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Communication

Total Synthesis of (±)-Rubriflordilactone A

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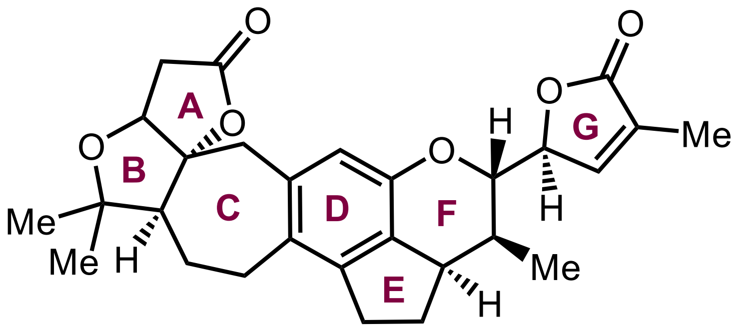
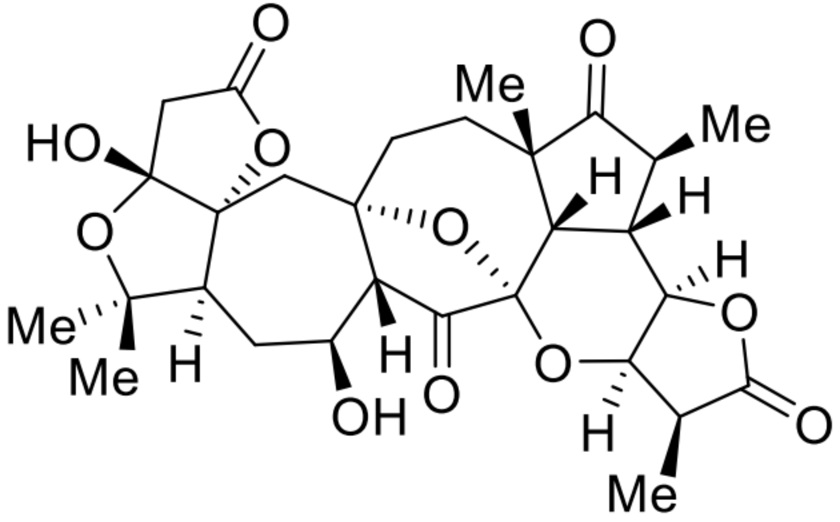
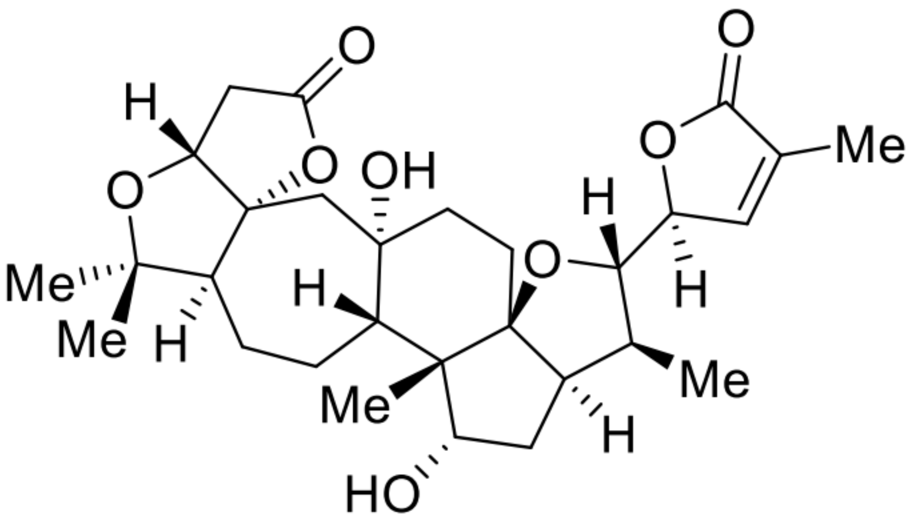


Rubriflordilactone A (**3**)

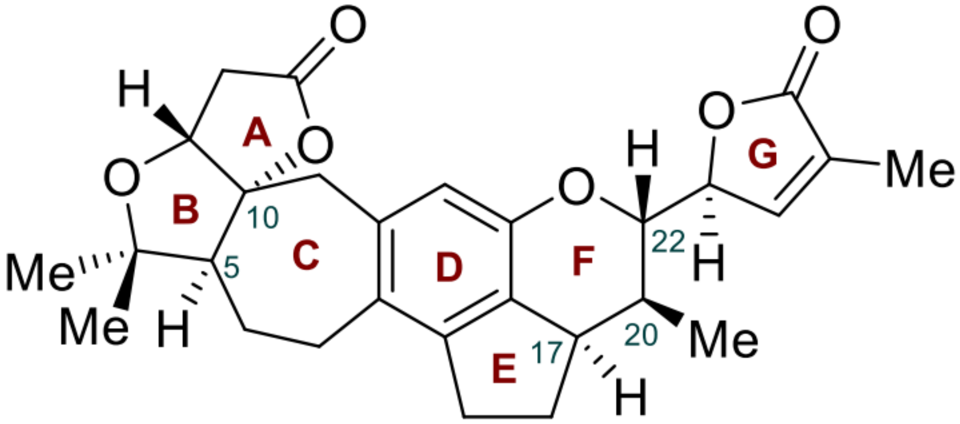
J. Am. Chem. Soc., **2024**, *146*, 7198.



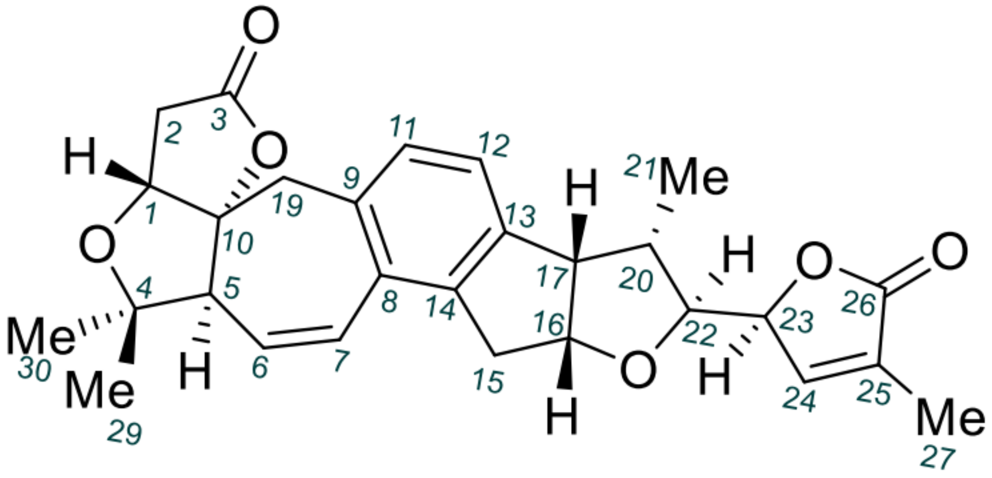
schindilactone A (**1**)



