1 + \sum_{i=1}^{z} [\varphi_{1,i} (\varepsilon_{1,i}..\varepsilon_{1,i-1}) - 1] \frac{\nu_{b1,i} M_{B1,i}}{\sum M} + (\sigma_2 - 1) \frac{\nu_{a2} M_{A2}}{\sum M} + \sum_{j=1}^{m} [\sigma_2 \varphi_{2,j} (\varepsilon_{2,1}..\varepsilon_{2,j-1}) - 1] \frac{\nu_{b2,j} M_{B2,j}}{\sum M} + (\sigma_3 - 1) \frac{\nu_{a3} M_{A3}}{\sum M} + \sum_{k=1}^{r} [\sigma_3 \varphi_{3,k} (\varepsilon_{3,1}..\varepsilon_{3,k-1}) - 1] \frac{\nu_{b3,k} M_{B3,k}}{\sum M} + \frac{S}{\frac{x_1}{\nu_{a1}} \sum M} \qquad \text{(S19)}$$

Therefore

$$GME = \frac{GAE \prod_{i=1}^{z} \varepsilon_{1,i}}{1 + a_2 + a_3 + \sum_{i=1}^{z} b_{1,i} + \sum_{j=1}^{m} b_{2,j} + \sum_{k=1}^{r} b_{3,k} + s} \qquad \text{(S20)}$$

where a_2, $b_{1,i}$, $b_{2,j}$, s are given by Eq. S10, S11, S12 and S13.

$$a_3 = (\sigma_3 - 1) \frac{\nu_{a3} M_{A3}}{\sum M} \qquad \text{(S21)}$$

$$b_{3,k} = [\sigma_3 \varphi_{3,k} (\varepsilon_{3,1}....\varepsilon_{3,k-1}) - 1] \frac{\nu_{b3,k} M_{B3,k}}{\sum M} \qquad \text{(S22)}$$

GRME is obtained by omitting in Eq.20 the term corresponding to the auxiliaries so that

$$GRME = \frac{GAE \prod_{i=1}^{z} \varepsilon_{1,i}}{1 + a_2 + a_3 + \sum_{i=1}^{z} b_{1,i} + \sum_{j=1}^{m} b_{2,j} + \sum_{k=1}^{r} b_{3,k}} \qquad (S23)$$

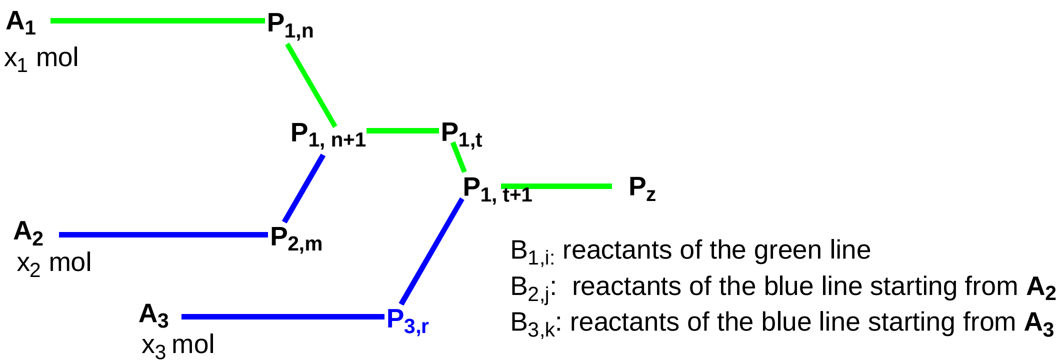


Figure S2 Convergent synthesis with two points of convergence. Two branches (in blue) converge to the main sequence (in green). **A1** is the reference molecule.

Calculation of GRME for the synthesis of discodermolide

To obtain 165 mg of discodermolide we need to start with x_1 = 6.96 mmol of $\mathbf{A_1}$, x_2 = 6.654 mmol of $\mathbf{A_2}$ and x_3 = 8.435 mmol of $\mathbf{A_3}$. The mass of reagents at this scale are displayed in Table S1

