文献报告

Synthesis of (-)-Quinocarcin by Gold(I)-Catalyzed Regioselective Hydroamination

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Fujii, N. *et al.*
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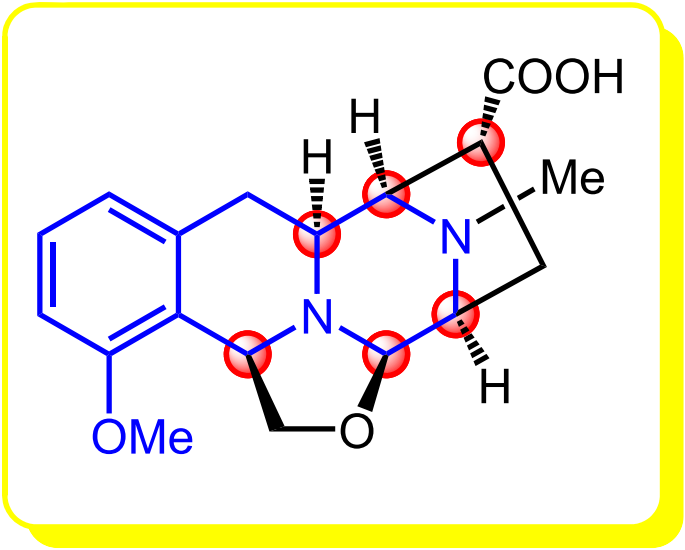
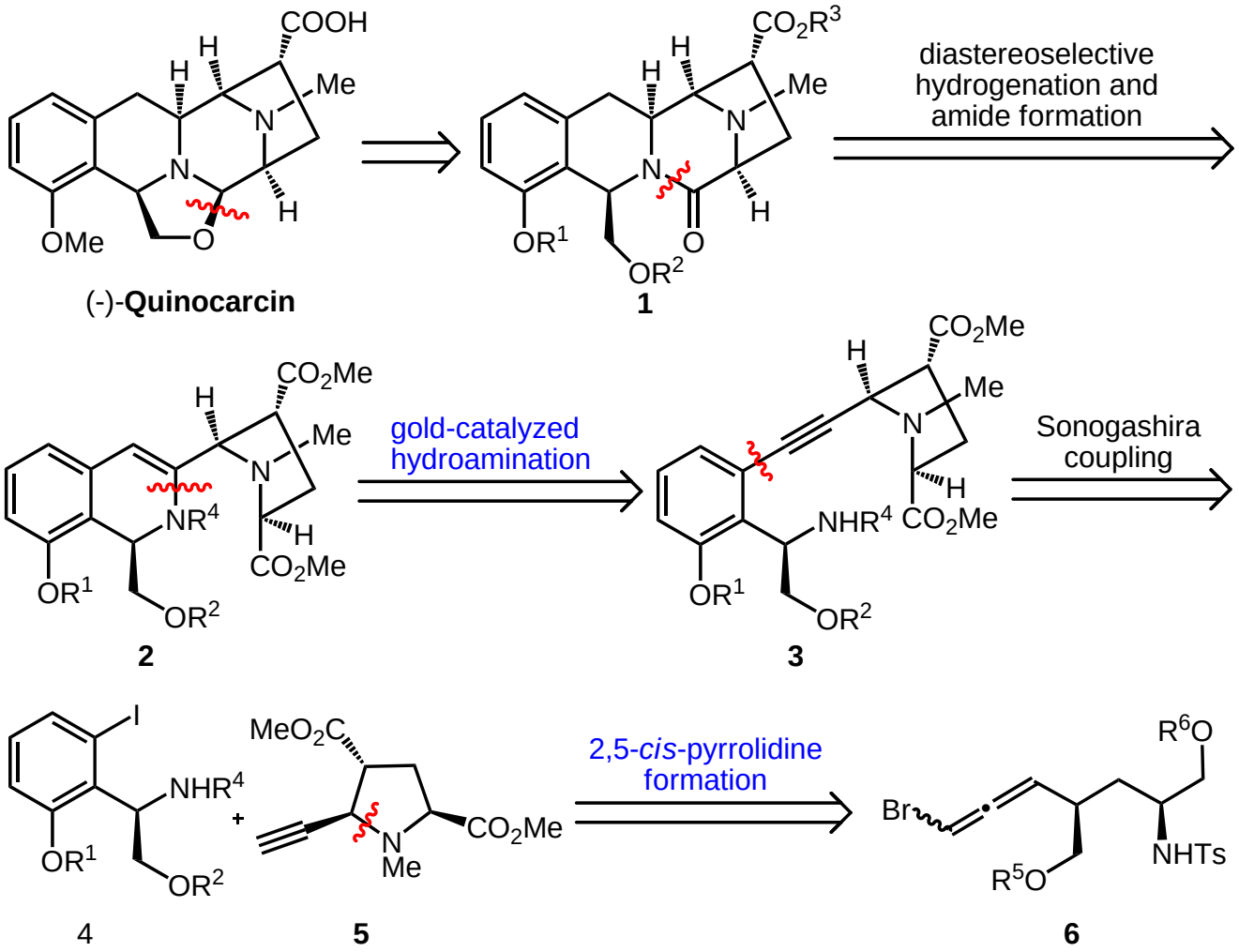
(-)-Quinocarcin