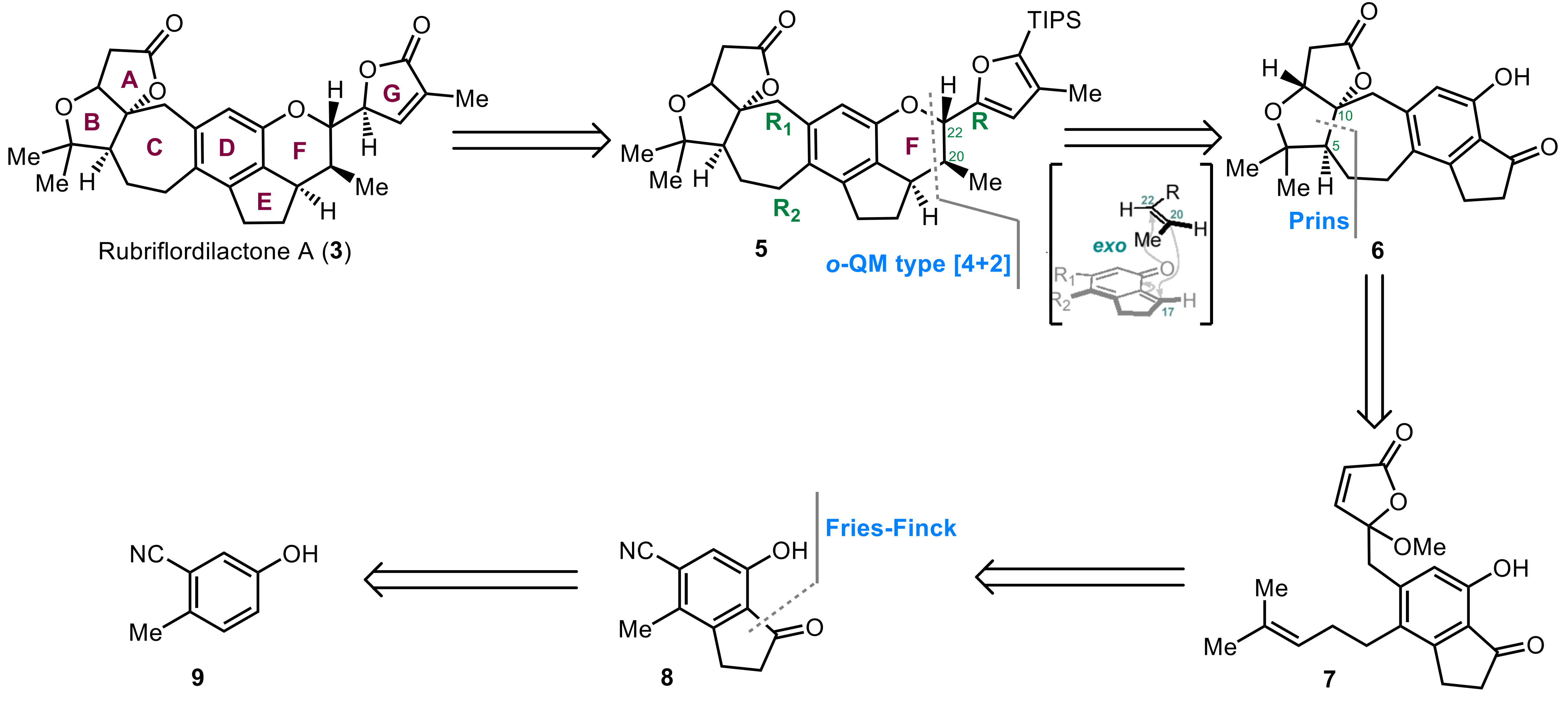
wuweizidilactone D (**2**)



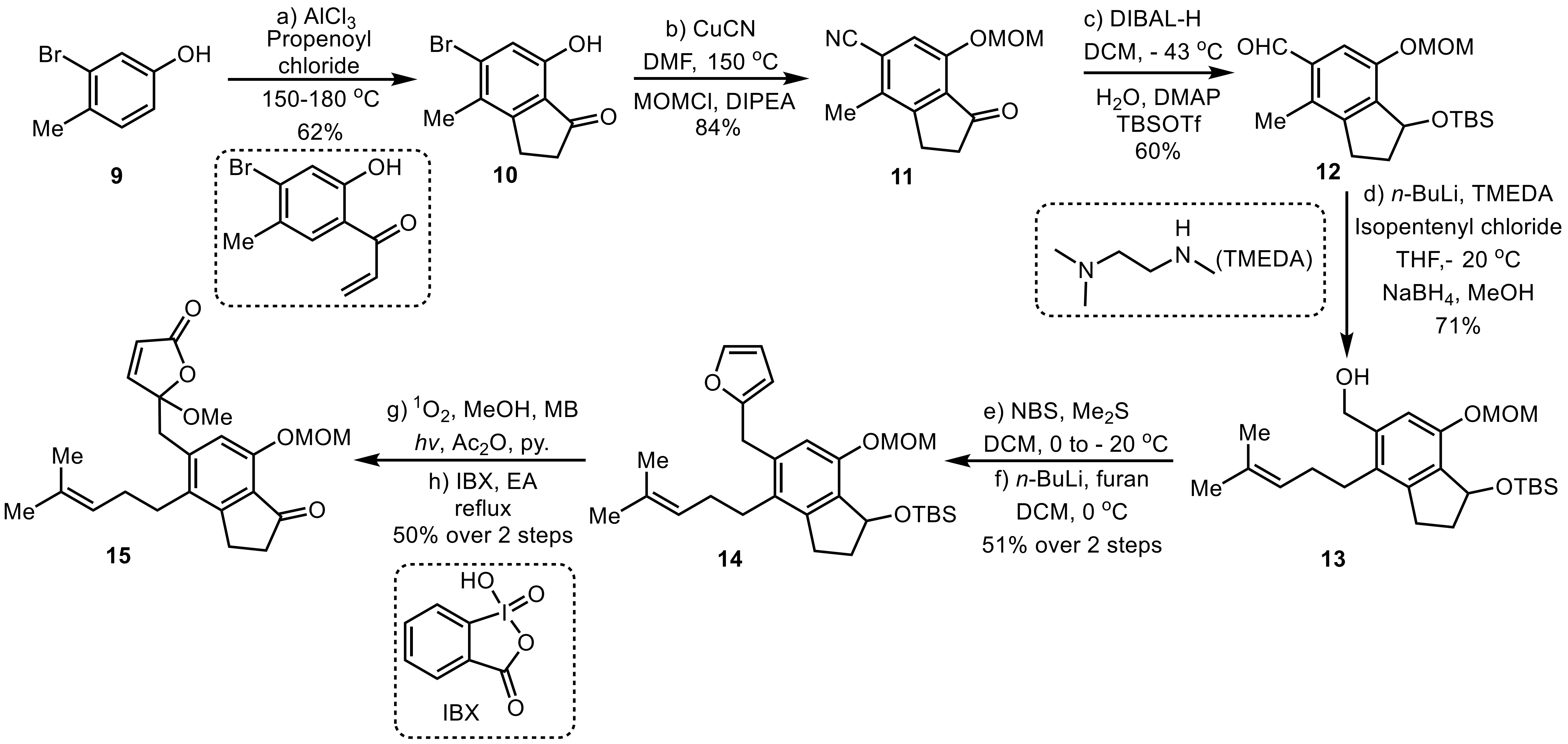
rubriflordilactone A (**3**)



rubriflordilactone B (**4**)



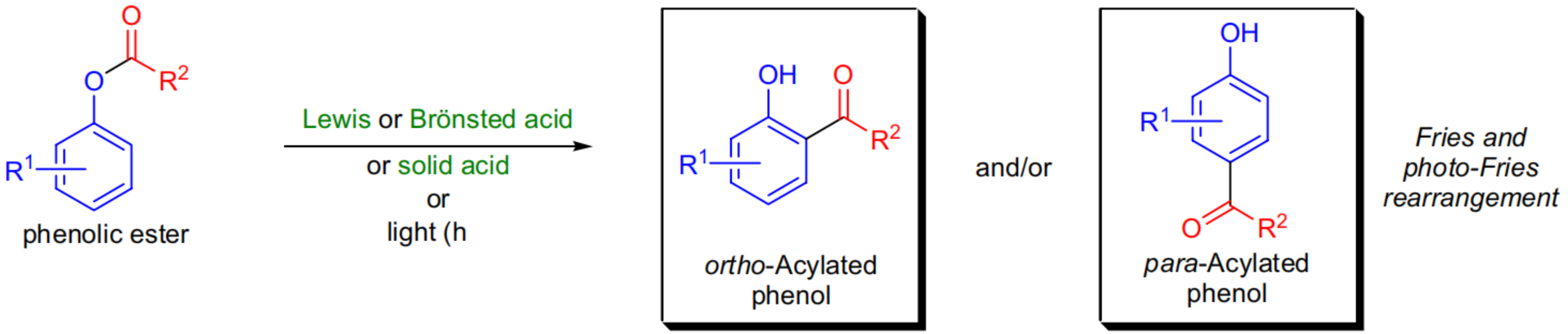
Rubriflordilactone A (3)
5
o-QM type [4+2]
exo
6
Prins
7
8
Fries-Finck
9

