Asymmetric Total Syntheses of Kopsia Indole Alkaloids

Lingying Leng, Xiaohan Zhou, Qi Liao, Falu Wang, Hao Song,* Dan Zhang, Xiao-Yu Liu, and Yong Qin*

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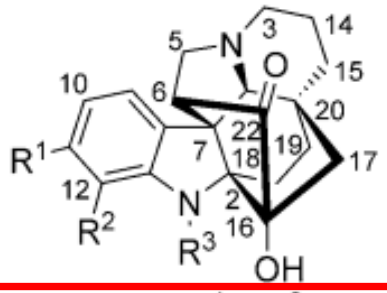
Structures of the Representative Kopsine-Related Alkaloids

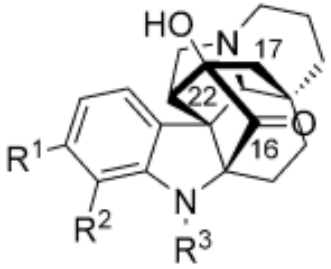


Kopsine (**1**), $R^1 = R^2 = H$, $R^3 = CO_2Me$

Methylenedioxykopsine (**2**)
$R^1, R^2 = OCH_2O$, $R^3 = CO_2Me$

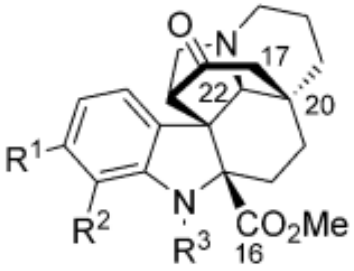
Kopsinidines A (**3**), $R^1, R^2 = OCH_2O$, $R^3 = H$;

Kopsinidines B (**4**), $R^1 = R^2 = OMe$, $R^3 = CO_2Me$



Isokopsine (**5**), $R^1 = R^2 = R^3 = H$;

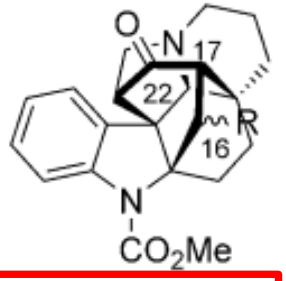
Dasyrachine (**6**)
$R^1, R^2 = OCH_2O$, $R^3 = H$



Methyl chanofruticosinate (**7**)
$R^1 = R^2 = H$, $R^3 = CO_2Me$;

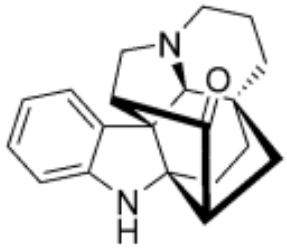
Methyl methylenedioxy-chanofruticosinate (**8**)
$R^1, R^2 = OCH_2O$, $R^3 = CO_2Me$;