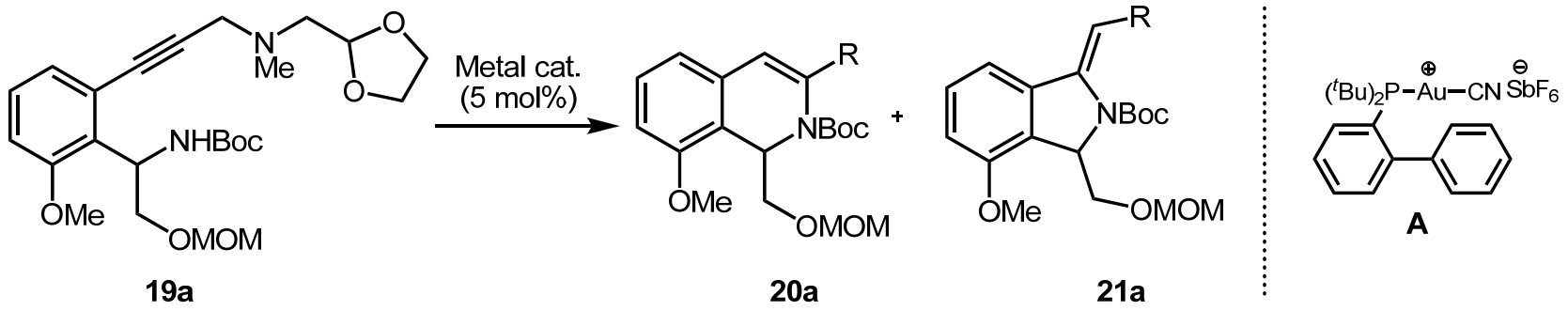


1. 四氢异喹啉类生物碱，1983年Takahashi与Tomita等从链霉菌melanovinaceus中分离得到。
2. 结构单元：五个并环、四氢异喹啉、六氢吡嗪，六个手性碳中心。
3. 研究表明，该类化合物具有强效的抗癌活性。
4. 目前已有六个课题组（Fukuyama, Garner, Terashima, Myers, Zhu和Stoltz）完成该化合物的全合成。