Table S1. Calculation of the mass of reagents at the appropriate scale

Reagent	MW (g.mol^{-1})	[illegible]	yield	Mass (mg)
A_1	258.43			1798,673
$B_{1,1a}$ (iPrMgCl)	158.95	3.002		3322.055
$B_{1,1b}$ (MeNHOMe)	61.08	1.55		659.053
$B_{1,1c}$ (HCl)	36.46	1.55	0.98	393.403
$B_{1,2a}$ (TESCl)	150.72	1.016		1044.479
$B_{1,2b}$ (imidazole)	68.08	1.128	0.92	523.798
$B_{1,3}$ (Red-Al)	202.16	2	0.97	2543.092
$B_{1,4a}$ ($EtP^+Ph_3I^-$)	418.25	1.804		4622.612
$B_{1,4b}$ (NaHMDS)	183.37	1.88		2111.0988
$B_{1,4c}$ (I_2)	253.81	1.804		2805.177
$B_{1,4d}$ (NaHMDS)	183.37	1.804	0.3	2026.654
A_2	258.43			1719.607
$B_{2,1a}$ (iPrMgCl)	158.95	3.11		3289.212
$B_{2,1b}$ (MeNHOMe)	61.08	1.71		694.804
$B_{2,1c}$ (HCl)	36.46	1.71	1	414.744
$B_{2,2a}$ (DMSO)	78.13	1		519.881
$B_{2,2b}$ (Pyridine)	79.1	3.037		1598.557
$B_{2,2c}$ (SO_3)	80.06	3.037		1617.958
$B_{2,2d}$ (NEt_3)	101.19	4.056	1	2730.723
$B_{2,3a}$ (Br-allylsilane)	193.16	4		5141.189
$B_{2,3b}$ (2 $CrCl_2$)	245.8	3		4906.70

$B_{2,3c}$ (H_2O)	18.02	1		119.906
$B_{2,3d}$ (KH)	40.11	1.097	0.77	292.800
$B_{2,4a}$ (DIBAH)	142.22	1.053		767.544
$B_{2,4b}$ (H_2O)	18.02	1	0.79	92.328
$B_{2,5a}$ (oxazoline)	233.26	1.425		1345.424
$B_{2,5b}$ (Bu_2OTf)	274.11	1.35		1497.831
$B_{2,5c}$ (NEt_3)	101.19	1.792		734.177
$B_{2,5d}$ (H_2O)	18.02	1	0.85	72.939
$B_{2,6a}$ (lutidine)	107.15	2.632		970.307
$B_{2,6b}$ (TBSOTf)	264.34	2.374	0.9	2158.967
$B_{2,7a}$ (mercaptan)	124.2	3.886		1494.37
$B_{2,7b}$ (BuLi)	64.06	2.857		566.741
$B_{2,7c}$ (H_2O)	18.02	1	1	55.798
$B_{2,8a}$ (1/2 $LiBH_4$)	10.89	16		539.527
$B_{2,8b}$ (2 EtOH)	92.14	1	0.84	285.308
$B_{2,9a}$ (Ph_3P)	262.29	1.711		1167.11
$B_{2,9b}$ (I_2)	253.81	1.496		987.522
$B_{2,9c}$ (imidazole)	68.08	1.504	0.86	266.349
$B_{1,5a}$ (tBuLi)	64.06	2.439		287.101
$B_{1,5b}$ (borane-OMe)	152.04	1.583	0.81	442.124
$B_{1,6}$ (2 CF_3COOH)	228.04	3.562	0.77	1209.105
$B_{1,7}$ ($PhI(OAc)_2$)	322.1	3	1	1107.391
$B_{1,8a}$ (K_2CO_3)	138.21	6		950.341
$B_{1,8b}$ (phosphonate)	318.11	3.99	0.87	1454.492
$B_{1,9a}$ (isocyanate)	188.4	4.55		854.619
$B_{1,9b}$ (MeOH)	32.04	1	0.98	31.945
$B_{1,10a}$ (2 DIBAH)	284.44	3.992		1109.62
$B_{1,10b}$ (H_2O)	18.02	1	0.92	17.607
$B_{1,11}$ (Dess-Martin)	424.14	1.504	0.96	573.554
A_3 (= A_1)	258.43			2179.91
$B_{3,1a}$ (iPrMgCl)	158.95	3		4026.17
$B_{3,1b}$ (MeNHOMe)	61.08	1.55		798.74
$B_{3,1c}$ (HCl)	36.46	1.55	0.98	476.79
$B_{3,2a}$ (DMSO)	78.13	1		645.861
$B_{3,2b}$ (pyridine)	79.1	3.0147		1971.254
$B_{3,2c}$ (SO_3)	80.06	3.0147		1995.178
$B_{3,2d}$ (NEt_3)	101.19	4.0147	0.84	3358.245
$B_{3,3a}$ (MeMgBr)	119.24	1.762		1458.83
$B_{3,3b}$ (H_2O)	18.02	1	1	125.128
$B_{3,4a}$ (DMSO)	78.13	1		542.523
$B_{3,4b}$ (pyridine)	79.1	4.914		2699.214
$B_{3,4c}$ (SO_3)	80.06	4.914		2731.973
$B_{3,4d}$ (NEt_3)	101.19	6.286	0.82	4416.646
$B_{1,12a}$ (chloroborane)	320.75	6.598		1484.869
$B_{1,12b}$ (NEt_3)	101.19	5.364		579.436
$B_{1,12c}$ (H_2O)	18.02	6.635	0.628	15.551
$B_{1,13a}$ (borohydride)	263.1	14.175		2021.107
$B_{1,13b}$ (AcOH)	60.05	1	0.733	32.544

$B_{1,z}$ (3 HCl)	109.38	406.564	0.7	17665.399
Total	9748,2			115161.686

By applying Eq S23 to the synthesis of discodermolide (Figure 7), we obtain Eq 35. The coefficients of Eq. 35 are displayed in Table 1.