Methyl *N*-decarbomethoxy chanofruticosinate (**9**)
$R^1 = R^2 = R^3 = H$



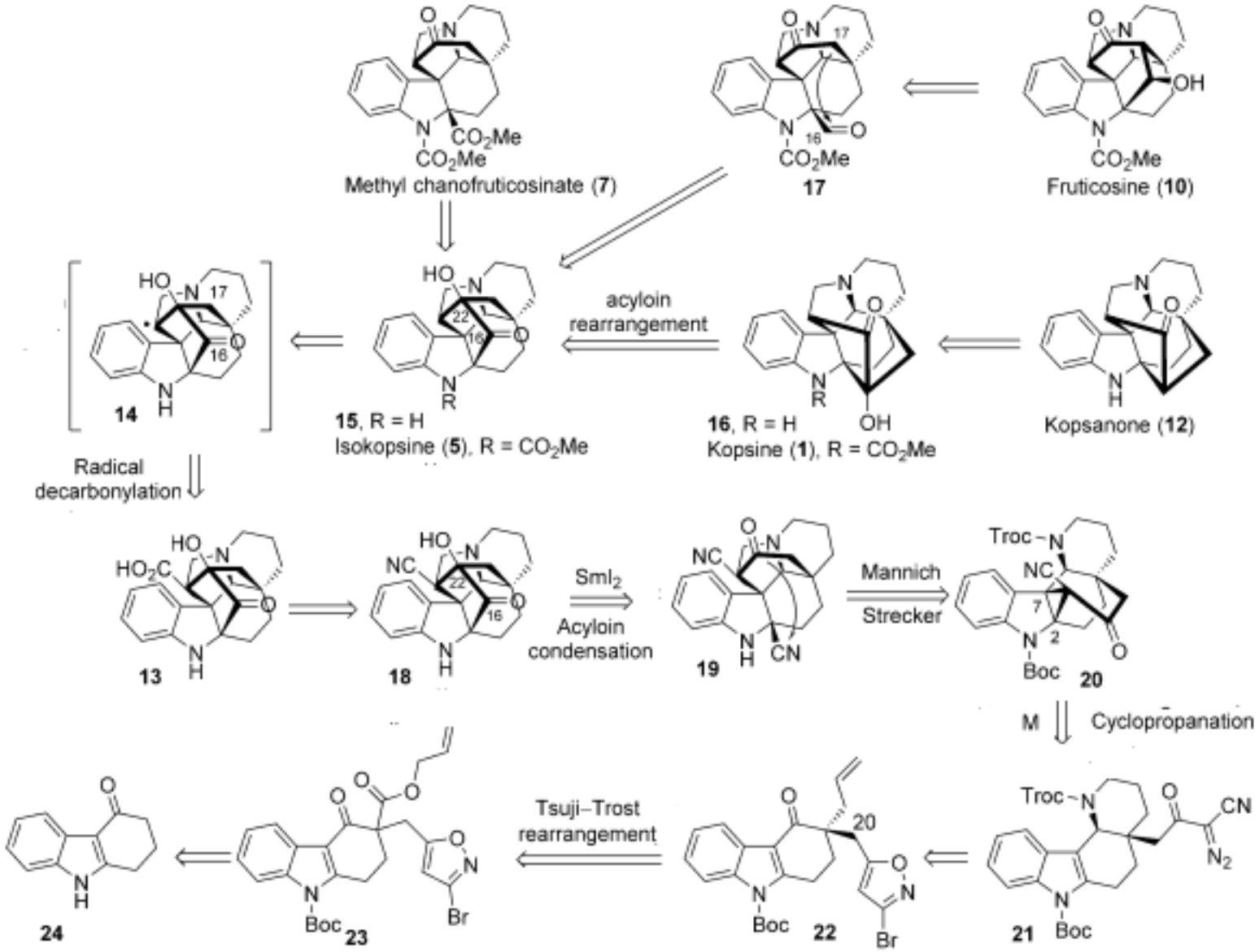
Fruticosine (**10**)
R = β-OH

Fruticosamine (**11**)