Retrosynthetic Analysis

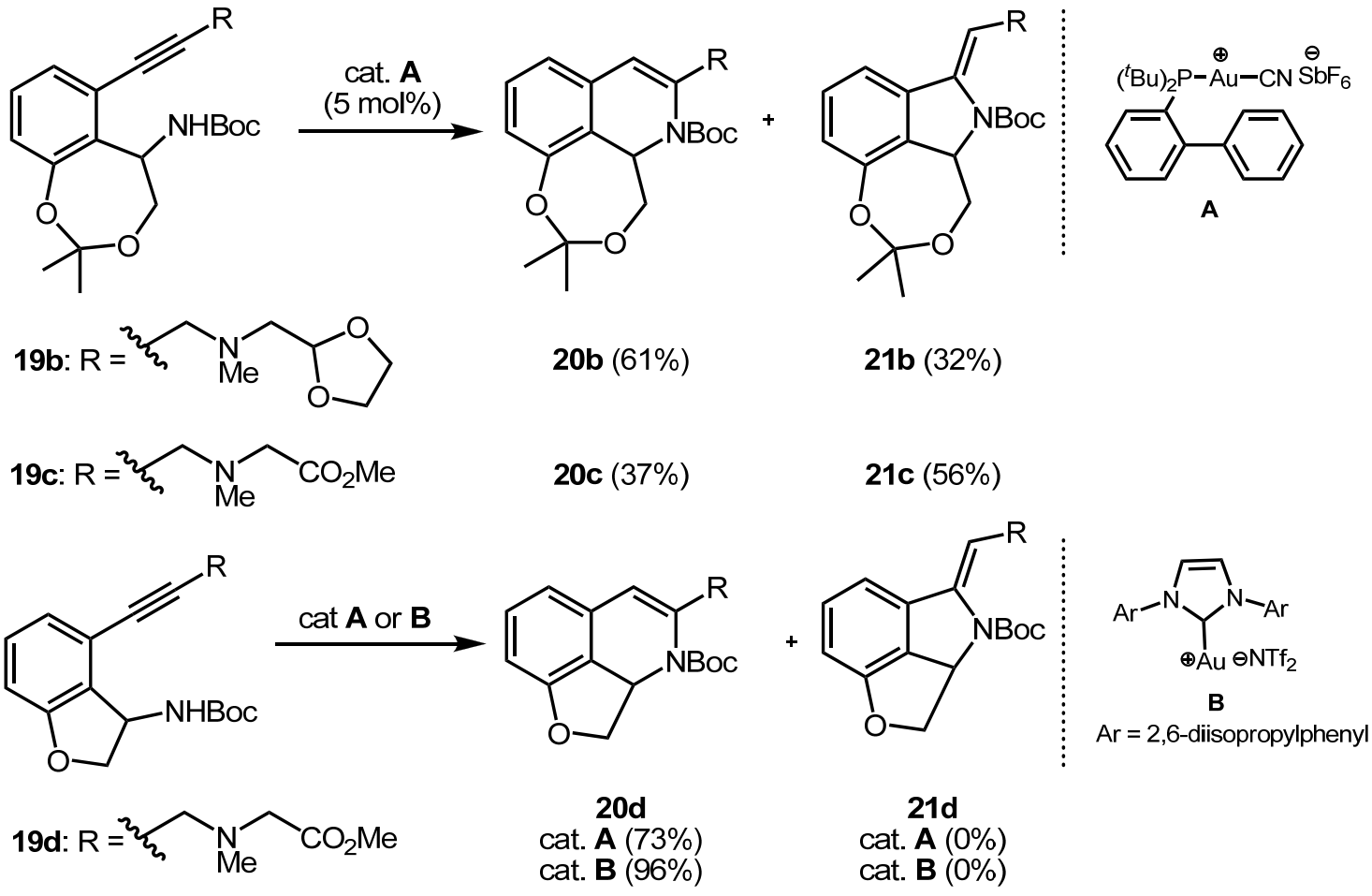


Gold-Catalyzed Hydroamination

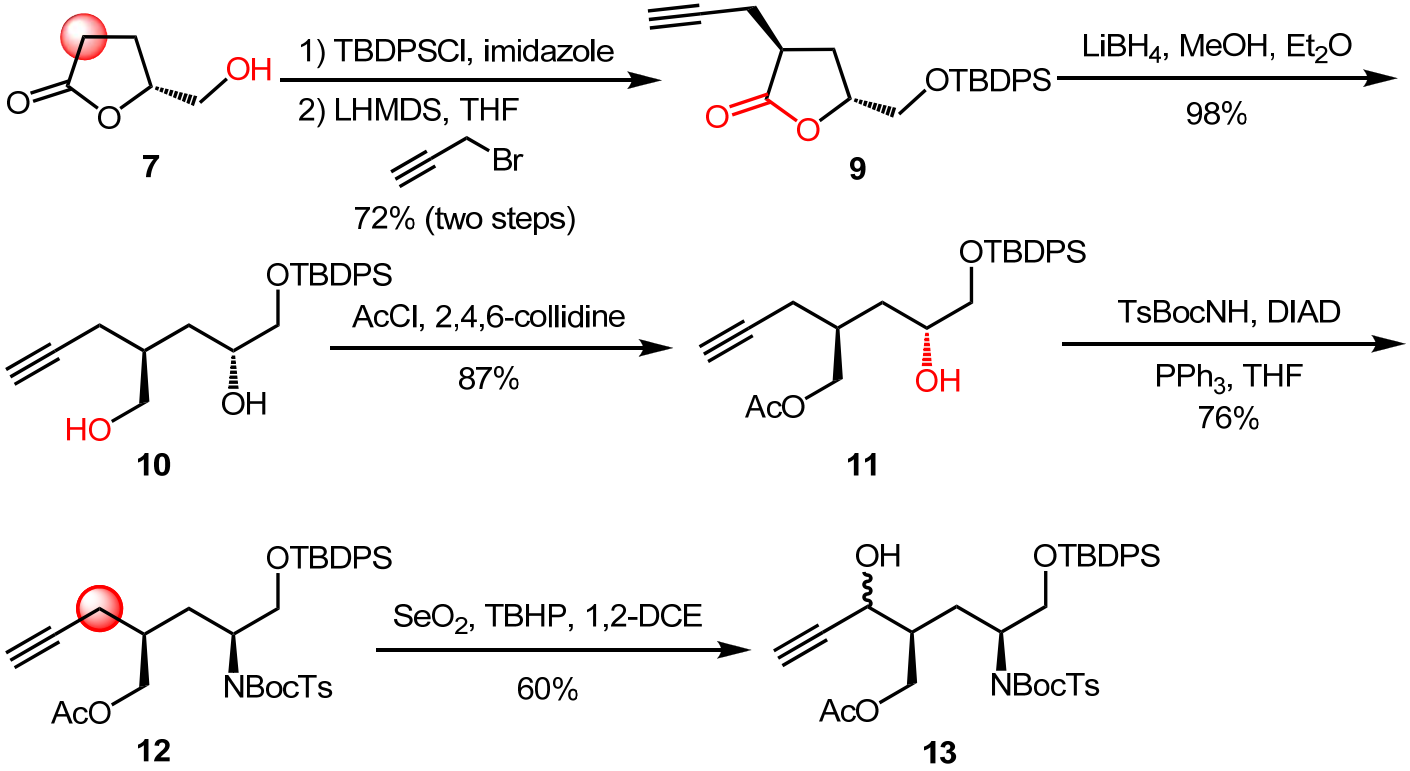


entry	cat.	additive	solvent	**20a** (%)	**21a** (%)
1	CuBr	TBAF	DMF	0	21
2	PPh_3AuCl	$AgNTf_2$	DCM	0	43
3	$PtCl_2$	$AgNTf_2$	DCM	0	0
4	cat. **A**	none	DCM	6	72
5	$In(OTf)_3$	none	1,2-DCE	0	0
6	$[RhCl(cod)]_2$	none	1,2-DCE	0	0