The coefficients of Eq. 36, 38 and 42 are displayed in Tables S2, S3 and S4 respectively

Table S2. Coefficients of Eq. 36

a_1 (**A_1**)	0.00121892			a_3 (**A_3**)	0.007096262
$b_{1,1a}$ (iPrMgCl)	0.03490929	$b_{2,1a}$ (iPrMgCl)	0.03440296	$b_{3,1a}$ (iPrMgCl)	0.045764431
$b_{1,1b}$ (MeNHOMe)	0.0038946	$b_{2,1b}$ (MeNHOMe)	0.004445753	$b_{3,1b}$ (MeNHOMe)	0.006048123
$b_{1,1c}$ (HCl)	0.00232477	$b_{2,1c}$ (HCl)	0.002653768	$b_{3,1c}$ (HCl)	0.003610258
$b_{1,2a}$ (TESCl)	0.00064103	$b_{2,2a}$ (DMSO)	0	$b_{3,2a}$ (DMSO)	0.001942178
$b_{1,2b}$ (imidazole)	0.00109134	$b_{2,2b}$ (pyridine)	0.016530032	$b_{3,2b}$ (pyridine)	0.022275752
$b_{1,3}$ (Red-Al)	0.0184677	$b_{2,2c}$ (SO_3)	0.016730649	$b_{3,2c}$ (SO_3)	0.022546103
$b_{1,4a}$ ($EtPh_3P^+I^-$)	0.0283597	$b_{2,2d}$ (NEt_3)	0.031718147	$b_{3,2d}$ (NEt_3)	0.041392417
$b_{1,4b}$ (NaHMDS)	0.01373536	$b_{2,3a}$ (Br-allylsilane)	0.059444821	$b_{3,3a}$ (MeMgBr)	0.010258232
$b_{1,4c}$ (I_2)	0.01720975	$b_{2,3b}$ ($CrCl_2$)	0.050429823	$b_{3,3b}$ (H_2O)	0.0000805075
$b_{1,4d}$ (NaHMDS)	0.01243352	$b_{2,3c}$ (H_2O)	0	$b_{3,4a}$ (DMSO)	0.000349059
$b_{2,10a}$ (${}^tBuLi$)	-0.0021453	$b_{2,3d}$ (KH)	0.000399386	$b_{3,4b}$ (pyridine)	0.033498435
$b_{2,10b}$ (borane-OMe)	-0.0087807	$b_{2,4a}$ (DIBAH)	-0.002756416	$b_{3,4c}$ (SO_3)	0.03390499
$b_{2,11}$ (CF_3CO_2H)	-0.00475272	$b_{2,4b}$ (H_2O)	-0.000425166	$b_{3,4d}$ (NEt_3)	0.057709381
$b_{2,12}$ ($PhI(OAc)_2$)	-0.01596977	$b_{2,5a}$ (oxazoline)	-0.003186621		
$b_{2,13a,}$ (K_2CO_3)	0.00047305	$b_{2,5b}$ (Bu_2OTf)	-0.005027543	1+ Σ a, b	1.775404066
$b_{2,13b}$ (phosphonate)	-0.01020935	$b_{2,5c}$ (NEt_3)	0.000938155	(Eq.36 denomin.)	
$b_{2,14a}$ (isocyanate)	-0.00615131	$b_{2,5d}$ (H_2O)	-0.000724076	GAE Π ε	0.00254552
$b_{2,14b}$ (MeOH)	-0.00279428	$b_{2,6a}$ (lutidine)	0.003967077	(Eq. 36 numerator)	
$b_{2,15a}$ (DIBAH)	-0.01207214	$b_{2,6b}$ (TBSOTf)	0.006167181	GRME	0.0014337711
$b_{2,15b}$ (H_2O)	-0.0015771	$b_{2,7a}$ (mercaptan)	0.010297319		
$b_{2,16}$ (Dess-Martin)	-0.03466731	$b_{2,7b}$ (BuLi)	0.002165759		
$b_{2,17a}$ (chloroborane)	-0.01001185	$b_{2,7c}$ (H_2O)	-0.000988326		
$b_{1,17b}$ (NEt_3)	-0.00144743	$b_{2,8a}$ ($LiBH_4$)	0.00720056		
$b_{1,17c}$ (H_2O)	-0.00160881	$b_{2,8b}$ (EtOH)	-0.005053517		
$b_{2,18a}$ (borohydride)	0.00416905	$b_{2,9a}$ (Ph_3P)	-0.00891362		
$b_{2,18b}$ (CH_3CO_2H)	-0.0056584	$b_{2,9b}$ (I_2)	-0.010812347		
$b_{2,,z}$ (HCl)	0.26112022	$b_{2,9c}$ (imidazole)	-0.002877657		