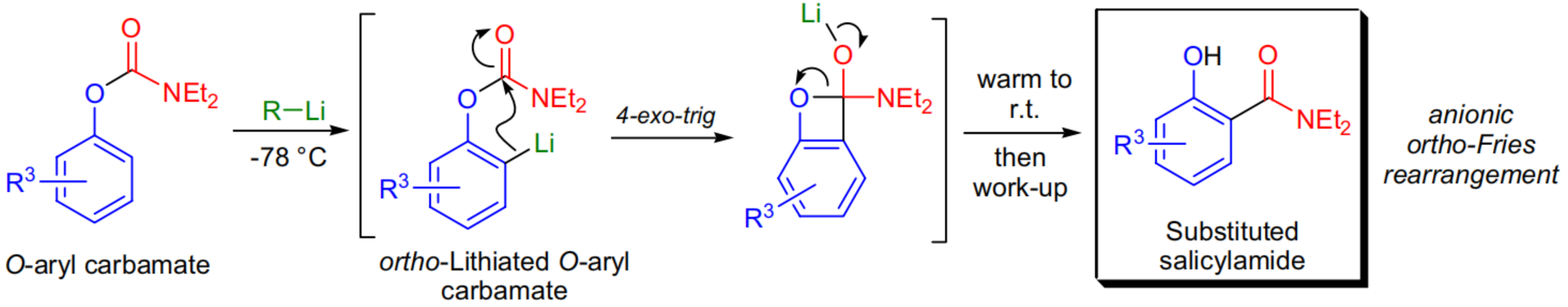


a) AlCl3
Propenoyl chloride
150-180 °C
62%
b) CuCN
DMF, 150 °C
MOMCl, DIPEA
84%
c) DIBAL-H
DCM, - 43 °C
H2O, DMAP
TBSOTf
60%
d) n-BuLi, TMEDA
Isopentenyl chloride
THF,- 20 °C
NaBH4, MeOH
71%
(TMEDA)
e) NBS, Me2S
DCM, 0 to - 20 °C
f) n-BuLi, furan
DCM, 0 °C
51% over 2 steps
g) 1O2, MeOH, MB
hv, Ac2O, py.
h) IBX, EA
reflux
50% over 2 steps
IBX
9
10
11
12
13
14
15

FRIES-, PHOTO-FRIES, AND ANIONIC ORTHO-FRIES REARRANGEMENT

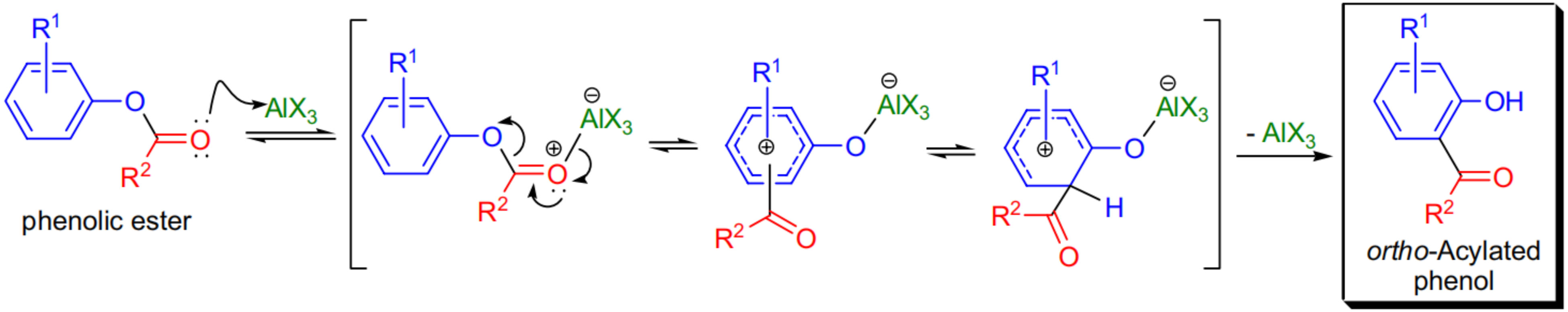
(References are on page 590)





R^1 = alkyl, -OR,-NR_2, -aryl; R^2 = alkyl, aryl; R^3 = alkyl, -OR, Cl

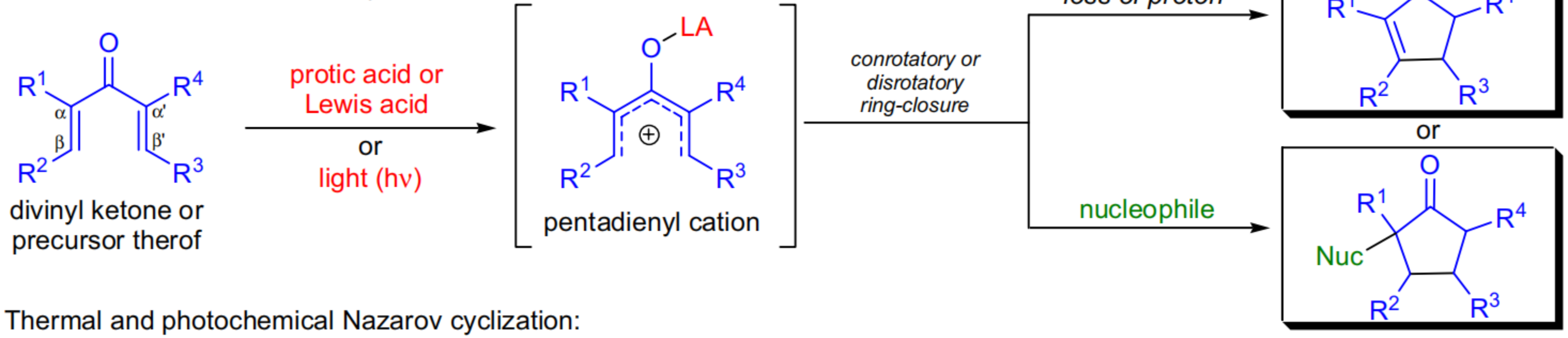
Mechanism:



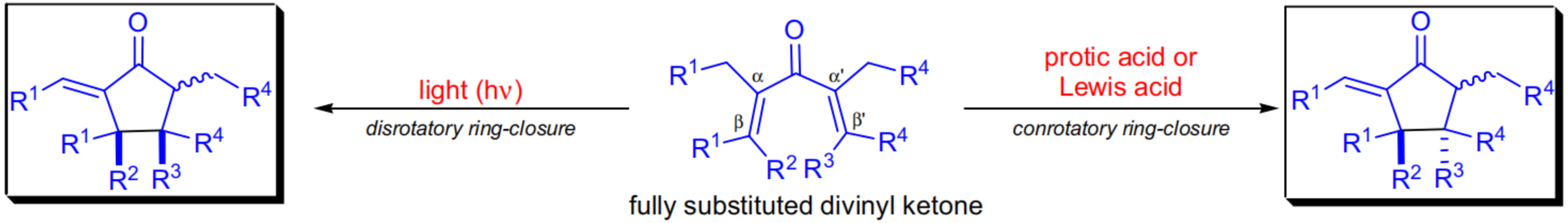
NAZAROV CYCLIZATION

(References are on page 635)

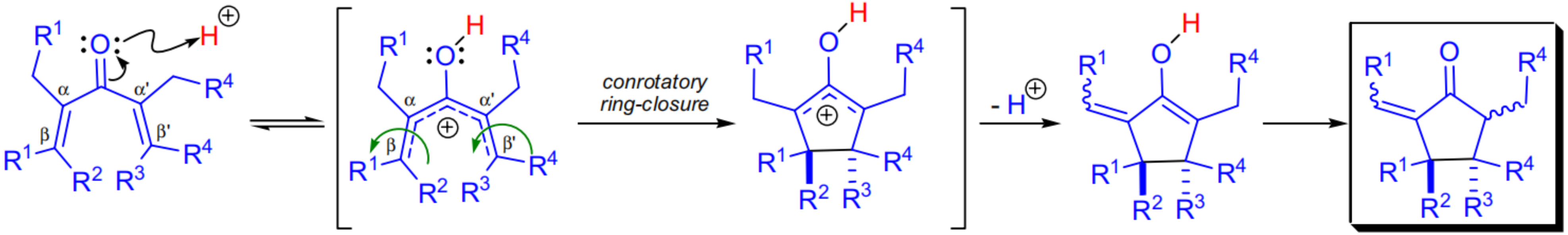
General scheme for Nazarov cyclization:

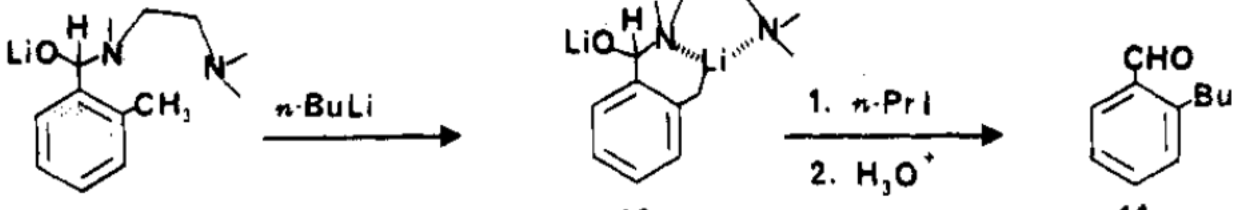


Thermal and photochemical Nazarov cyclization:



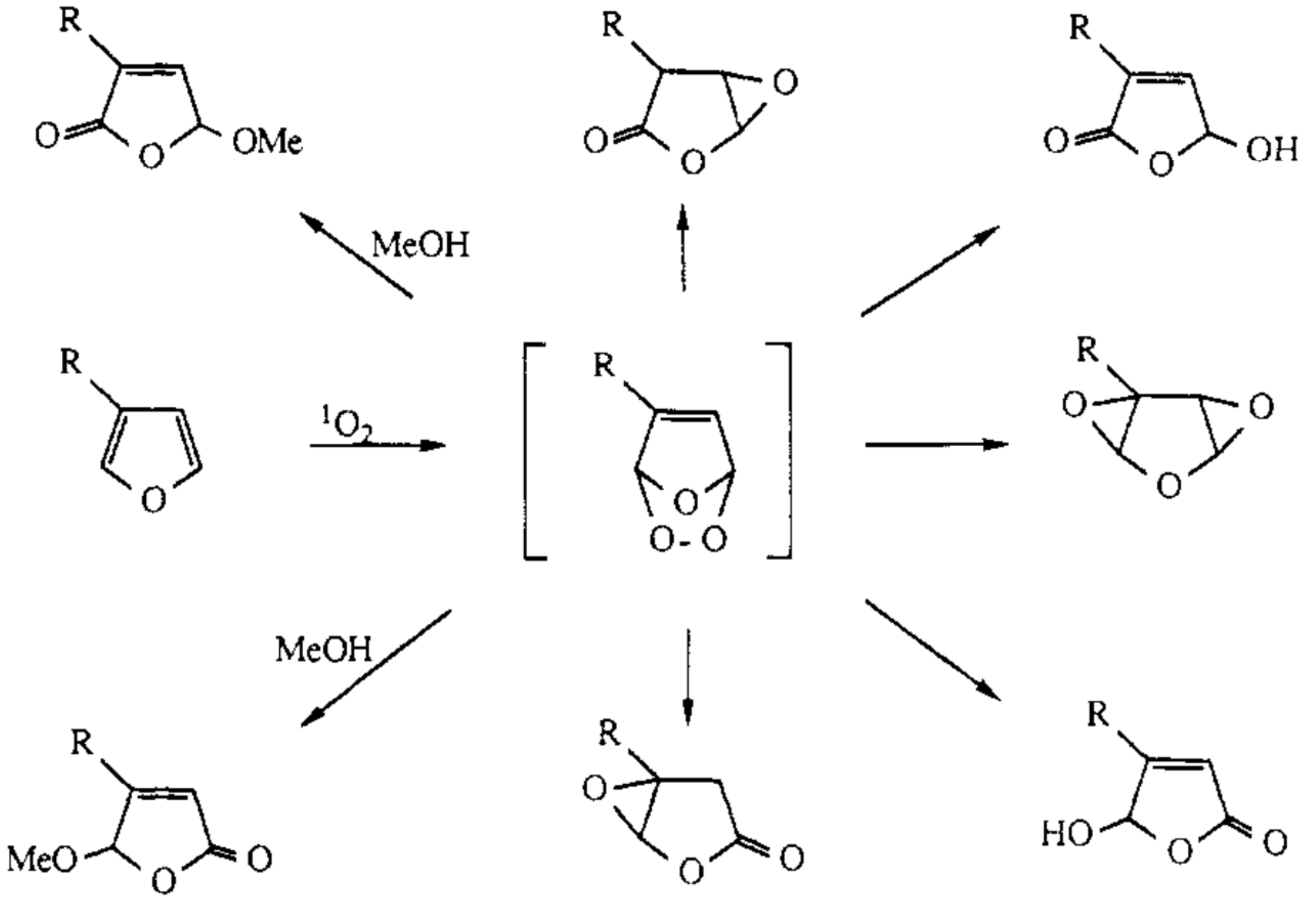
Mechanism:

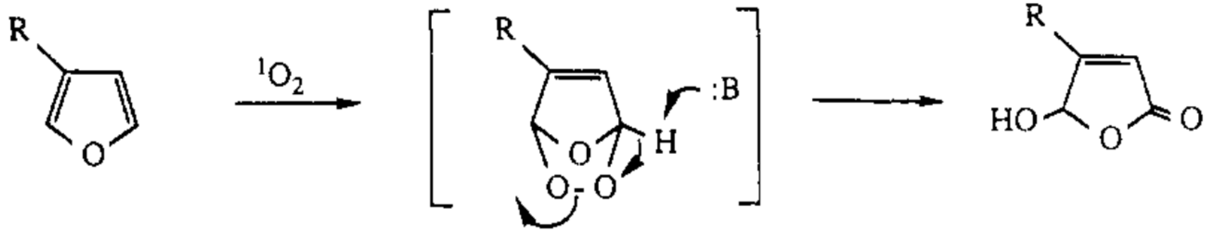




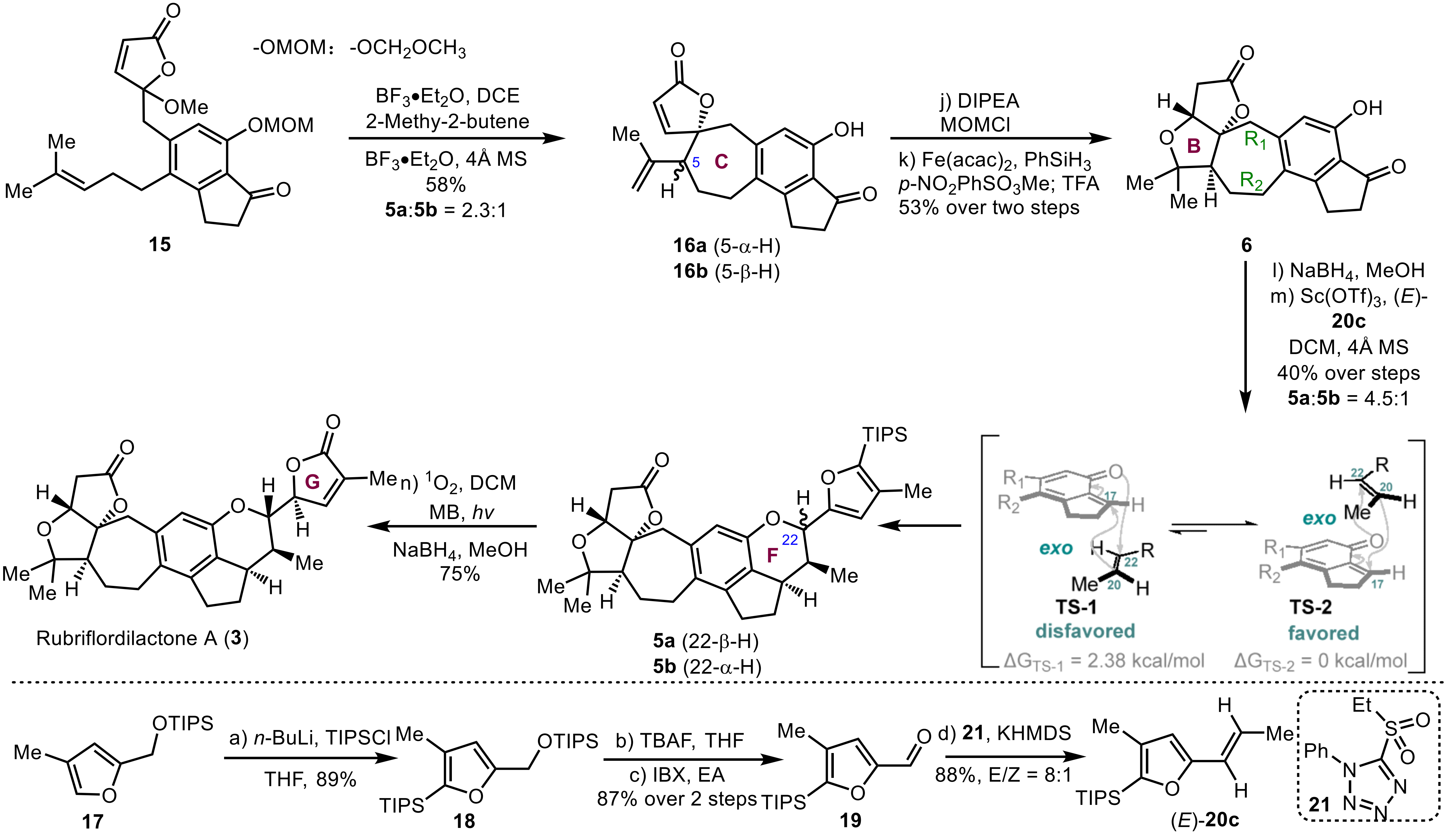
9 10 11

J. Org. Chem., **1984**, *49*, 1078.

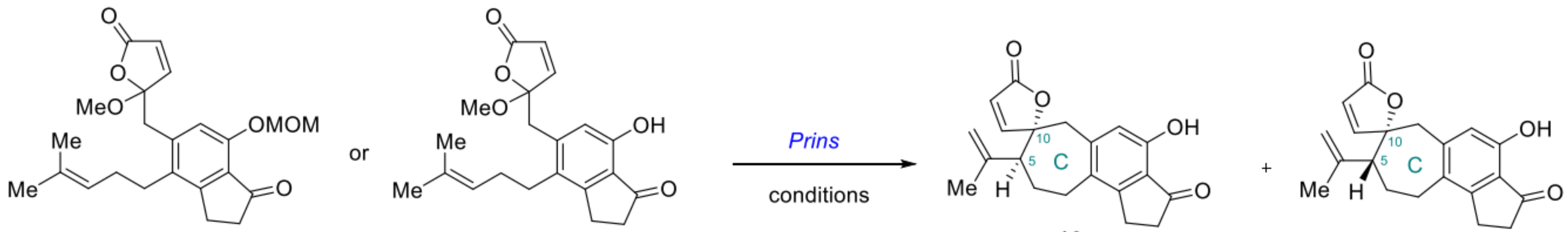




J. Org. Chem., **1988**, *53*, 2773.

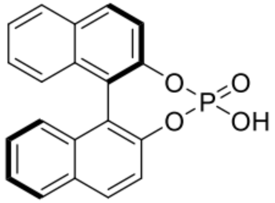


-OMOM: -OCH2OCH3
BF3•Et2O, DCE
2-Methy-2-butene
BF3•Et2O, 4Å MS
58%
5a:5b = 2.3:1
15
16a (5-α-H)
16b (5-β-H)
j) DIPEA
MOMCl
k) Fe(acac)2, PhSiH3
p-NO2PhSO3Me; TFA
53% over two steps
6
l) NaBH4, MeOH
m) Sc(OTf)3, (E)-
20c
DCM, 4Å MS
40% over steps
5a:5b = 4.5:1
TS-1
disfavored
ΔGTS-1 = 2.38 kcal/mol
TS-2
favored
ΔGTS-2 = 0 kcal/mol
exo
5a (22-β-H)
5b (22-α-H)
n) 1O2, DCM
MB, hv
NaBH4, MeOH
75%
Rubriflordilactone A (3)
a) n-BuLi, TIPSCl
THF, 89%
b) TBAF, THF
c) IBX, EA
87% over 2 steps
d) 21, KHMDS
88%, E/Z = 8:1
17
18
19
(E)-20c
21

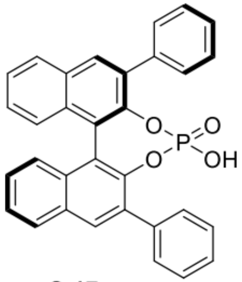


15	BF_3•OEt_2	100	0.006	reflux	DCE	isobutene	48	58	—
15	BF_3•OEt_2	100	0.006	reflux	DCE	isobutene	36	52	—
15	BF_3•OEt_2	100	0.006	reflux	DCE	isobutene	24	34	—
15	BF_3•OEt_2	100	0.006	reflux	DCE	isobutene	12	18	—
S-15	BF_3•OEt_2	100	0.006	reflux	DCE	isobutene	48	57	—
S-15	BF_3•OEt_2	100	0.006	reflux	DCE	—	48	43	—

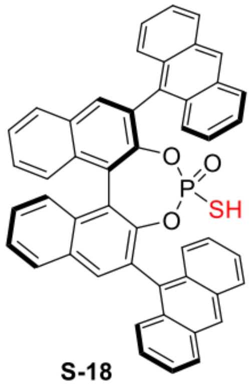
15	**S-16**	10	0.006	reflux	DCE	isobutene	48	NR	0
15	**S-17**	10	0.006	reflux	DCE	isobutene	48	NR	0
15	**S-18**	10	0.006	reflux	DCE	isobutene	48	NR	0
15	**S-19**	10	0.006	reflux	DCE	isobutene	48	NR	0
15	BF_3•OEt_2 +**S-17**	100 (BF_3•OEt_2) +10 (**S-17**)	0.006	reflux	DCE	isobutene	48	35	0



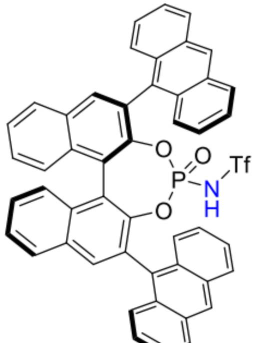
S-16



S-17



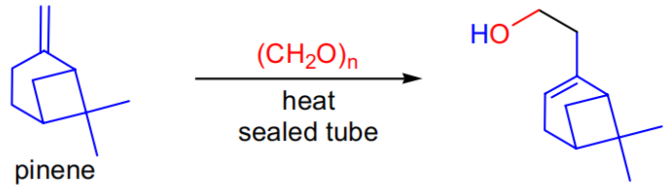
S-18



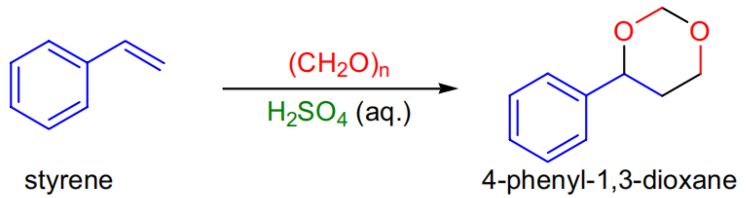
S-19

PRINS REACTION

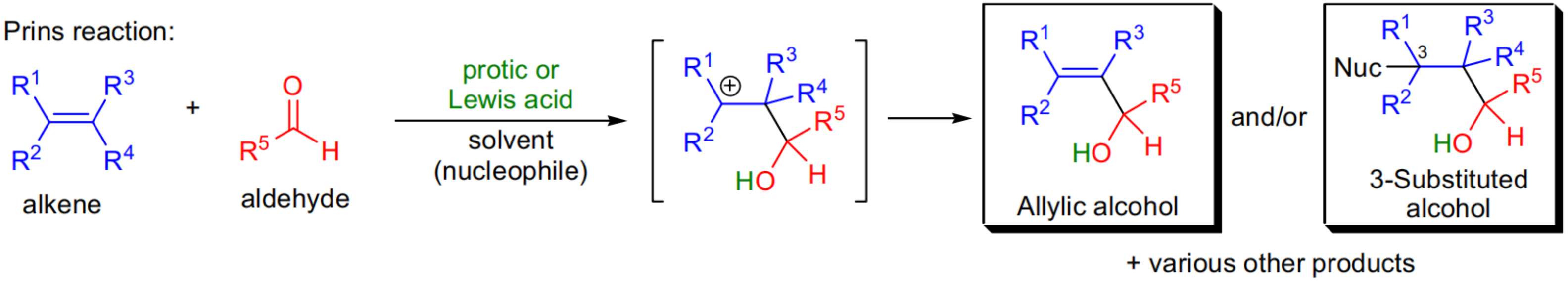
Kriewitz (1899):