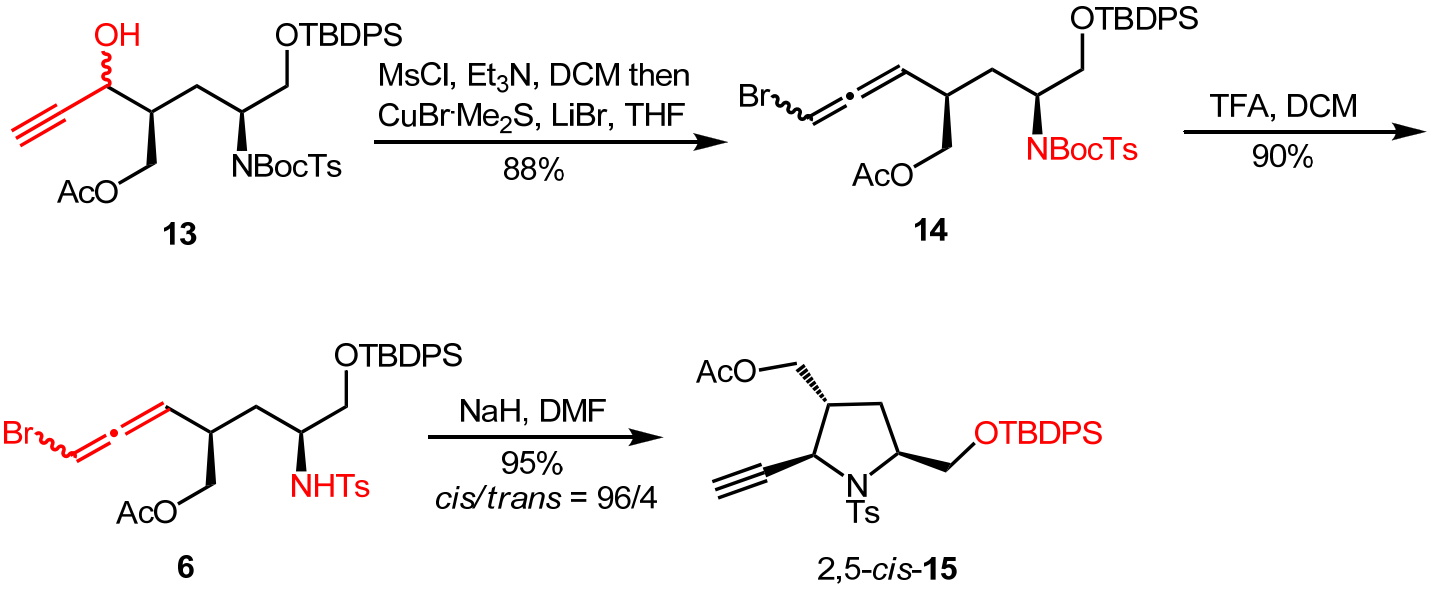
Gold-Catalyzed Hydroamination



Synthesis of 5

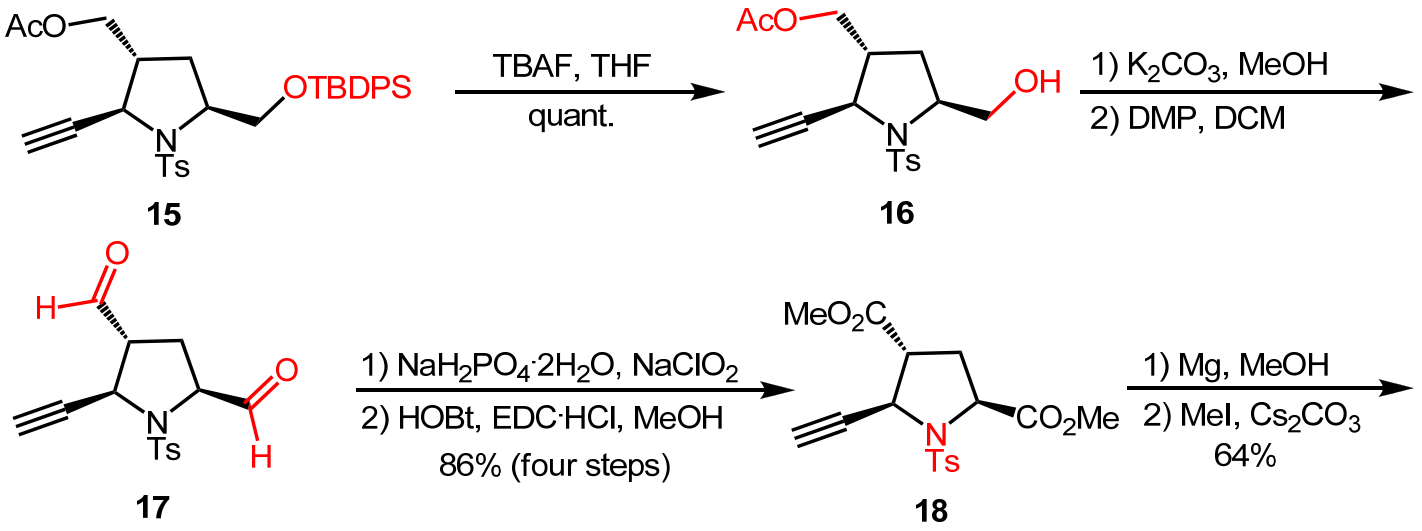