R = α-OH

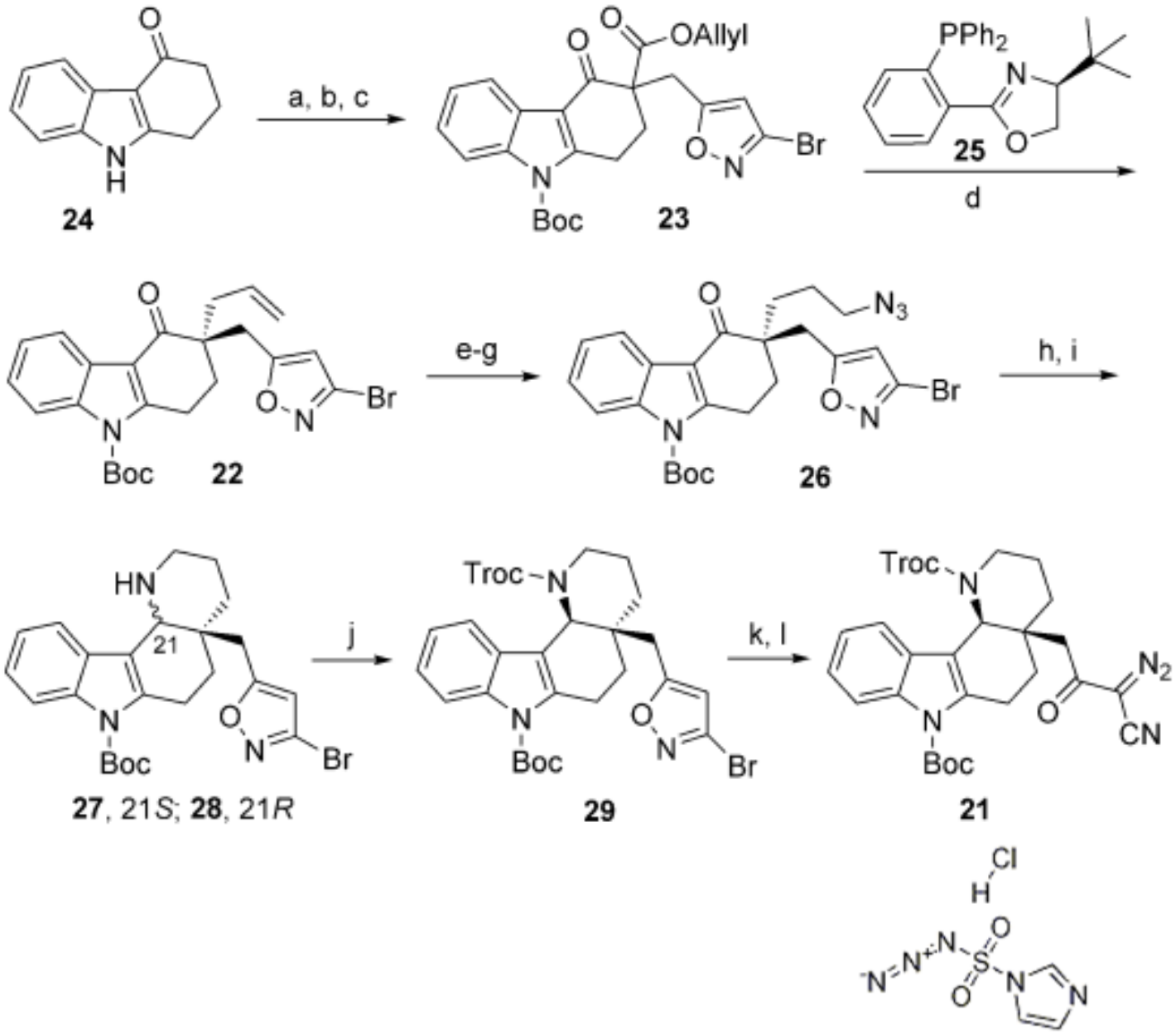


Kopsanone (**12**)

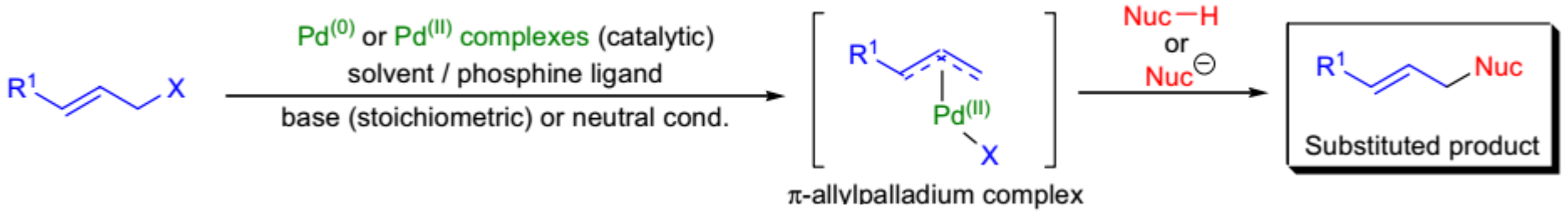
Retrosynthetic Analysis of Kopsine-Related Alkaloids

