JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Subscriber access provided by CHANGCHUN INST APPL CHEM

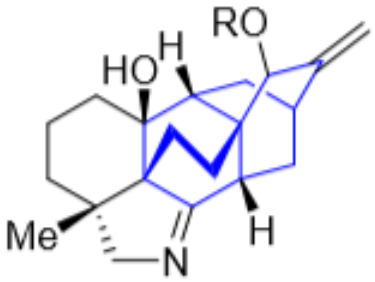
Communication

Asymmetric Total Synthesis of Arcutinidine, Arcutinine, and Arcutine

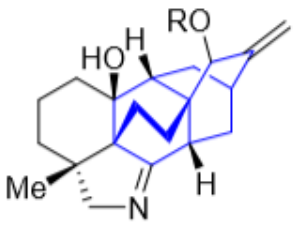
Shupeng Zhou, Kaifu Xia, Xuebing Leng, and Ang Li

J. Am. Chem. Soc., **Just Accepted Manuscript** • DOI: 10.1021/jacs.9b05818 • Publication Date (Web): 05 Jul 2019

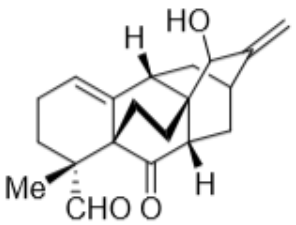
Downloaded from http://pubs.acs.org on July 7, 2019



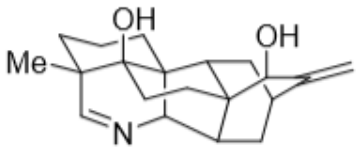
1: the originally described structure of arcutine; R = (*R*)-*s*-BuCO
2: arcutinine; R = *i*-PrCO
3: arcutinidine; R = H



1: the originally described structure of arcutine; R = (*R*)-*s*-BuCO
2: arcutinine; R = *i*-PrCO
3: arcutinidine; R = H