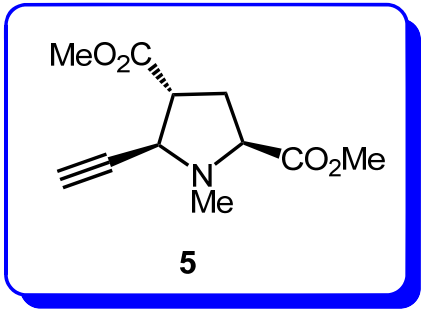
Synthesis of 5



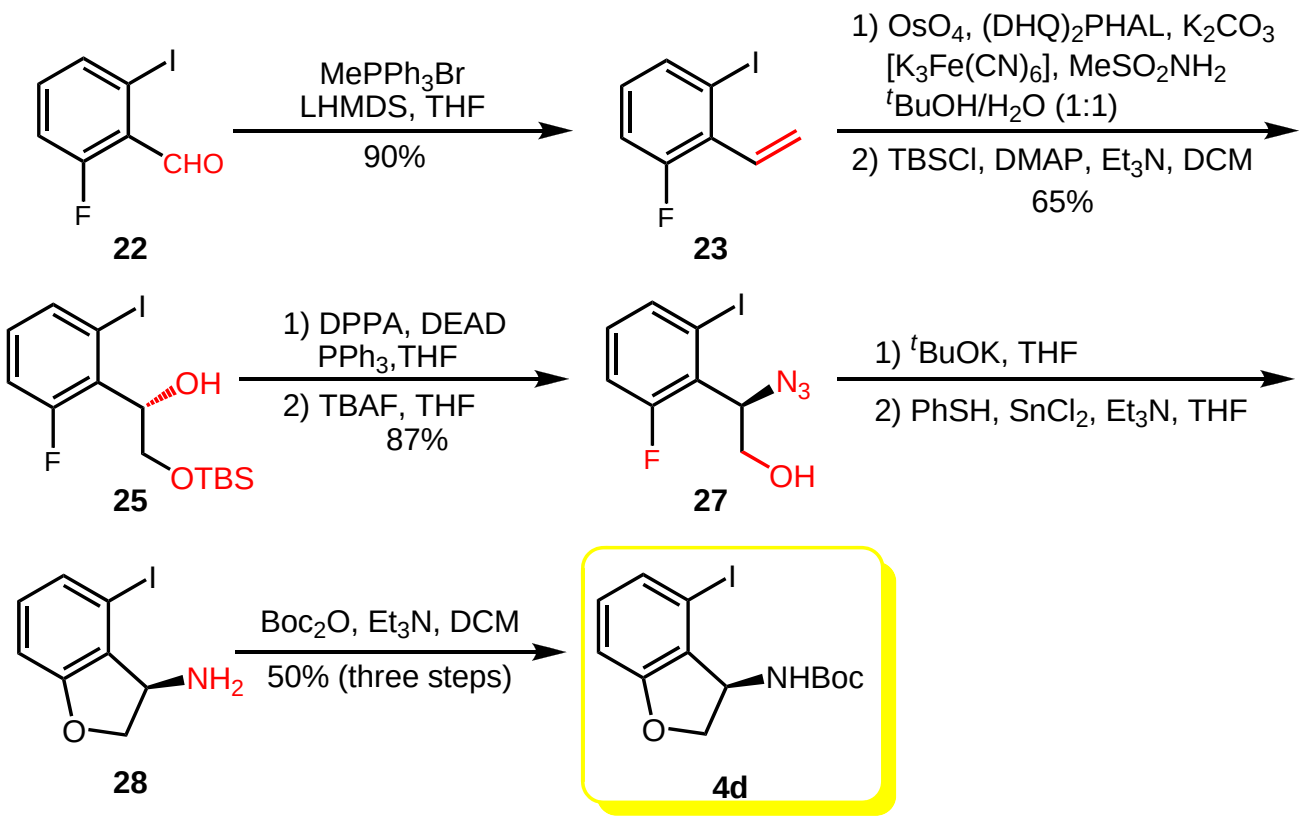
Tanaka, T. et al. *J. Am. Chem. Soc.* **2002**, *124*, 15255.