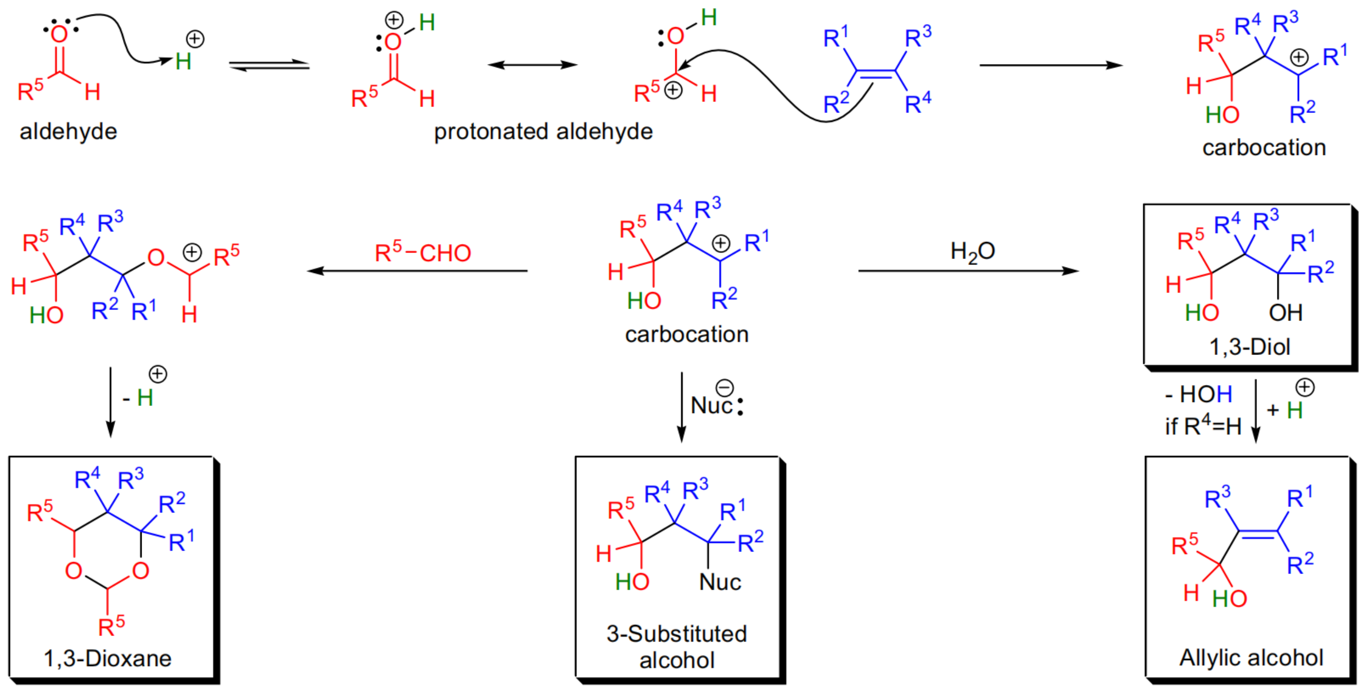
Prins (1919):

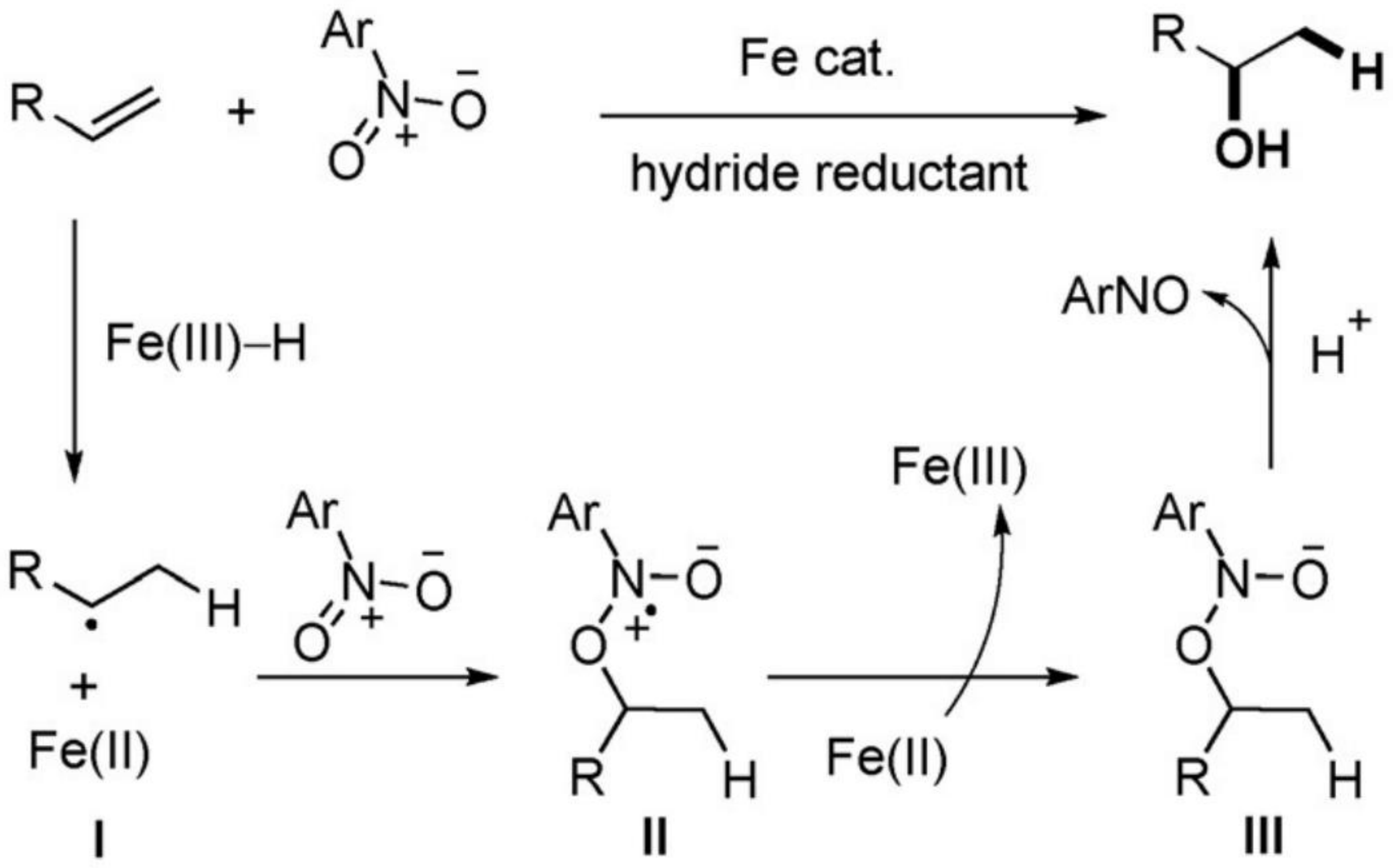


Prins reaction:

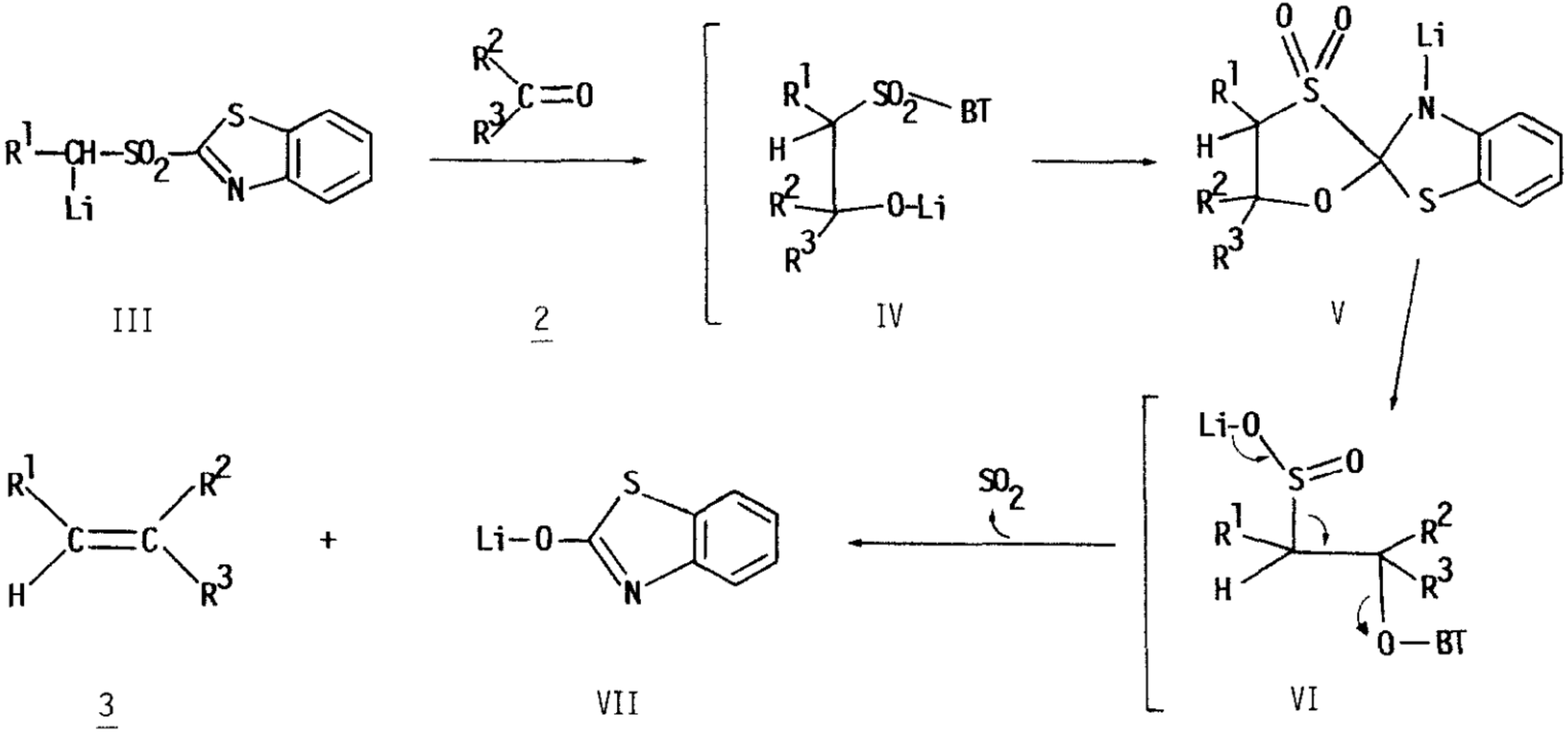


Mechanism: [16-29]

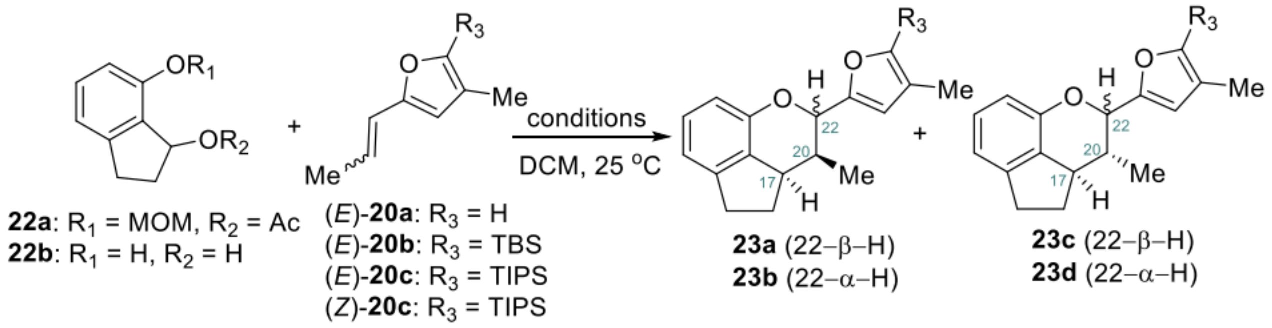




Angew. Chem. Int. Ed., **2021**, *60*, 8313.



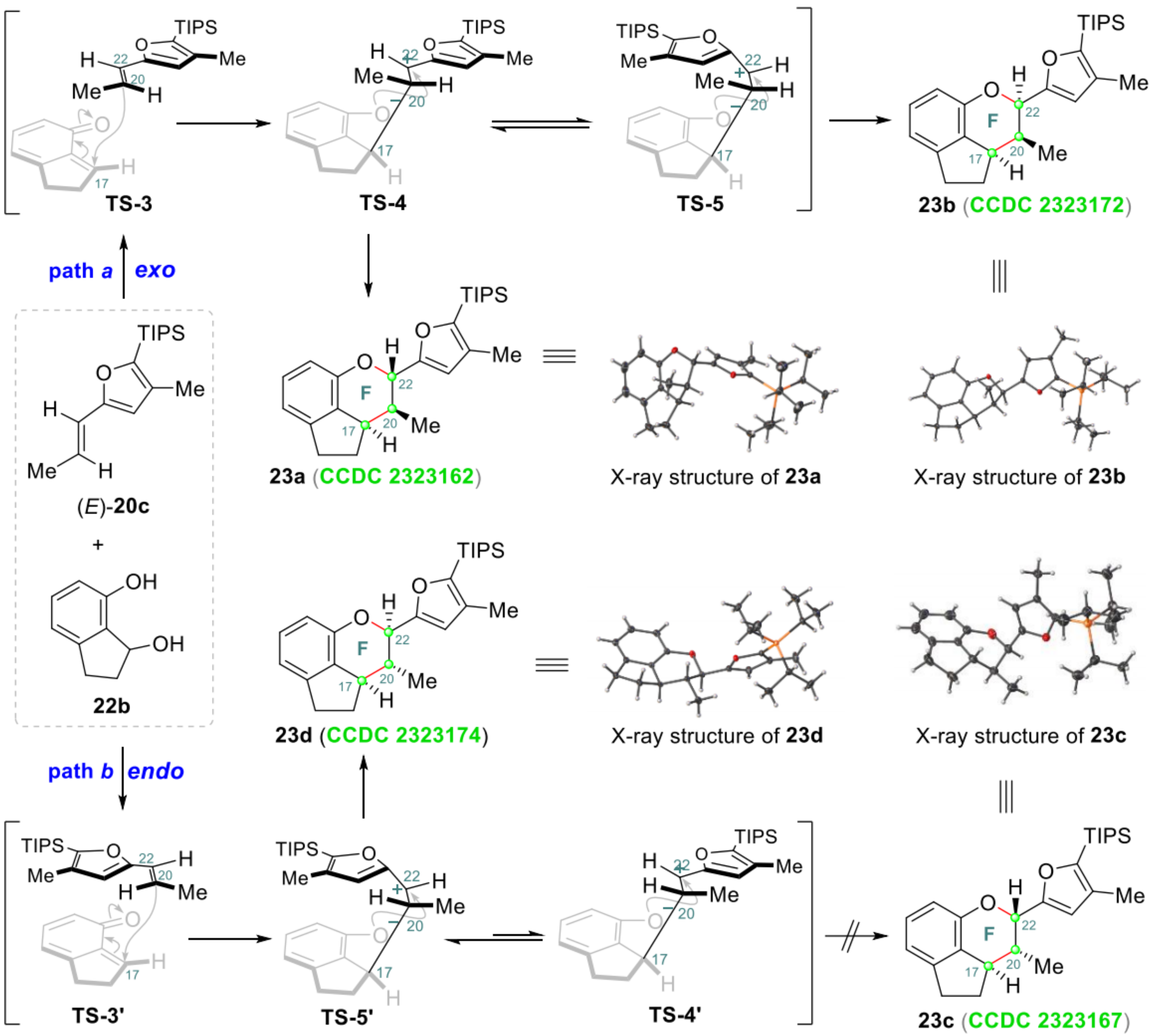
Tetrahedron Lett., **1991**, *32*, 1175.