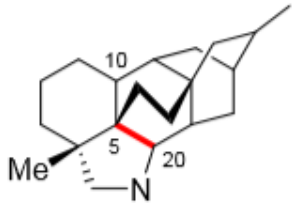


4: atropurpuran

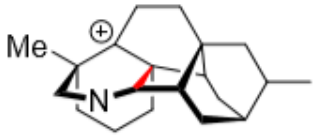


5: tongolinine

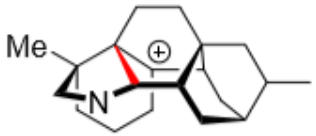
the hetidine skeleton

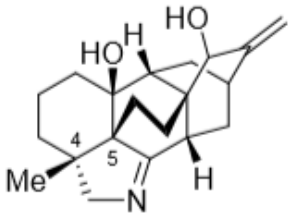


the arcutine skeleton



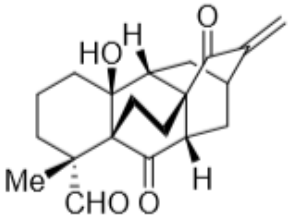
1,2-alkyl shift





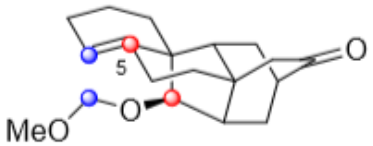
3: arcutinidine