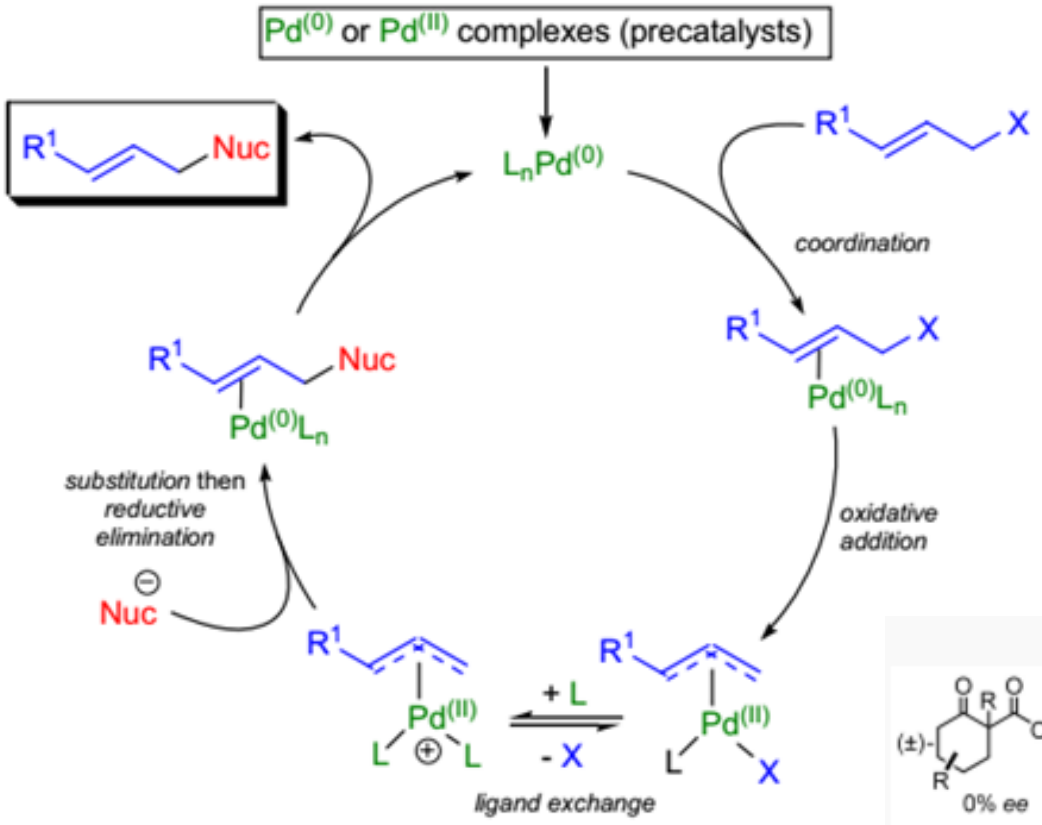


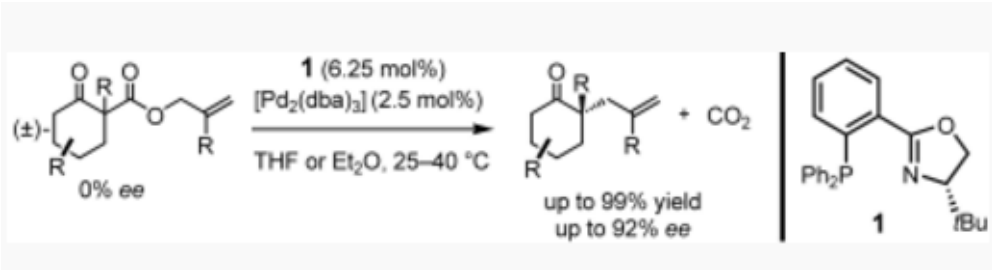
Preparation of the Diazo **21**



Tsuji-Trost Reaction