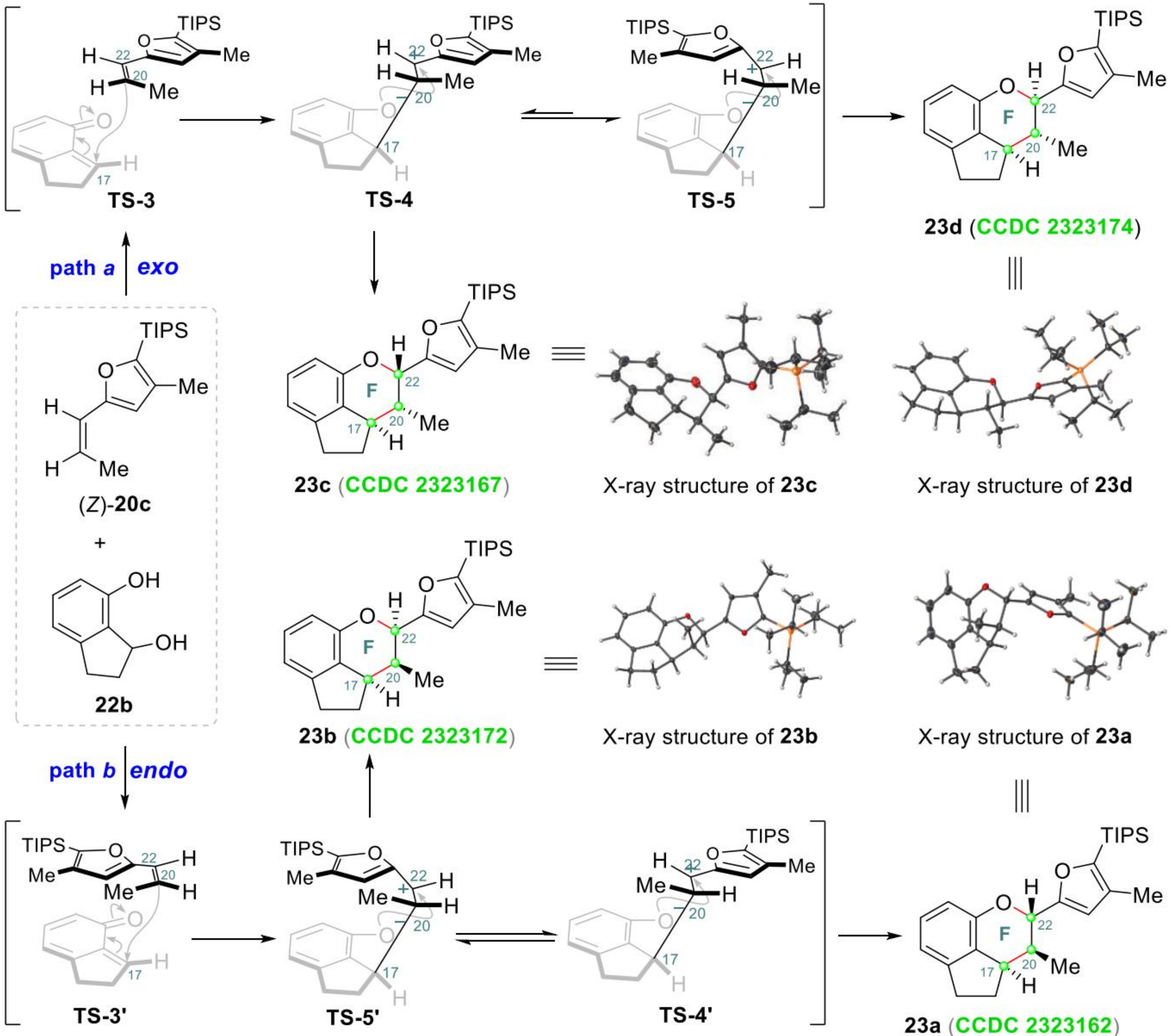
Entry	Substrates	Cat.	Yield (%)[b] (**23a**:**23b**:**23c**:**23d**)
1	**22a**, (*E*)-**20a**	$PtCl_4$	NA
2	**22a**, (*E*)-**20b**	$PtCl_4$	NA
3	**22a**, (*E*)-**20c**	$PtCl_4$	3 (1.5:1.0:0:0.8)
4	**22b**, (*E*)-**20c**	$PtCl_4$	6 (1.5:1.0:0:0.8)
5[c]	**22b**, (*E*)-**20c**	$PtCl_4$	14 (1.5:1.0:0:0.8)
6[c]	**22b**, (*E*)-**20c**	CSA	23 (3.7:1.0:0:0.3)
7[c]	**22b**, (*E*)-**20c**	$Zn(OTf)_2$	28 (3.2:1.0:0:0.6)
8[c]	**22b**, (*E*)-**20c**	$In(OTf)_3$	31 (2.2:1.0:0:0.5)
9[c]	**22b**, (*E*)-**20c**	$Sc(OTf)_3$	33 (1.1:1.0:0:0.4)
10[c]	**22b**, (*E*)-**20c**	$Bi(OTf)_3$	57 (3.0:1.0:0:0.4)
11[c]	**22b**, (*Z*)-**20c**	$Sc(OTf)_3$	63 (2.1:1.0:1.0:7.0)
12[c,d]	**22b**, **20c**	$Sc(OTf)_3$	30 (1.5:1.0:0.2:1.0)

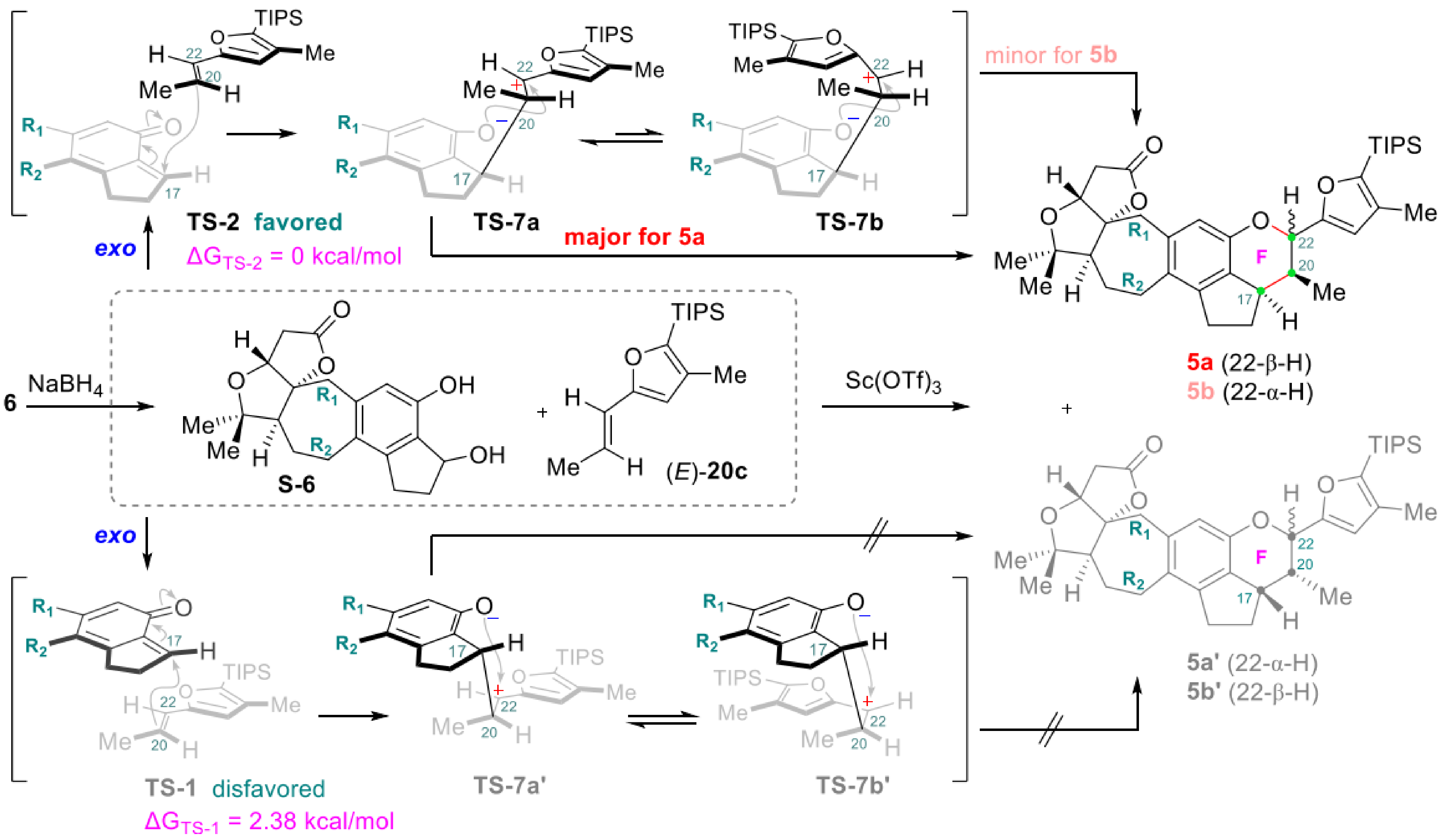
[a]Reaction conditions: **22** (0.07 mmol), **20** (0.2 mmol), Cat. (10 mol %), DCM (5 mL), 25 °C. [b]Isolated yield. [c]4 Å MS (50 mg) was added. [d]**20c**: *E*:*Z* = 1:1.

Scheme S5. Proposed Mechanism of *o*-QM type [4+2] Cyclization by Using (*E*)-**20**.



Scheme S6. Proposed Mechanism of *o*-QM type [4+2] Cyclization by Using (*Z*)-**20**.





TS-2 favored
ΔG(TS-2) = 0 kcal/mol
TS-7a
TS-7b
major for 5a
minor for 5b
exo
6
NaBH4
S-6
(E)-20c
Sc(OTf)3
5a (22-β-H)
5b (22-α-H)
5a' (22-α-H)
5b' (22-β-H)
TS-1 disfavored
ΔG(TS-1) = 2.38 kcal/mol
TS-7a'
TS-7b'