reductive amination

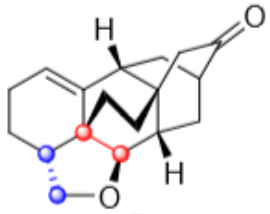


6

Prins/Wagner–Meerwein

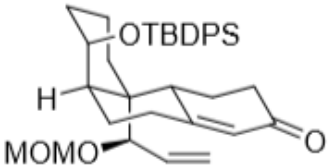


8

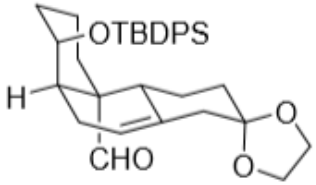


7

anionic Diels–Alder

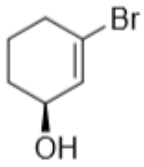


9

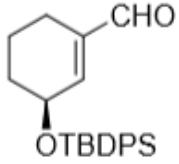


10

Diels–Alder

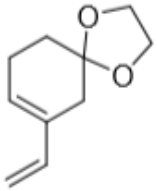


13

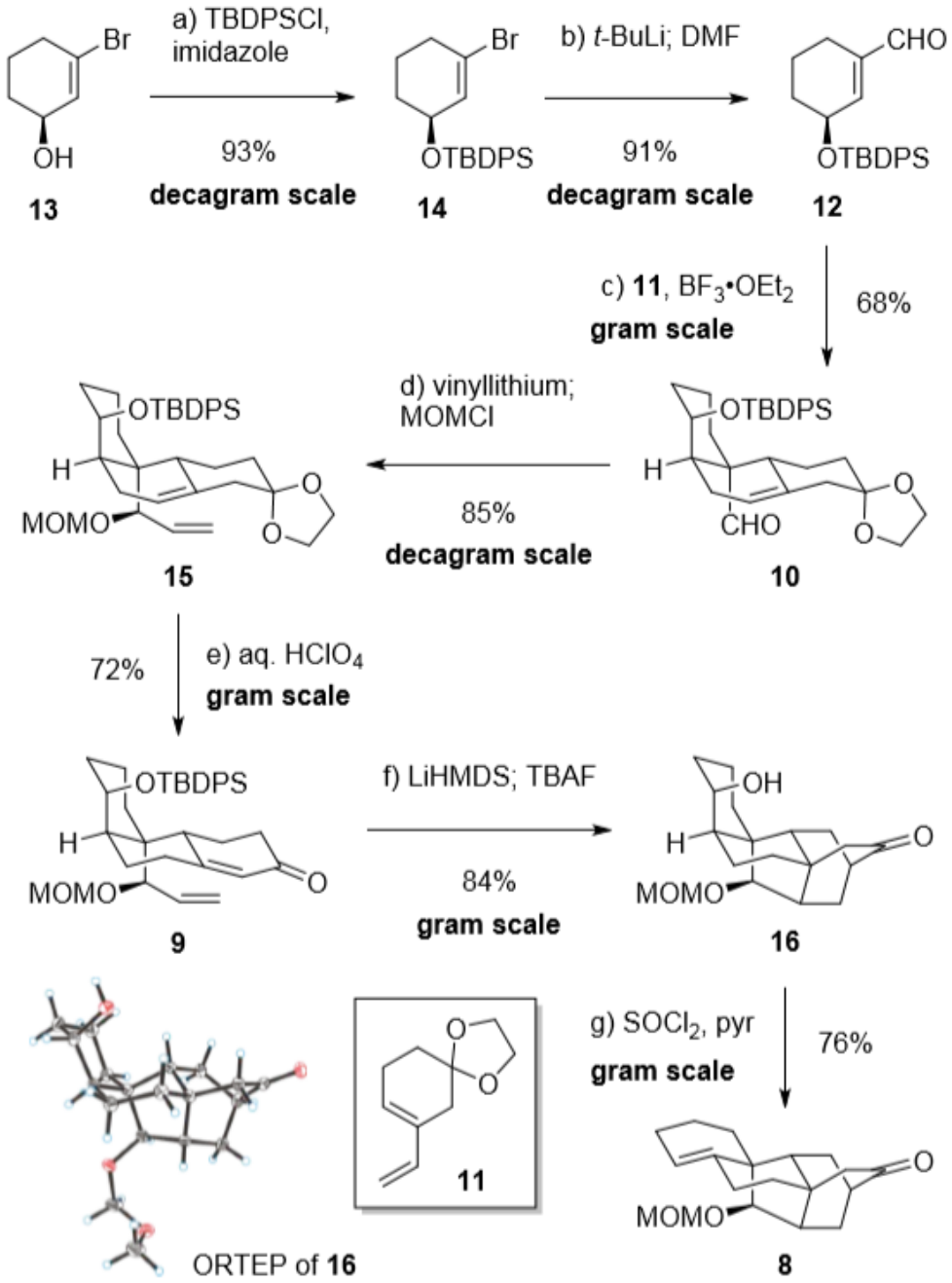