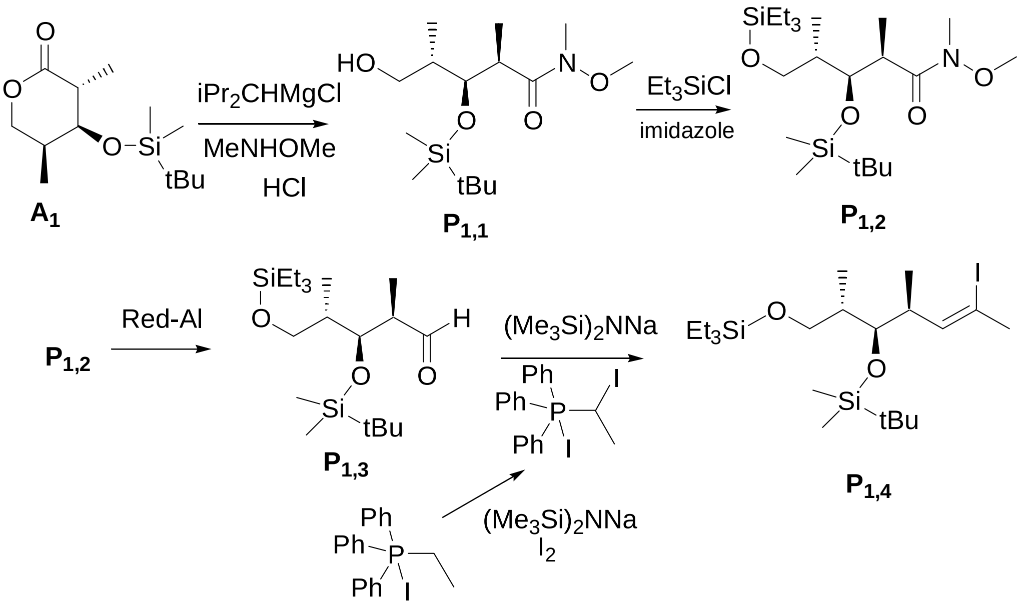
Table S3. Coefficients of Eq. 38

a_1 (**A_1**)	-0.00463631	a_2 (**A_2**)	-0.005597847		
$b_{1,1a}$ (iPrMgCl)	0.02409499	$b_{2,1a}$ (iPrMgCl)	0.023695571	$b_{3,1a}$ (iPrMgCl)	0.032658004
$b_{1,1b}$ (MeNHOMe)	0.00174918	$b_{2,1b}$ (MeNHOMe)	0.002183955	$b_{3,1b}$ (MeNHOMe)	0.003447975
$b_{1,1c}$ (HCl)	0.00104413	$b_{2,1c}$ (HCl)	0.001303651	$b_{3,1c}$ (HCl)	0.002058172
$b_{1,2a}$ (TESCl)	-0.00275907	$b_{2,2a}$ (DMSO)	-0.001692372	$b_{3,2a}$ (DMSO)	-0.000160296
$b_{1,2b}$ (imidazole)	-0.00061378	$b_{2,2b}$ (pyridine)	0.01132624	$b_{3,2b}$ (pyridine)	0.01585872
$b_{1,3}$ (Red-Al)	0.01018916	$b_{2,2c}$ (SO_3)	0.011463701	$b_{3,2c}$ (SO_3)	0.01605119
$b_{1,4a}$ ($EtPh_3P^+I^-$)	0.01331169	$b_{2,2d}$ (NEt_3)	0.022828809	$b_{3,2d}$ (NEt_3)	0.030460303
$b_{1,4b}$ (NaHMDS)	0.00686309	$b_{2,3a}$ (Br-allylsilane)	0.042708681	$b_{3,3a}$ (MeMgBr)	0.005509294
$b_{1,4c}$ (I_2)	0.08807804	$b_{2,3b}$ ($CrCl_2$)	0.034457016	$b_{3,3b}$ (H_2O)	-0.000326823