Synthesis of 5

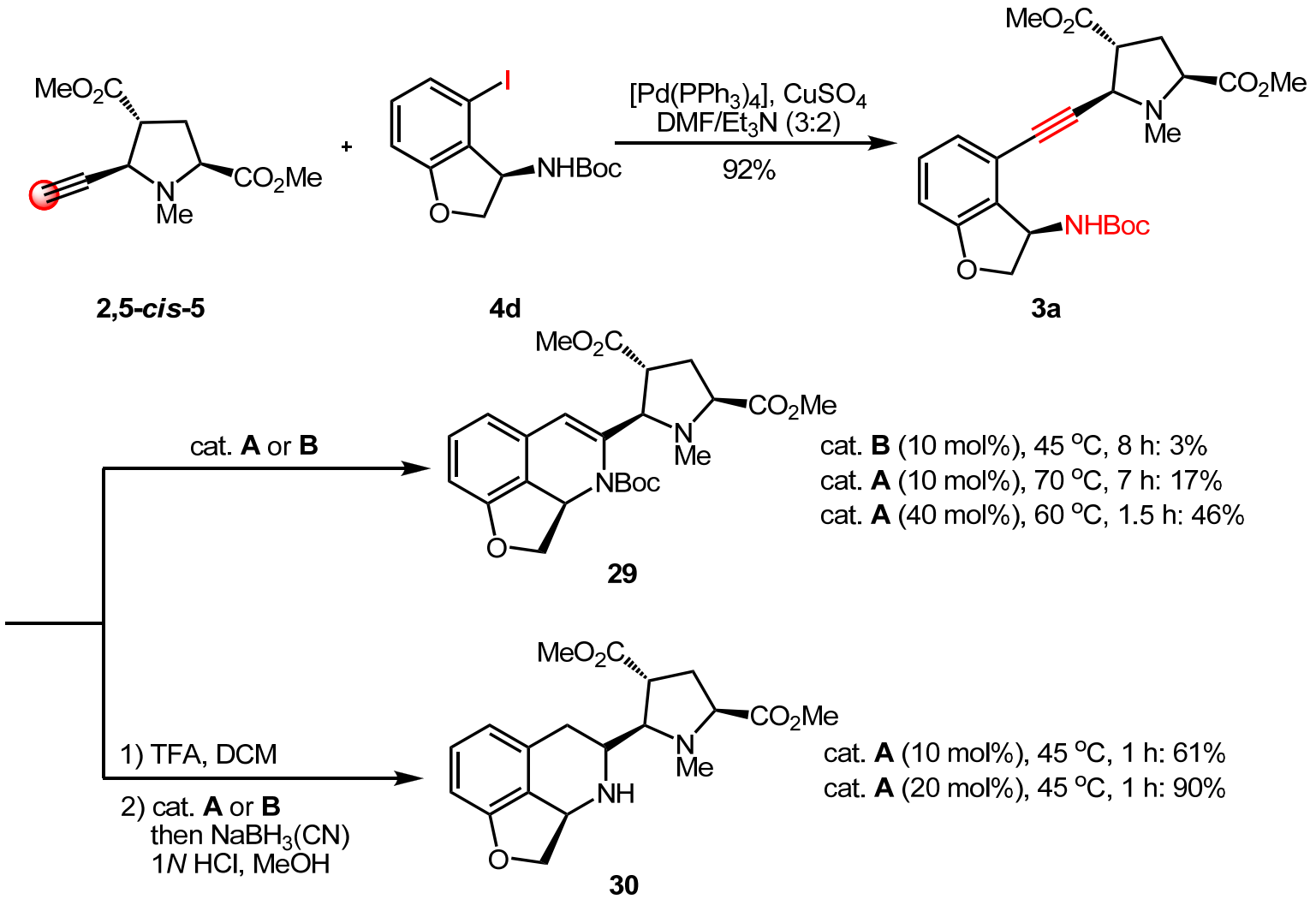