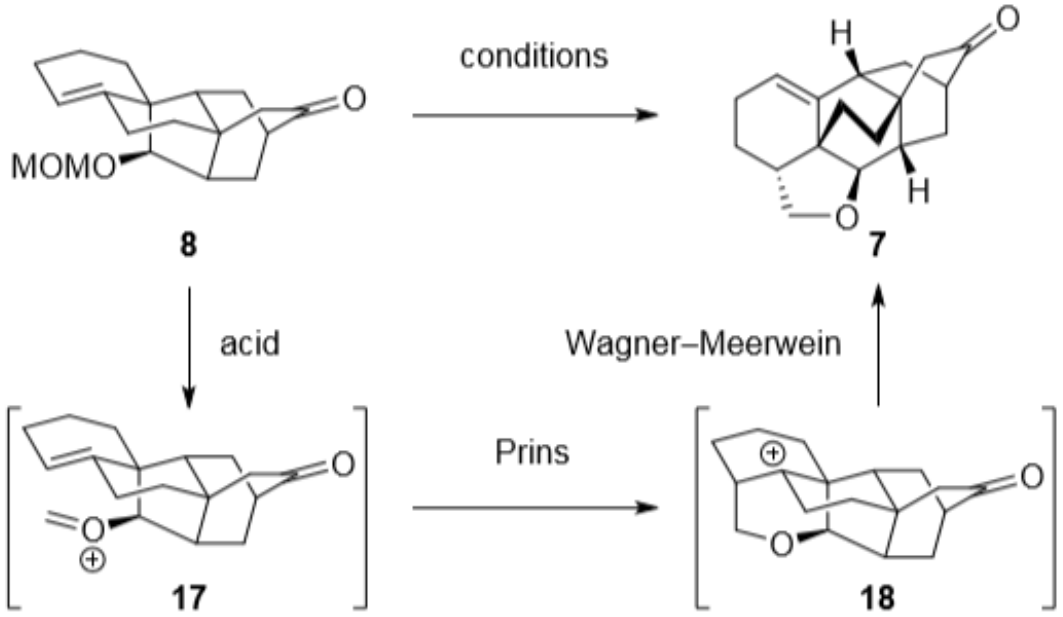
12

+



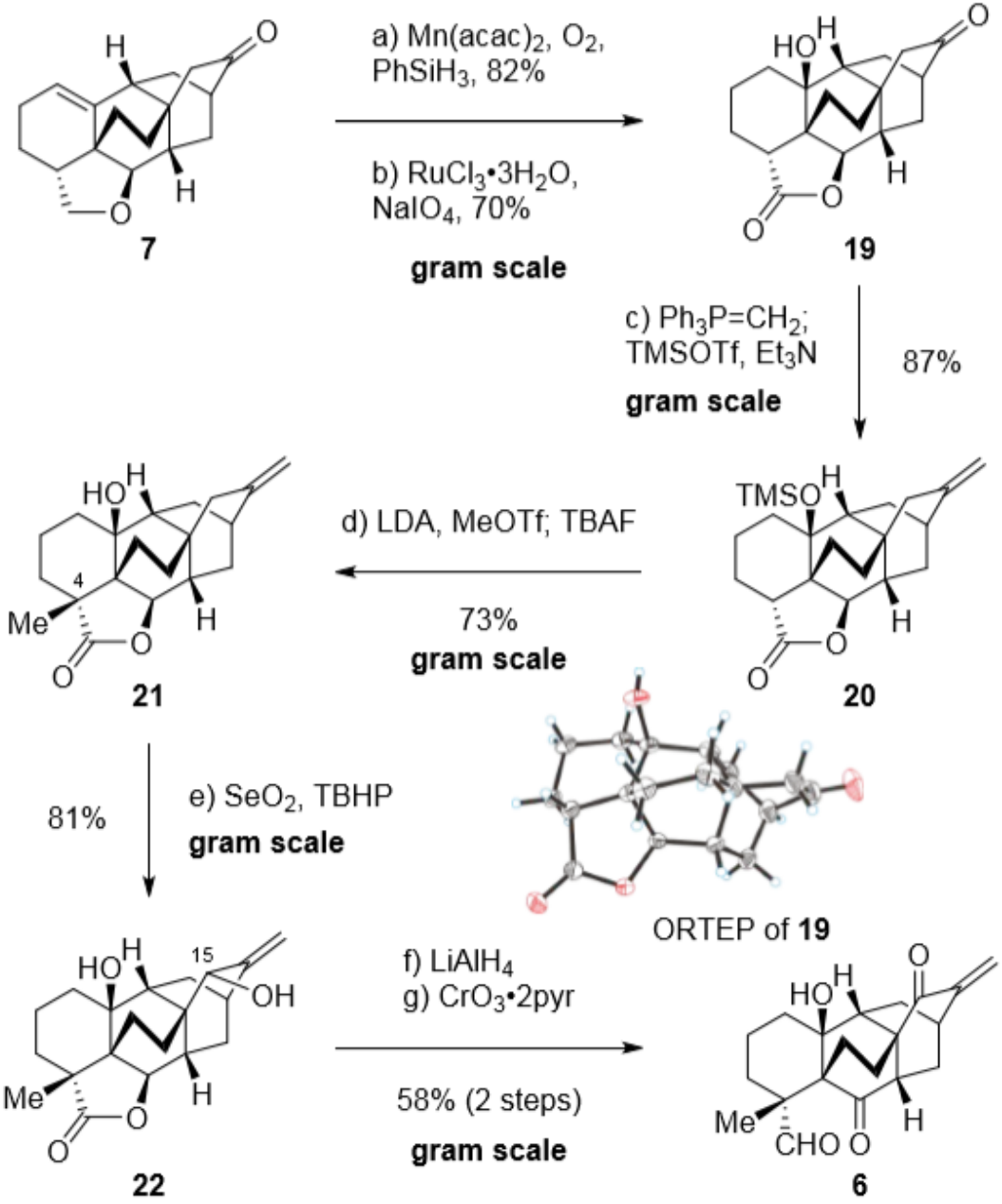
11


a) TBDPSCl, imidazole
93%
decagram scale
b) t-BuLi; DMF
91%
decagram scale
c) 11, BF3•OEt2
gram scale
68%
d) vinyllithium; MOMCl
85%
decagram scale
e) aq. HClO4
gram scale
72%
f) LiHMDS; TBAF
84%
gram scale
g) SOCl2, pyr
gram scale
76%
13
14
12
10
15
9
16
8
11
ORTEP of 16

