Synthesis of (+)-Saxitoxin Facilitated by a Chiral Auxiliary for Photocycloadditions Involving Alkenylboronate EstersClick to copy article link

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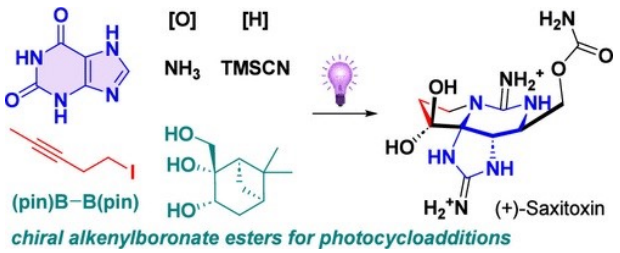
Kishi's groundbreaking total synthesis in 1977

Jacobi, Du Bois, Nagasawa, Looper, Chida

summary

strategic equivalency of the Michael addition for 1,5-dicarbonyl motif.
the efficient and quantitative exchange of the pinacol ligand on B(pin) with 15.



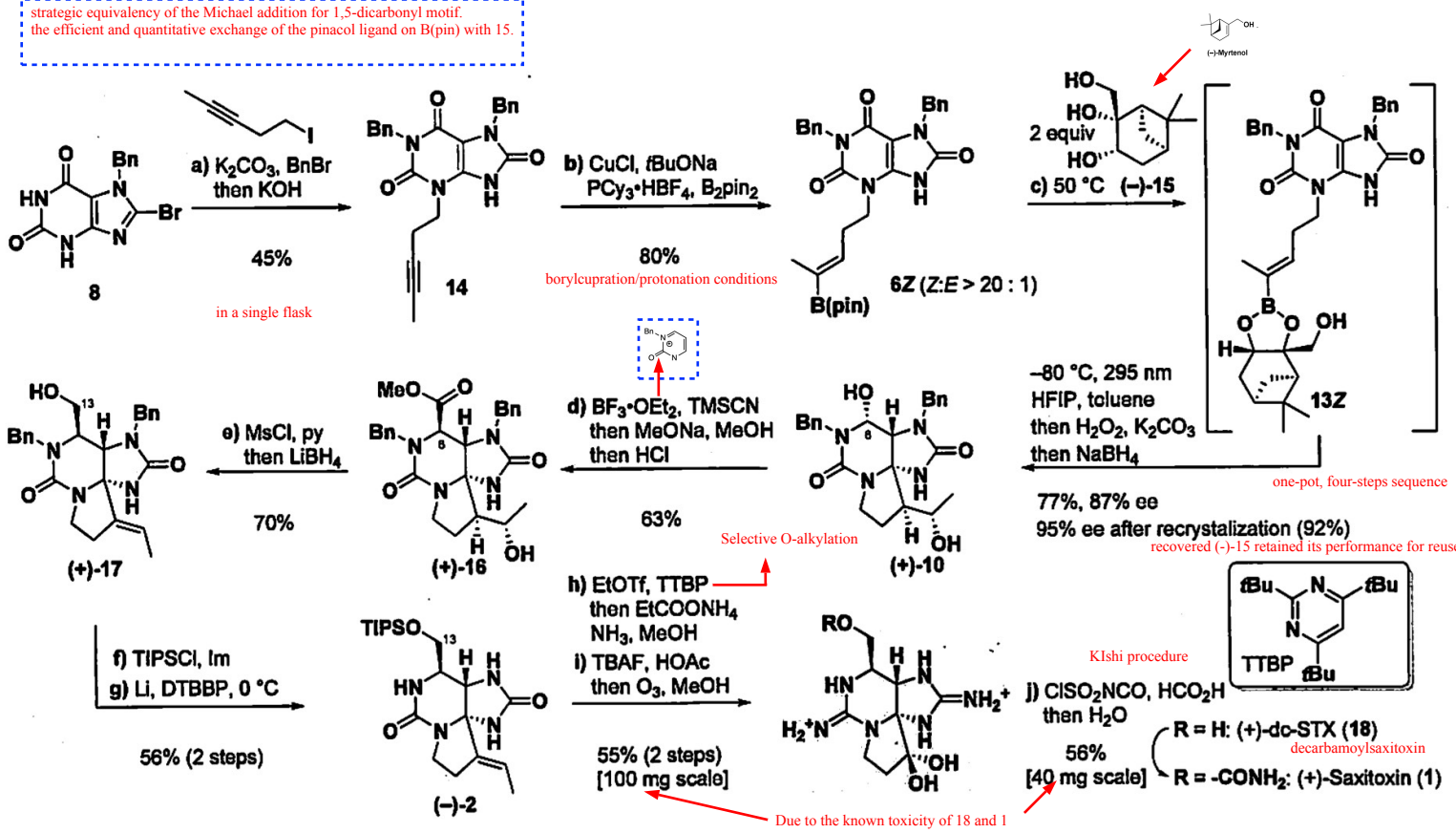
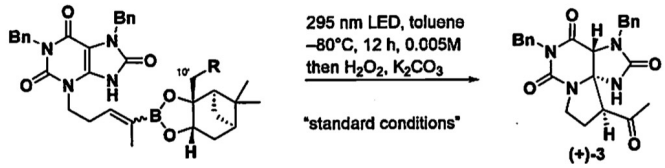


Figure 2. Total synthesis of (+)-saxitoxin (1). All reactions were carried out on a gram-scale if not specified.

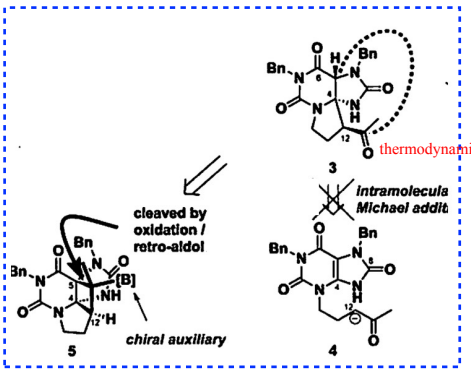
the preferential oxidation of the major

Table 1. Enantioselective Synthesis of (+)-3 via Identification of a Chiral Auxiliary[a]



entry	R	ratio (Z/E)	conditions	yield (%)	ee (%)
1	H (*ent*-11)	1 : 0.8	standard	76	–30
2	OTBDPS (12)	1 : 0.8	standard	71	50
3	OTBDPS (12)	1 : 0.8	$NaBO_3$ instead of H_2O_2, K_2CO_3	55	75
4	OTBDPS (12)	1 : 0.8	H_2O_2, $NaHCO_3$ instead of H_2O_2, K_2CO_3	50	84
5	OH (13)	1 : 0.75	standard	69	65
6	OH (13)	1 : 0.75	TFE (60 equiv)	65	74
7	OH (13)	1 : 0.75	HFIP (60 equiv)	70	83
8	OH (13)	1 : 0.75	HFIP (60 equiv), –40 °C	71	65
9	OH (13)	1 : 0.75	HFIP (60 equiv), toluene/ether = 4 : 1	58	47
10	OH (13)	1 : 0.75	HFIP (9 equiv)	73	76
11	OH (13*E*)	*E*	HFIP (60 equiv)	77	74
12	OH (13*Z*)	*Z*	HFIP (60 equiv)	70	90
13[b]	OH (13*Z*)	*Z*	HFIP (60 equiv)	75	89

be converted into a tertiary alcohol, thereby



Attempts to isolate the cycloaddition product were un-successful.

the C8-carbonyl, being a stronger H-bond acceptor, may better