Catalytic Asymmetric Synthesis of α-Alkylidene-β-hydroxy Esters via Dynamic Kinetic Asymmetric Transformation Involving Ba-Catalyzed Direct Aldol Reaction

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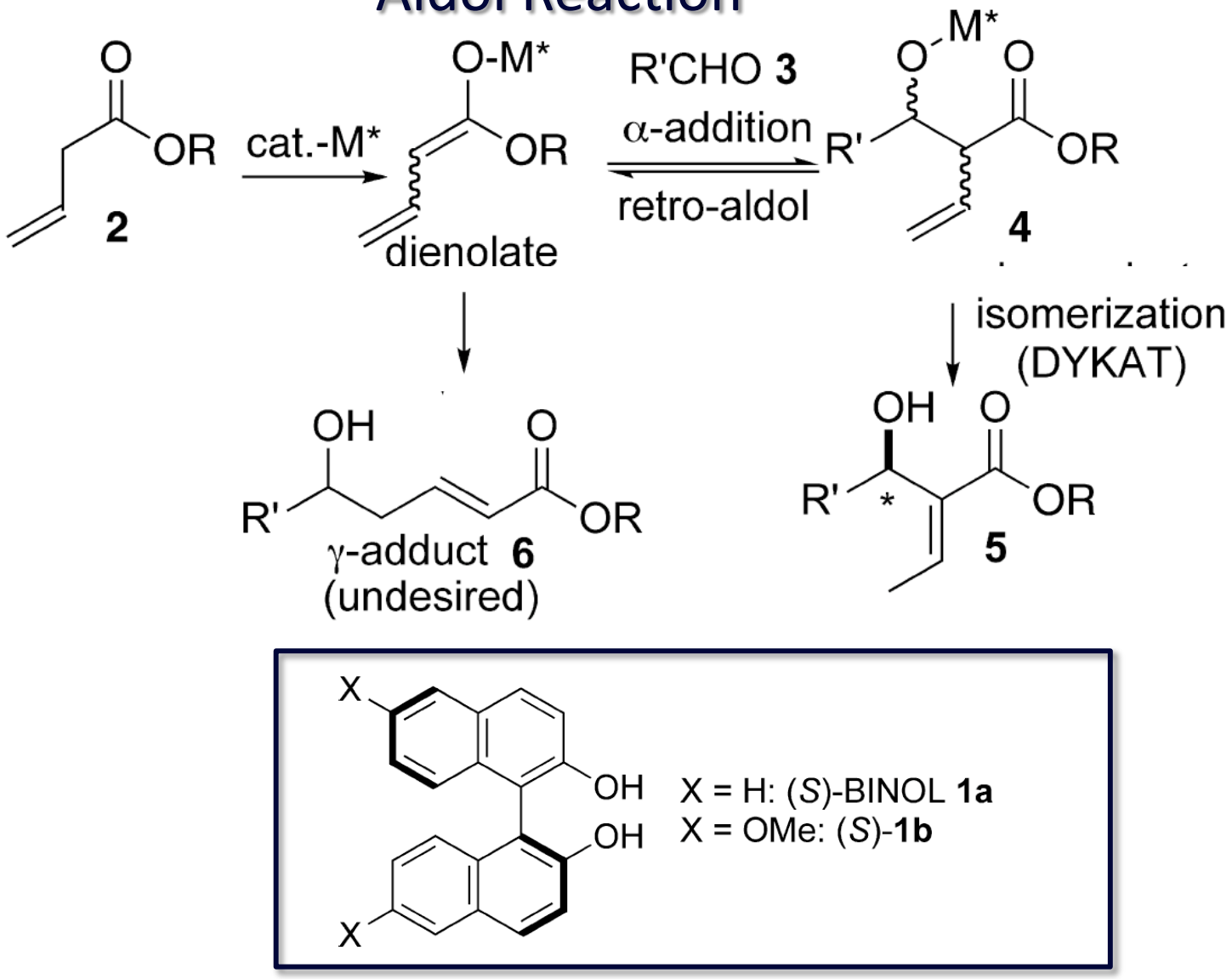
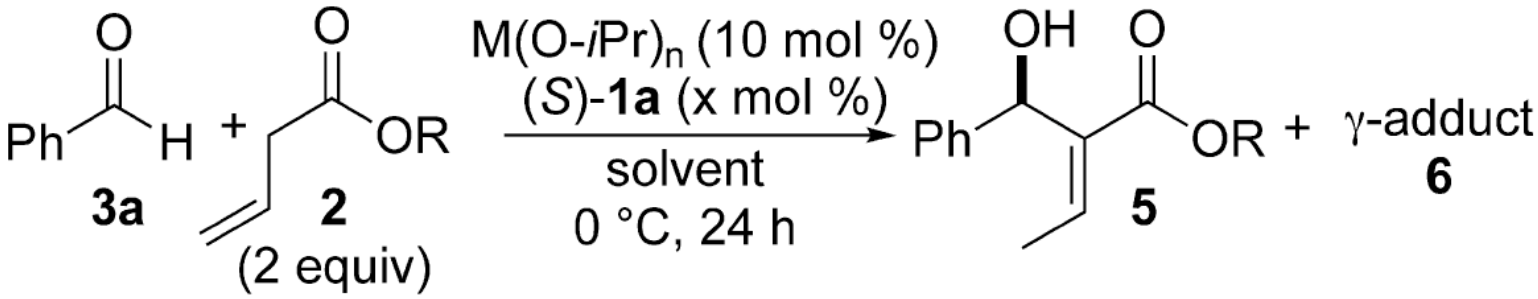
Working Hypothesis of DYKAT Involving Direct Aldol/Retro-Aldol Reaction