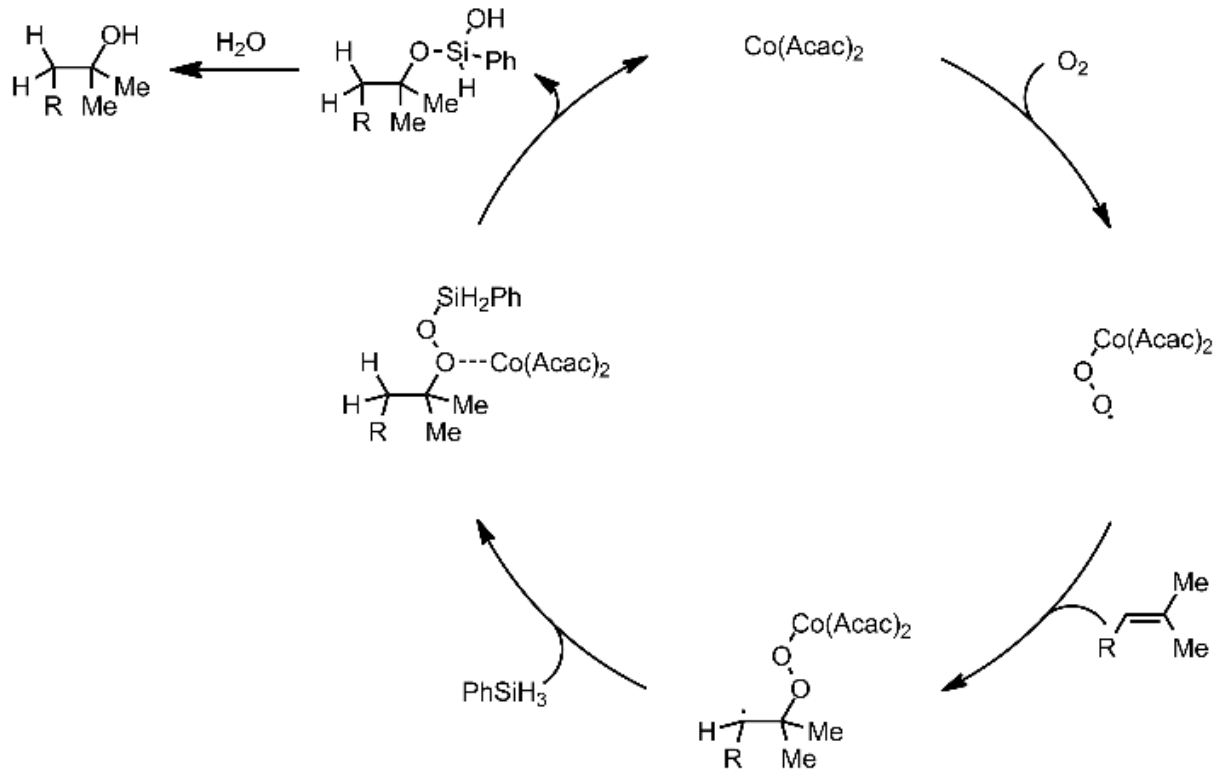


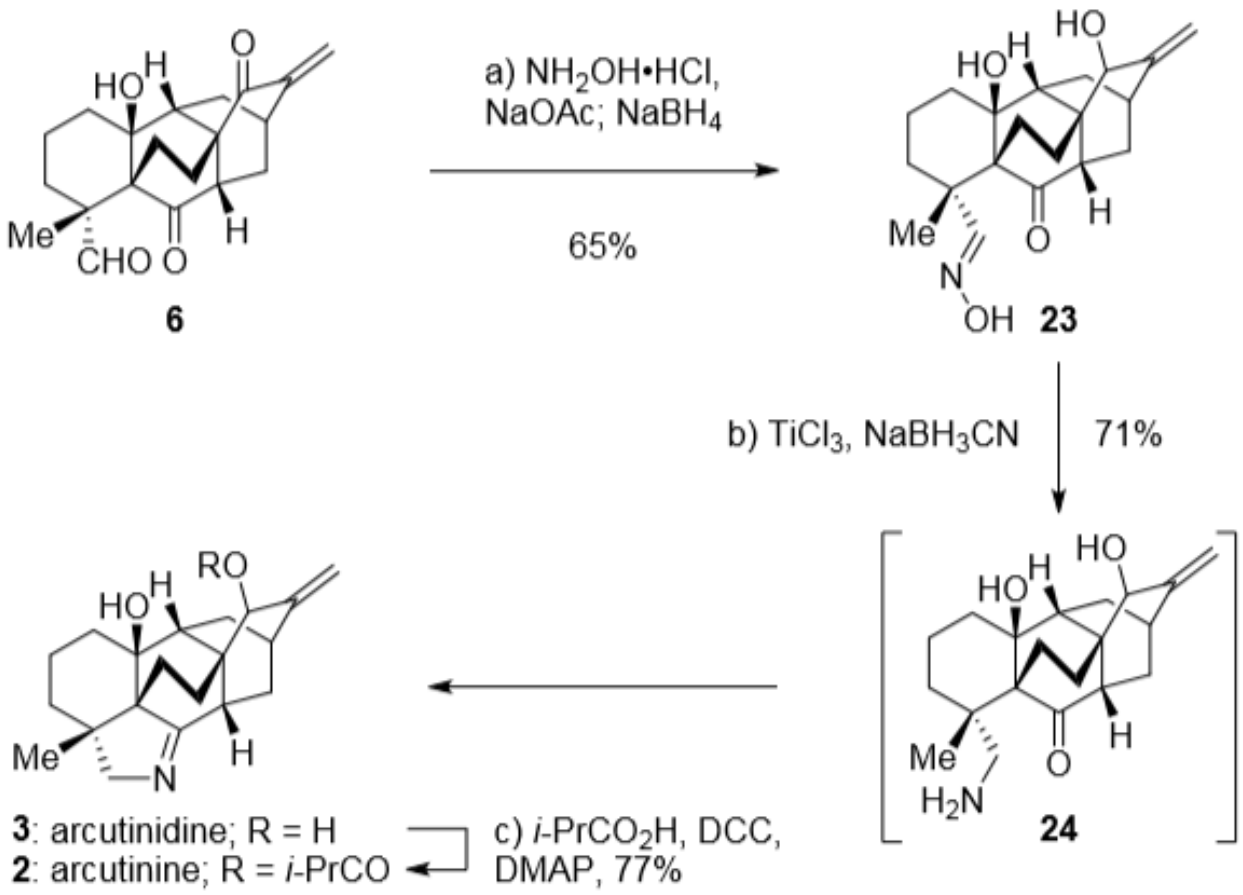
entry	conditions[a]	yield (%)
1	TFA, 0 °C, 24 h	22
2	TESOTf, 0 °C, 1 h	16
3	BF_3•OEt_2, –15 °C, 6 h	37
4	$TiCl_4$, –15 °C, 1 h	24
5	$SnCl_4$, –15 °C, 1 h	63
6	$SnCl_4$, TMSOAc, –15 °C, 1 h	55