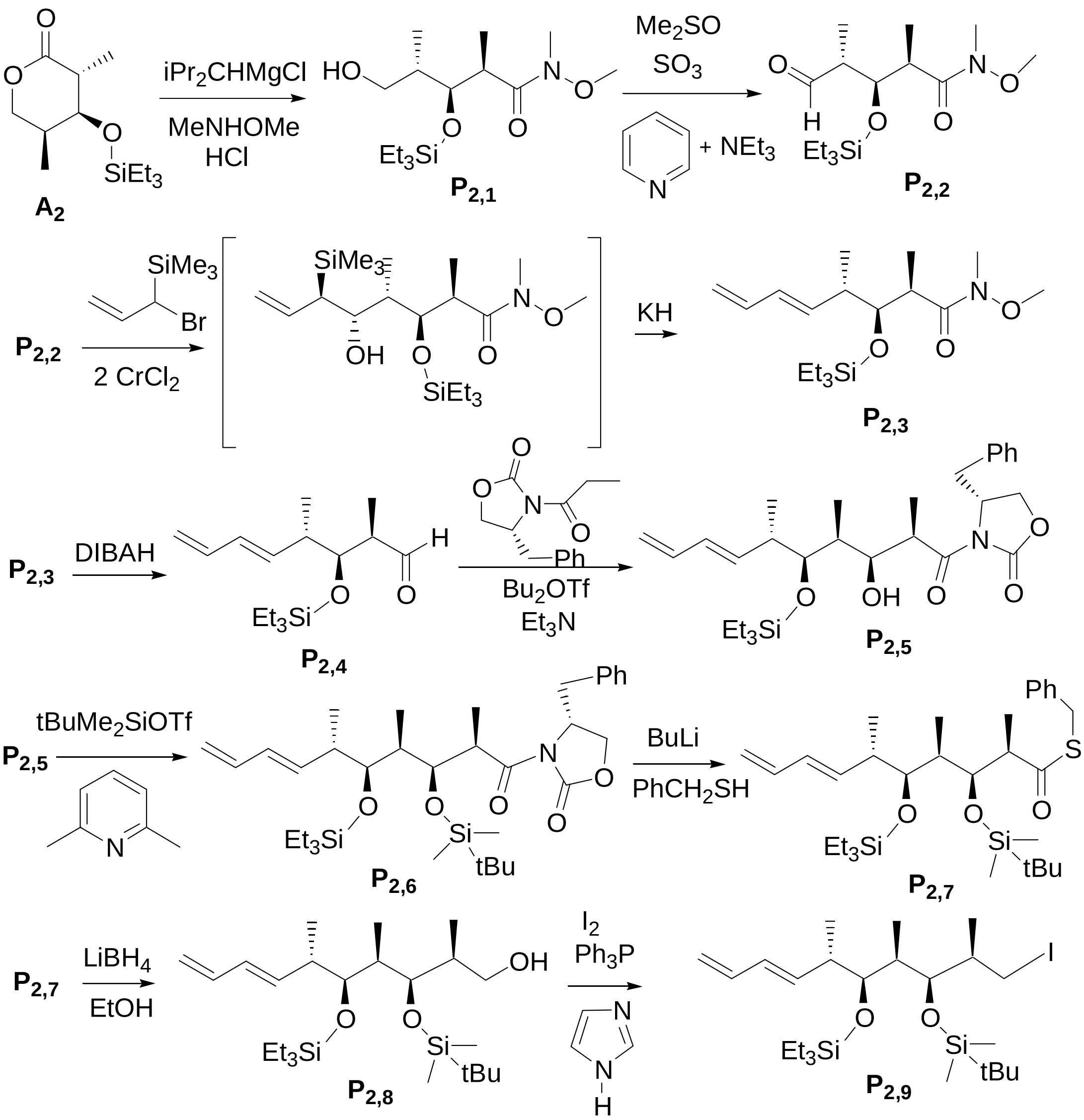
$b_{1,4d}$ (NaHMDS)	0.00583614	$b_{2,3c}$ (H_2O)	-0.000390331	$b_{3,4a}$ (DMSO)	-0.001417019
$b_{2,10a}$ (^tBuLi)	-0.00307994	$b_{2,3d}$ (KH)	-0.000553768	$b_{3,4b}$ (pyridine)	0.02471167
$b_{2,10b}$ (borane-OMe)	-0.01021991	$b_{2,4a}$ (DIBAH)	-0.005255008	$b_{3,4c}$ (SO_3)	0.025011584
$b_{2,11}$ (CF_3CO_2H)	-0.008668873	$b_{2,4b}$ (H_2O)	-0.00072572	$b_{3,4d}$ (NEt_3)	0.04333185
$b_{2,12}$ ($PhI(OAc)_2$)	-0.01957467	$b_{2,5a}$ (oxazoline)	-0.007566388	$b_{3,5a}$ (chloroborane)	-0.01484555
$b_{2,13a,}$ (K_2CO_3)	-0.0026206	$b_{2,5b}$ (Bu_2OTf)	-0.009903441	$b_{3,5b}$ (NEt_3)	-0.00333367
$b_{2,13b}$ (phosphonate)	-0.0149442	$b_{2,5c}$ (NEt_3)	-0.001451816	$b_{3,5c}$ (H_2O)	-0.00165943
$b_{2,14a}$ (isocyanate)	-0.00893335	$b_{2,5d}$ (H_2O)	-0.000961514	$b_{3,6a}$ (borohydride)	-0.00241027
$b_{2,14b}$ (MeOH)	-0.00289827	$b_{2,6a}$ (lutidine)	0.000808433	$b_{3,6b}$ (CH_3CO_2H)	-0.00576434
$b_{2,15a}$ (DIBAH)	-0.0156843	$b_{2,6b}$ (TBSOTf)	-0.000860917	$b_{3,,z}$ (HCl)	0.20361396
$b_{2,15b}$ (H_2O)	-0.00163442	$b_{2,7a}$ (mercaptan)	0.005432689		
$b_{2,16}$ (Dess-Martin)	-0.0365344	$b_{2,7b}$ (BuLi)	0.000320845	1+ Σ a, b	1.40051761
		$b_{2,7c}$ (H_2O)	-0.001169967	(Eq.38 denomin.)	
		$b_{2,8a}$ ($LiBH_4$)	0.005444233	GAE Π ε	0.00200802
		$b_{2,8b}$ (EtOH)	-0.005982282	(Eq. 38 numerator)	
		$b_{2,9a}$ (Ph_3P)	-0.012712918	GRME	0.0014337711
		$b_{2,9b}$ (I_2)	-0.014027033		
		$b_{2,9c}$ (imidazole)	-0.003744704		