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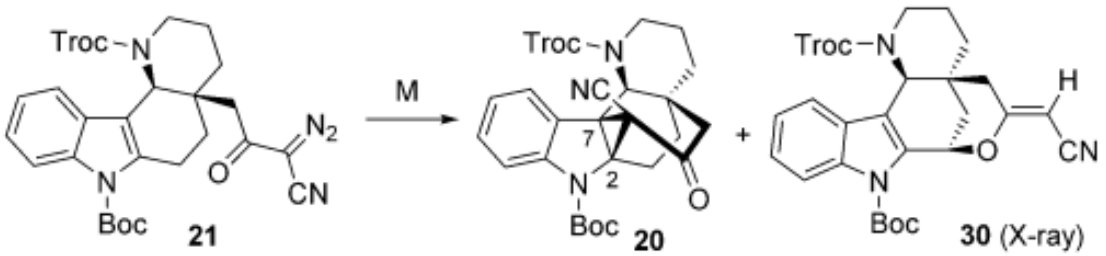
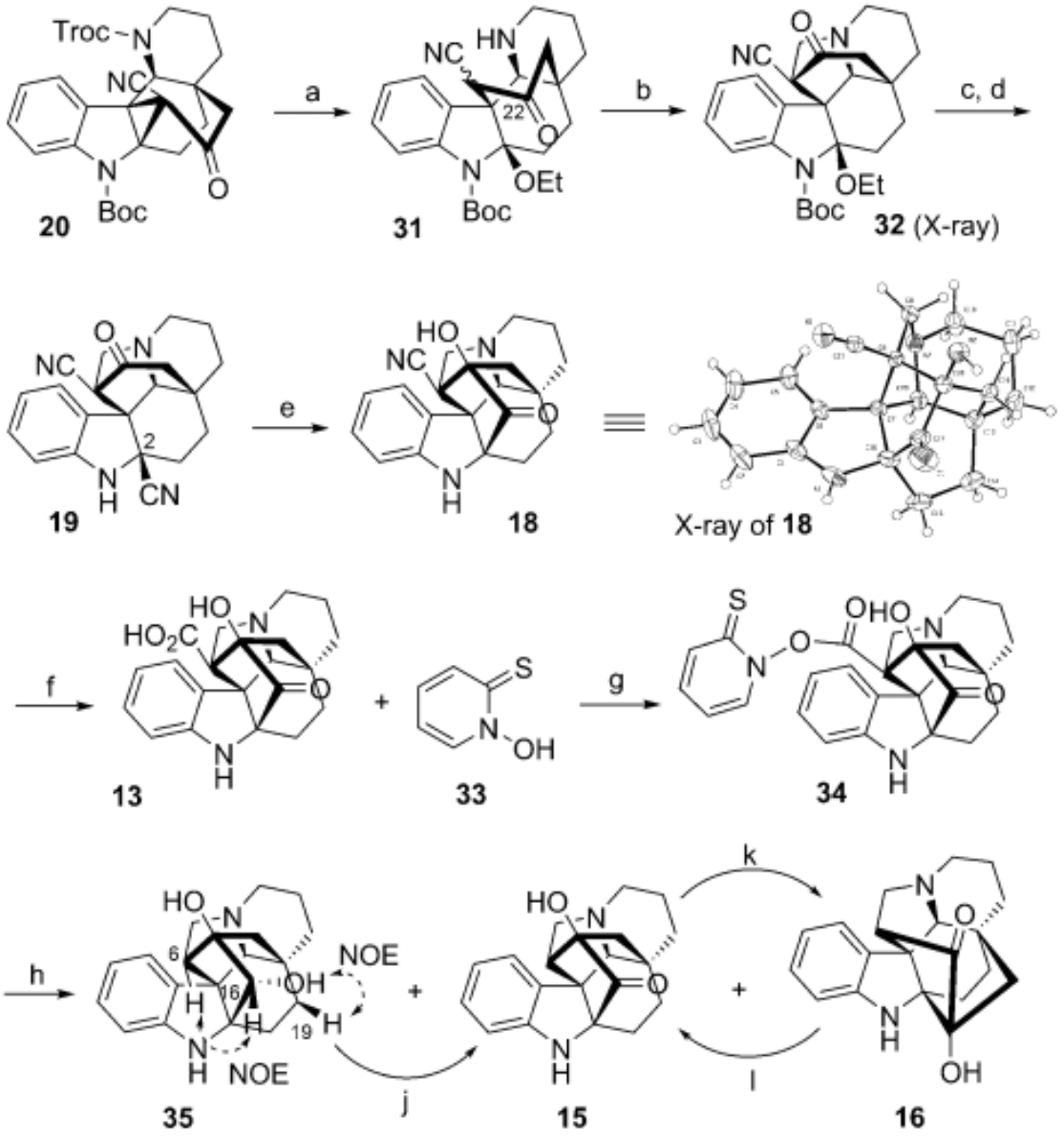
Optimization of Cyclopropanation Reactions