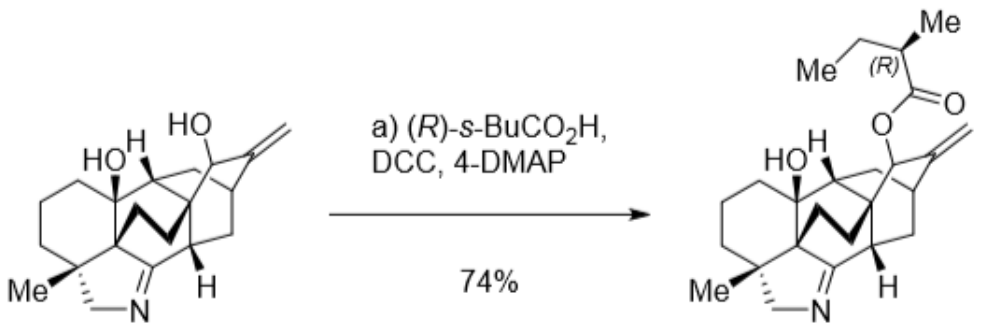
[a] 1.0 equiv. acid. Reactions performed in CH_2Cl_2.


a) Mn(acac)2, O2, PhSiH3, 82%
b) RuCl3•3H2O, NaIO4, 70%
gram scale
7
19
c) Ph3P=CH2; TMSOTf, Et3N
gram scale
87%
d) LDA, MeOTf; TBAF
73%
gram scale
21
20
81%
e) SeO2, TBHP
gram scale
ORTEP of 19
f) LiAlH4
g) CrO3•2pyr
58% (2 steps)
gram scale
22
6

Mechanism of the Mukaiyama Hydration

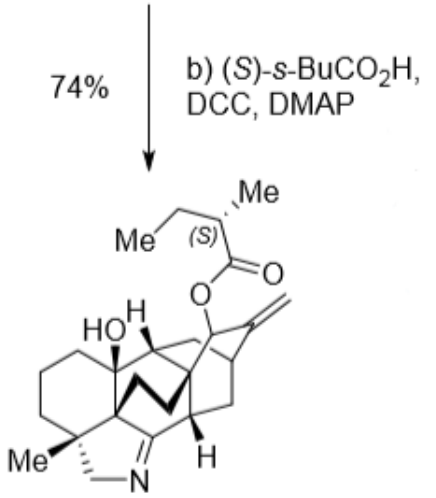



HO
H
O
Me
CHO
O
H
6
a) NH2OH•HCl,
NaOAc; NaBH4
65%
HO
HO
H
Me
N
OH
O
H
23
b) TiCl3, NaBH3CN
71%
HO
HO
H
Me
H2N
O
H
24
RO
HO
H
Me
N
H
3: arcutinidine; R = H
2: arcutinine; R = i-PrCO
c) i-PrCO2H, DCC,
DMAP, 77%



3: arcutinidine

1: the originally described structure of arcutine



25: arcutine