Table S4. Coefficients of Eq. 42

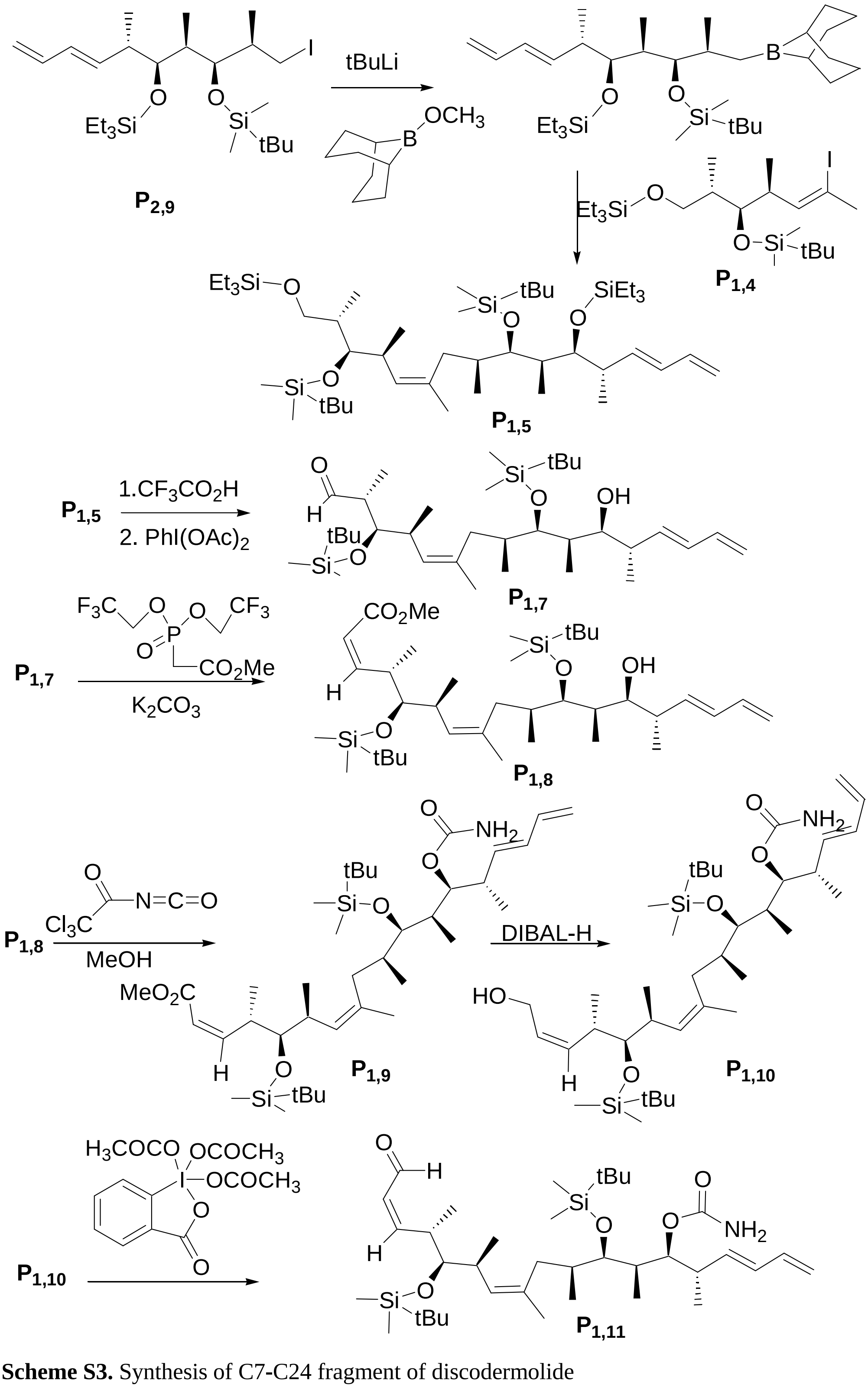
a_1 (**A_1**)	-0.00463631	a_2 (**A_2**)	-0.005597847		
$b_{1,1a}$ (iPrMgCl)	0.02409499	$b_{2,1a}$ (iPrMgCl)	0.023695571	$b_{3,1a}$ (iPrMgCl)	0.032658004
$b_{1,1b}$ (MeNHOMe)	0.00174918	$b_{2,1b}$ (MeNHOMe)	0.002183955	$b_{3,1b}$ (MeNHOMe)	0.003447975
$b_{1,1c}$ (HCl)	0.00104413	$b_{2,1c}$ (HCl)	0.001303651	$b_{3,1c}$ (HCl)	0.002058172
$b_{1,2a}$ (TESCl)	-0.00275907	$b_{2,2a}$ (DMSO)	-0.001692372	$b_{3,2a}$ (DMSO)	-0.000160296
$b_{1,2b}$ (imidazole)	-0.00061378	$b_{2,2b}$ (pyridine)	0.01132624	$b_{3,2b}$ (pyridine)	0.01585872
$b_{1,3}$ (Red-Al)	0.01018916	$b_{2,2c}$ (SO_3)	0.011463701	$b_{3,2c}$ (SO_3)	**0.01605119**
$b_{1,4a}$ ($EtPh_3P^+I^-$)	0.01331169	$b_{2,2d}$ (NEt_3)	0.022828809	$b_{3,2d}$ (NEt_3)	0.030460303
$b_{1,4b}$ (NaHMDS)	0.00686309	$b_{2,3a}$ (Br-allylsilane)	0.042708681	$b_{3,3a}$ (MeMgBr)	0.005509294
$b_{1,4c}$ (I_2)	0.08807804	$b_{2,3b}$ ($CrCl_2$)	0.034457016	$b_{3,3b}$ (H_2O)	-0.000326823
$b_{1,4d}$ (NaHMDS)	0.00583614	$b_{2,3c}$ (H_2O)	-0.000390331	$b_{3,4a}$ (DMSO)	-0.001417019
$b_{1,5a}$ (^tBuLi)	-0.00307994	$b_{2,3d}$ (KH)	-0.000553768	$b_{3,4b}$ (pyridine)	0.02471167
$b_{1,5b}$ (borane-OMe)	-0.01021991	$b_{2,4a}$ (DIBAH)	-0.005255008	$b_{3,4c}$ (SO_3)	0.025011584
$b_{1,6}$ (CF_3CO_2H)	-0.008668873	$b_{2,4b}$ (H_2O)	-0.00072572	$b_{3,4d}$ (NEt_3)	0.04333185
$b_{1,7}$ ($PhI(OAc)_2$)	-0.01957467	$b_{2,5a}$ (oxazoline)	-0.007566388	$b_{3,5a}$ (chloroborane)	-0.01484555
$b_{1,8a,}$ (K_2CO_3)	-0.0026206	$b_{2,5b}$ (Bu_2OTf)	-0.009903441	$b_{3,5b}$ (NEt_3)	-0.00333367
$b_{1,8b}$ (phosphonate)	-0.01494416	$b_{2,5c}$ (NEt_3)	-0.001451816	$b_{3,5c}$ (H_2O)	-0.00165943
$b_{1,9a}$ (isocyanate)	-0.00893335	$b_{2,5d}$ (H_2O)	-0.000961514	$b_{3,6a}$ (borohydride)	-0.00241027
$b_{1,9b}$ (MeOH)	-0.00289827	$b_{2,6a}$ (lutidine)	0.000808433	$b_{3,6b}$ (CH_3CO_2H)	-0.00576434
$b_{1,10a}$ (DIBAH)	-0.01568429	$b_{2,6b}$ (TBSOTf)	-0.000860917	$b_{3,,z}$ (HCl)	0.20361396
$b_{1,10b}$ (H_2O)	-0.00163442	$b_{2,7a}$ (mercaptan)	0.005432689		
$b_{1,11}$ (Dess-Martin)	-0.0365344	$b_{2,7b}$ (BuLi)	0.000320845	1+ Σ a, b	1.40051761
		$b_{2,7c}$ (H_2O)	-0.001169967	(Eq.38 denomin.)	
		$b_{2,8a}$ ($LiBH_4$)	0.005444233	GAE Π ε	0.00200802
		$b_{2,8b}$ (EtOH)	-0.005982282	(Eq. 38 numerator)	
		$b_{2,9a}$ (Ph_3P)	-0.012712918	GRME	0.0014337711
		$b_{2,9b}$ (I_2)	-0.014027033		
		$b_{2,9c}$ (imidazole)	-0.003744704		



