Enantioselective Total Synthesis of (–)-Cyathin B2: A Desymmetric Double-Allylboration Approach

Jianping Wang, Jiacheng Yin, Hayatullah Imtiaz, Hongyu Wang, and Yun Li*
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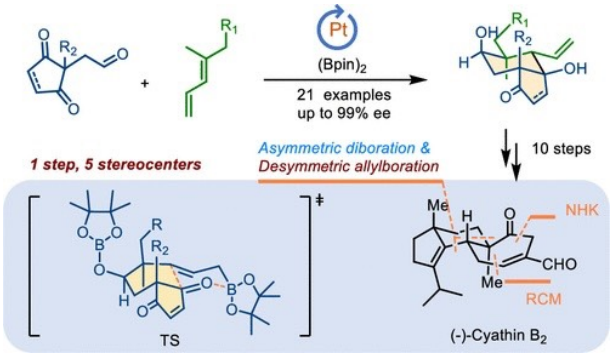
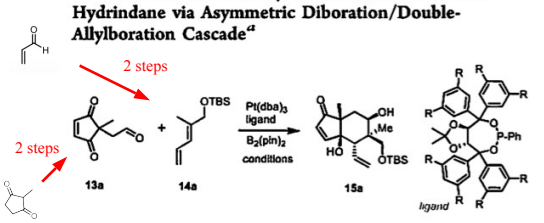


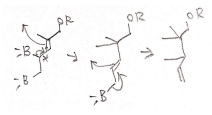
Table 1. Studies on the Synthesis of Functionalized Hydrindane via Asymmetric Diboration/Double-Allylboration Cascade[a]



entry	ligand	-R	solvent	temp. (°C)	yield[c] (%)	ee (%)
1	none	-	toluene	100	0	N.D.
2	PPh_3	-	toluene	100	0	N.D.
3	$P(OEt)_3$	-	toluene	100	0	N.D.
4	L1	H	toluene	100	trace	1
5	L2	Me	toluene	100	21	25
6	L3	Et	toluene	100	32	37
7	L4	CF_3	toluene	100	0	N.D.
8	L5	*i*-Pr	toluene	100	75	90
9	L6	*t*-Bu	toluene	100	52	90
10	L5	*i*-Pr	xylene	100	25	69
11	L5	*i*-Pr	THF	100	60	83
12	L5	*i*-Pr	PhCl	100	18	67
13	L5	*i*-Pr	toluene	80	27	90
14	L5	*i*-Pr	toluene	120	72	90
15	L5	*i*-Pr	toluene	160	64	86

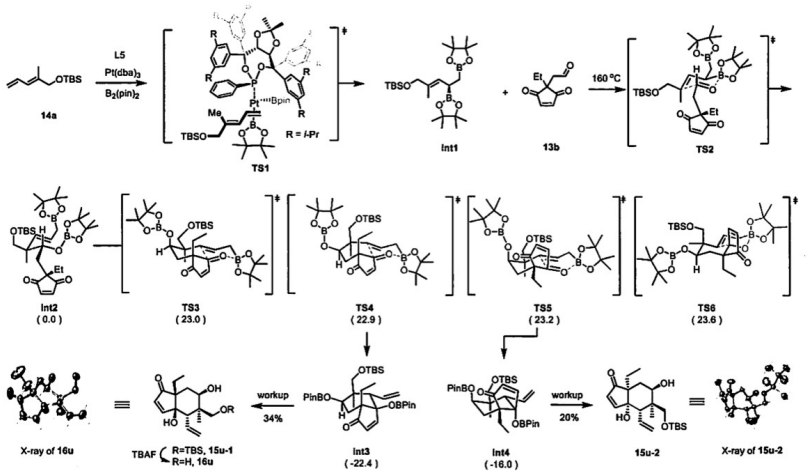
[a]The reactions were conducted by combining a catalyst (2.0 mol %), ligand (2.4 mol %), and $B_2(pin)_2$ (1.05 equiv) with a solution of 14a (1.0 equiv) under an argon atmosphere in a solvent (1.0 M) at 60 °C. The mixture was stirred until TLC indicated a complete consumption of 14a. Subsequently, 13a (1.0 equiv) was introduced into the reaction mixture and stirred for an additional 24 h at the specified temperature. [b]$B_2(pin)_2$ = Bis(pinacolato)diboron.

mechanism

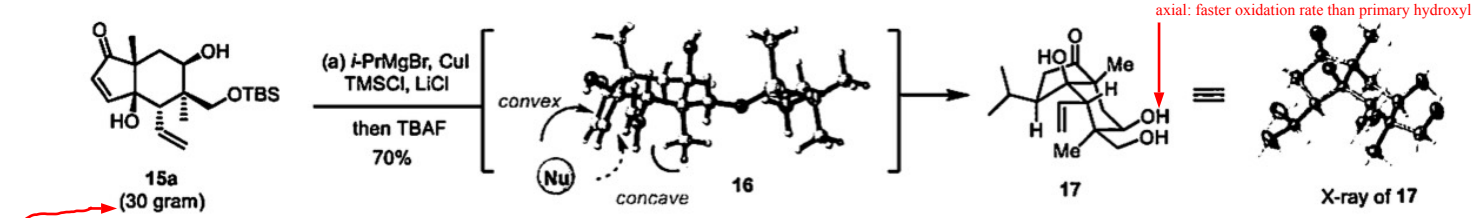


introduce an additional quaternary stereocenter through

Scheme 3. Stereochemical Model for the Double-Allylboration Step[a]