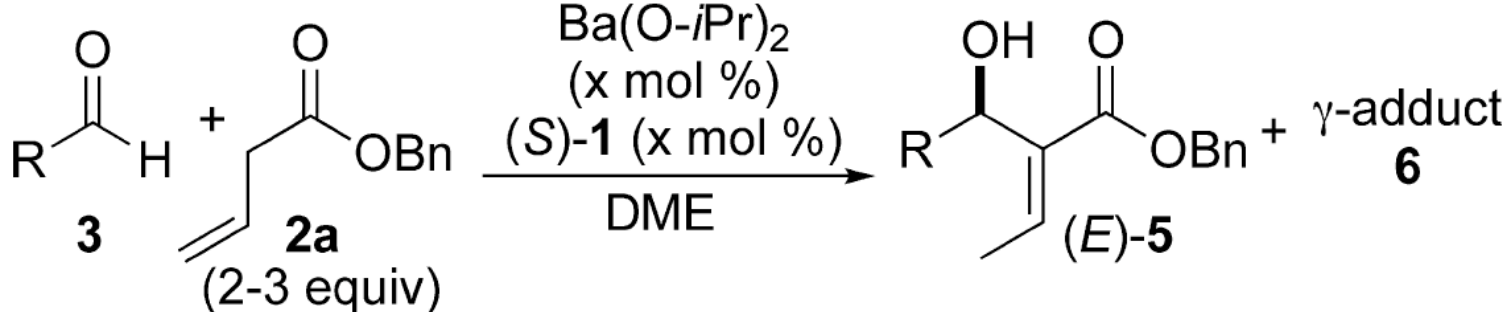
Optimization of Reaction Conditions



2a: R = Bn; **2b**: R = Et; **2c**: R = *t*Bu

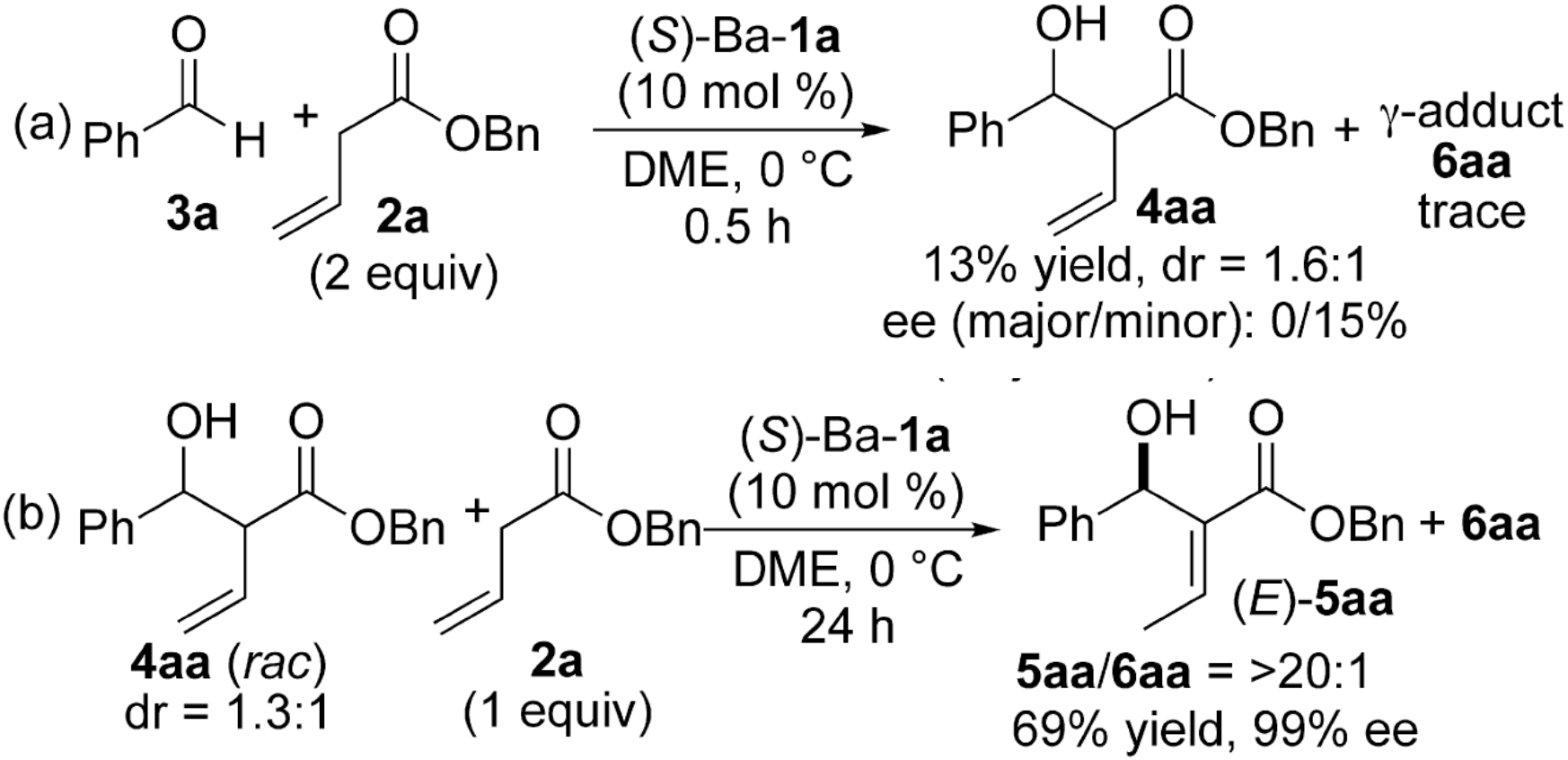
entry	M	*x*	**2**	solvent	**5**/**6**[a]	% yield of **5**	% ee of **5**
1	Ba(O-*i*Pr)$_2$	10	**2a**	THF	1.8:1	41	91
2	Ba(O-*i*Pr)$_2$	10	**2a**	1:9 THF/toluene	–	trace	–
3	Ba(O-*i*Pr)$_2$	10	**2a**	1:9 THF/EtOAc	0.8:1	4	69
4	Ba(O-*i*Pr)$_2$	10	**2a**	1:9 THF/DME	11:1	79	98
5	Li(O-*i*Pr)	5	**2a**	1:9 THF/DME	1.6:1	8	9[b]
6	La(O-*i*Pr)$_3$	15	**2a**	1:9 THF/DME	–	0	–
7	Ba(O-*i*Pr)$_2$	10	**2a**	DME	>20:1	85	99
8	Ba(O-*i*Pr)$_2$	10	**2b**	DME	5.6:1	69	99
9	Ba(O-*i*Pr)$_2$	10	**2c**	DME	–	trace	–

Ba-Catalyzed Asymmetric Synthesis of α-Alkylidene-β-hydroxy Esters via DYKAT