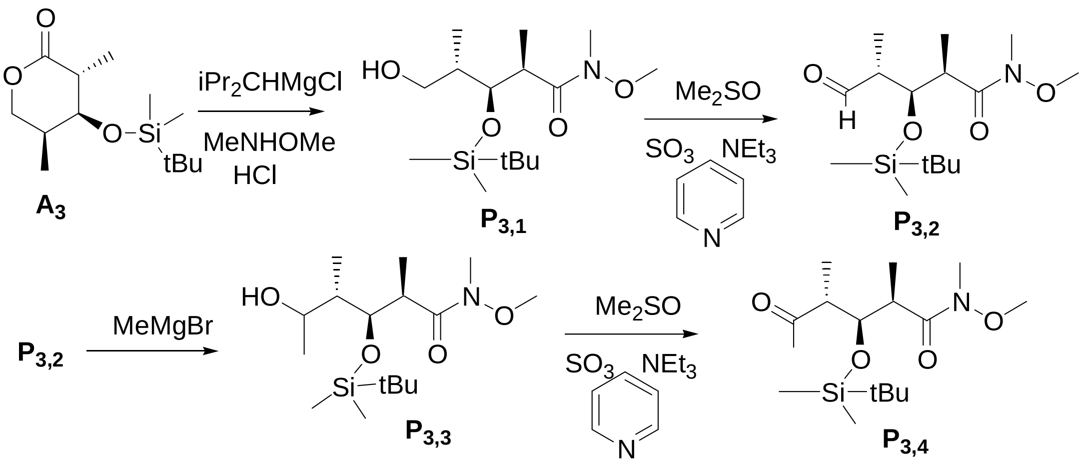
Scheme S1. Synthesis of C9-C14 fragment of discodermolide