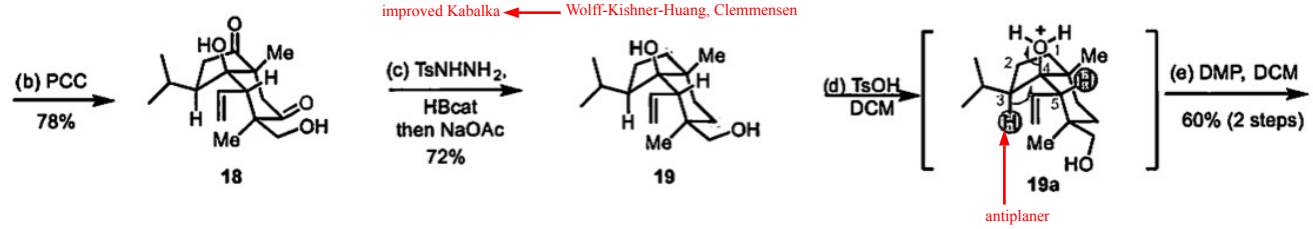


Scheme 4. Enantioselective Total Synthesis of (–)-Cyathin B_2[a]



scalability was crudial for early stage synthetic strategies

improved Kabalka ← Wolff-Kishner-Huang, Clemmensen



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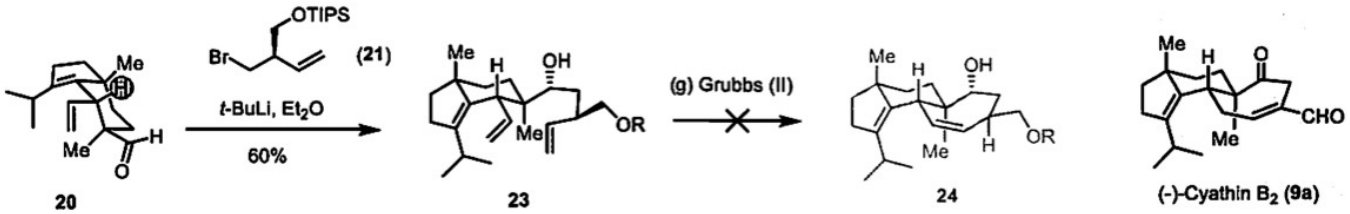
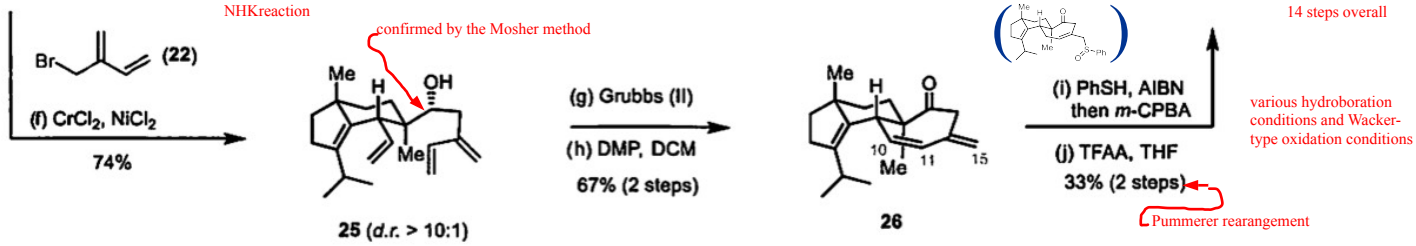


NHKreaction

confirmed by the Mosher method



14 steps overall

various hydroboration conditions and Wacker-type oxidation conditions

Pummerer rearangement

[a]Reagents and conditions: (a) LiCl (15.0 equiv), CuI (10.0 equiv), HMPA (5.0 equiv), TMSCl (5.0 equiv), ^{i}PrMgBr (5.0 equiv), THF (0.2 M), −78 °C, 4 h, then TBAF (1.5 equiv), THF (0.2 M), 0 °C, 15 min (70%); (b) PCC (1.1 equiv), DCM (0.2 M), 0 °C, 1 h, (78%); (c) $TsNHNH_2$ (2.1 equiv), toluene (0.1 M), 130 °C, 5 h; then HBCat (5.0 equiv), DCM (0.1 M), 0 °C, 12 h, then AcOH (2.0 equiv) 24 h; then $NaOAc{\cdot}3H_2O$ (30.0 equiv), 55 °C, 24 h (72%); (d) TsOH (0.1 equiv), DCM (0.1 M), 0 °C, 1 h, (71%); (e) DMP (1.0 equiv), DCM (0.1 M), − 10 °C, 3 h (85%); (f) $CrCl_2$ (5.0 equiv), $NiCl_2$ (0.15 equiv), Mn (1.0 equiv), 22 (5.0 equiv), TMSCl (5.0 equiv). THF, r.t. 4 h, (74%); (g) Grubbs-II (0.2 equiv), toluene (0.01 M), 45 °C, 1.5 h (73%); (h) DMP (1.0 equiv), DCM (0.1 M), −10 °C, 1 h (92%); (i) AIBN (1.0 equiv), PhSH (3.0 equiv), toluene (0.1 M), 80 °C, 1.5 h then *m*-CPBA (1.0 equiv), DCM (0.1 M), −78 °C, 10 min (55% in 2 steps); (j) TFAA (2.0 equiv), THF (0.1 M), 0 °C to r.t, 4 h, (60%).