entry	R	3	1 (*x*)	temp (°C)	time (h)	5	5/6[b]	% yield of 5[c]	% ee
1	Ph	**3a**	**1a** (10)	0	24	**5aa**	>20:1	85	99
2	4-MeC_6H_4	**3b**	**1a** (10)	0	42	**5ba**	17:1	77	98
3	3-$MeOC_6H_4$	**3c**	**1b** (10)	−20	24	**5ca**	15:1	81	99
4	3-BrC_6H_4	**3d**	**1a** (10)	0	42	**5da**	>20:1	78	96
5	2-thienyl	**3e**	**1a** (10)	0	34	**5ea**	>20:1	80	98
6	3-thienyl	**3f**	**1b** (10)	−20	40	**5fa**	>20:1	85	97
7	3-furyl	**3g**	**1a** (10)	0	34	**5ga**	>20:1	82	98
8	(*E*)-PhCH=CH	**3h**	**1b** (10)	−20	28	**5ha**	>20:1	63	99
9	*i*Bu	**3i**	**1b** (10)	0	42	**5ia**	>20:1	76	91
10	*n*Pr	**3j**	**1a** (10)	0	48	**5ja**	>20:1	53	87
11	Ph	**3a**	**1a** (5)	0	55	**5aa**	>20:1	84	99

Mechanistic Studies of Ba-Catalyzed DYKAT



Mechanistic Studies of Ba-Catalyzed DYKAT