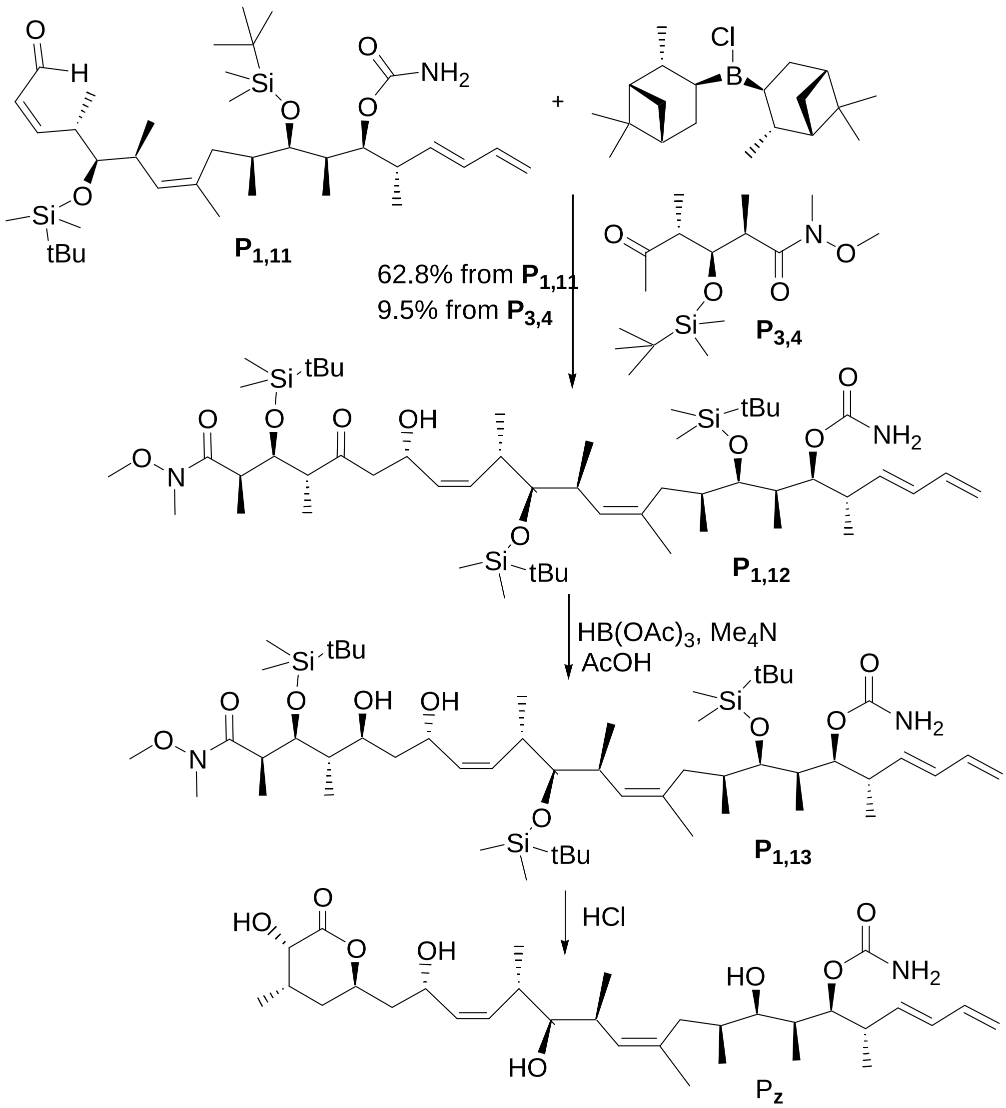
Scheme S2. Synthesis of C15-C24 fragment of discodermolide



Scheme S3. Synthesis of C7-C24 fragment of discodermolide



Scheme S4. Synthesis of C1-C6 fragment of discodermolide



Scheme S5. Final steps of the synthesis of discodermolide