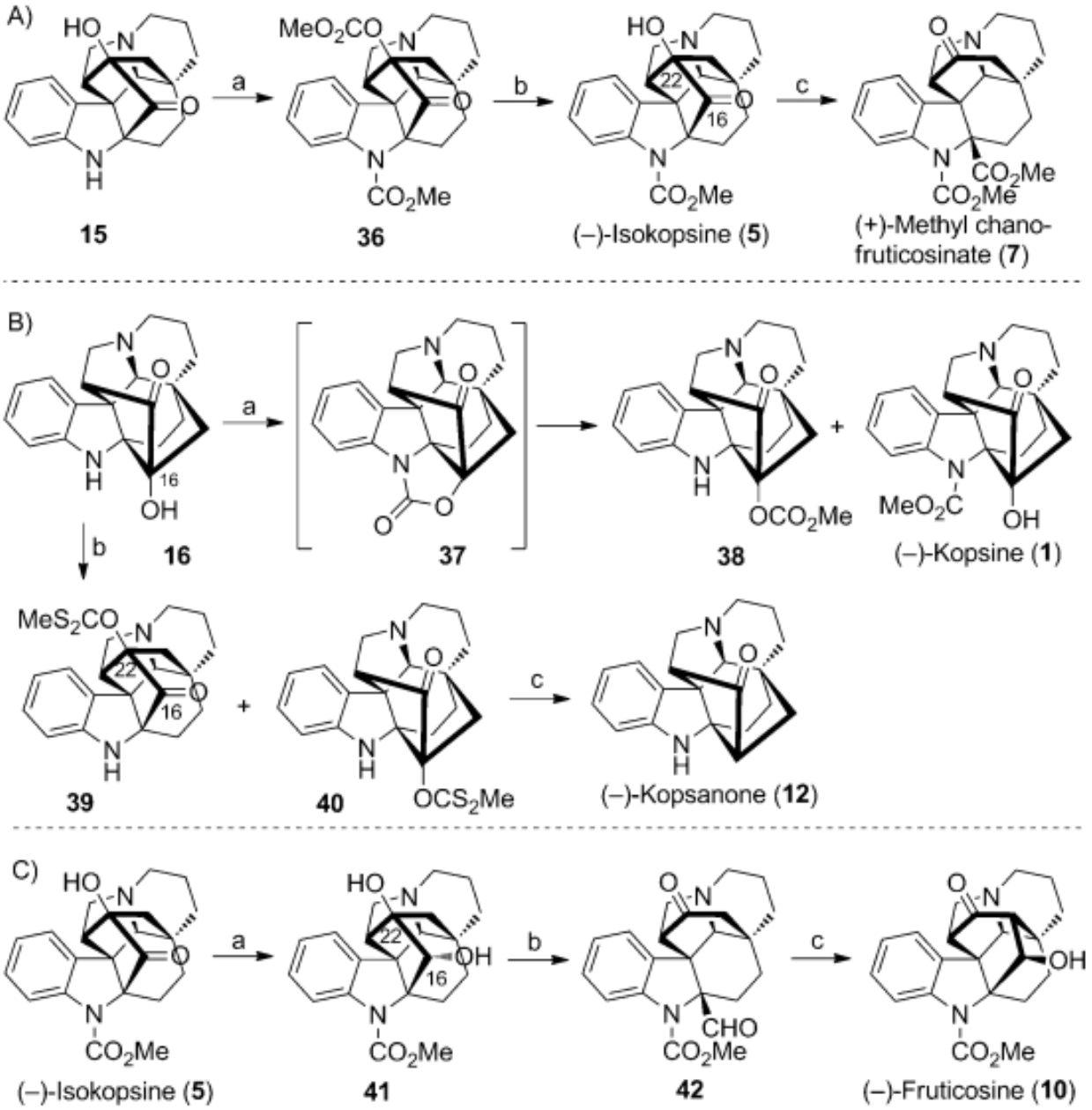


Entry	Catalyst	Solvent	*T* [°C]/*t*	Yield [%]	
				20	**30**
1	$[Rh(OAc)_2]$	DCM	25/3 h	trace	16
2	$Rh(C_3F_7CO_2)_2$	DCM	25/3 h	none	23
3	CuOTf	DCM	25/3 h	trace	22
4	$Cu(OTf)_2$	DCM	25/3 h	none	18
5	$Cu(TBS)_2$	DCE	80/2 h	none	15
6	$[Cu(acac)_2]$	DCE	80/2 h	10	15
7	$[Cu(tfacac)_2]$	DCE	80/2 h	17	12
8	$[Cu(hfacac)_2]$	DCE	80/2 h	22	13
9[b]	$[Cu(hfacac)_2]$	DCE	120/5 min	38	12
10	$[Cu(hfacac)_2]$	benzene	80/2 h	40	5
11	$[Cu(hfacac)_2]$	chlorobenzene	100/1 h	45	17
12	$[Cu(hfacac)_2]$	chlorobenzene	120/30 min	52	13
13	$[Cu(hfacac)_2]$	chlorobenzene	130/15 min	49	15
14	$[Cu(hfacac)_2]$	1,2-dichloro-benzene	150/10 min	34	13

Asymmetric Approach to the Core Structure



Syntheses of Kopsia Alkaloids



Summary

1. asymmetric total syntheses of a group of Kopsia alkaloids which belong to four subfamilies within 23 steps.
2. construction of the molecular complexity in the targets mainly relied on an asymmetric Tsuji–Trost rearrangement, a metal-salt-catalyzed intramolecular cyclopropanation, and a SmI2-promoted acyloin condensation.