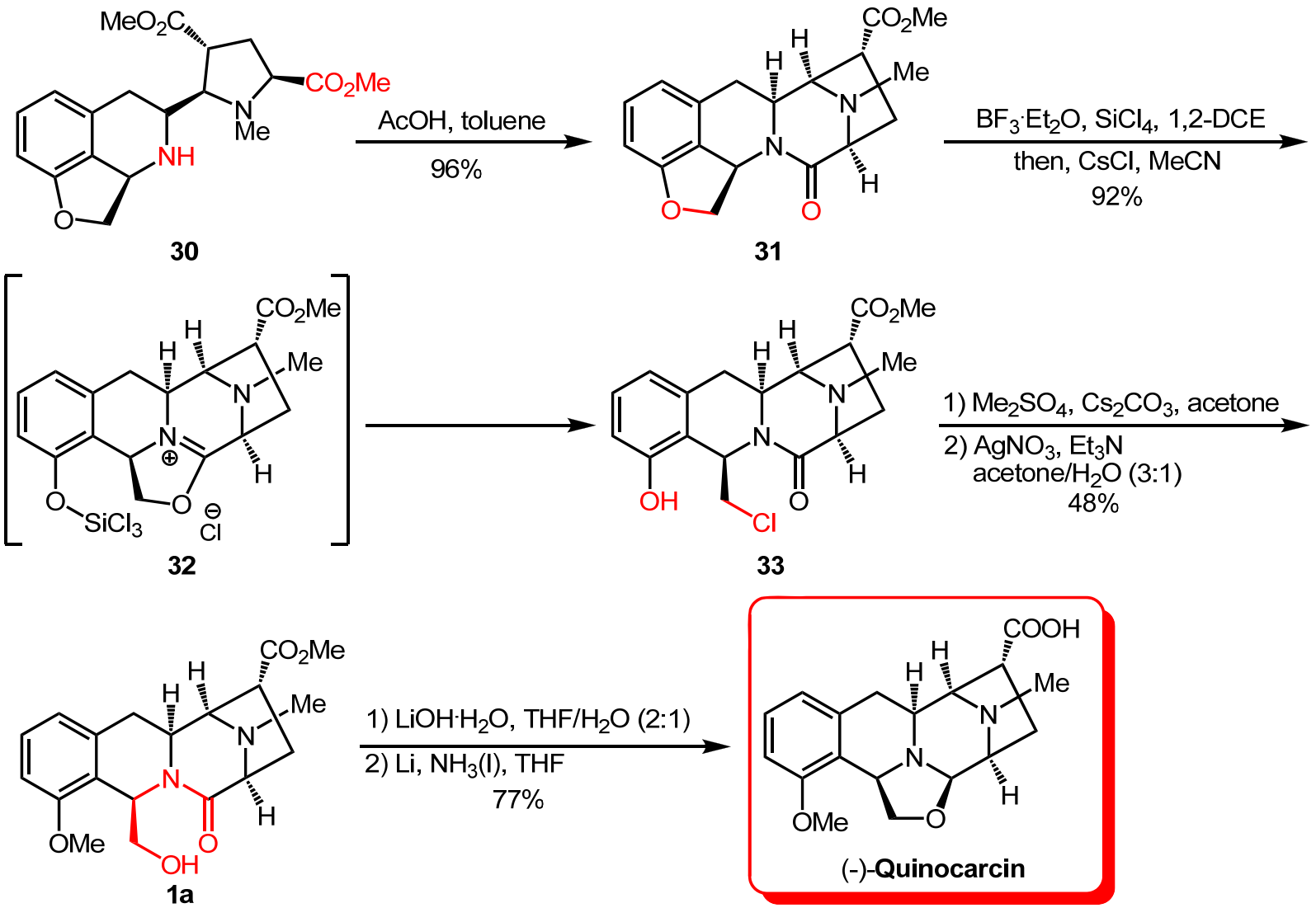
Synthesis of 4d



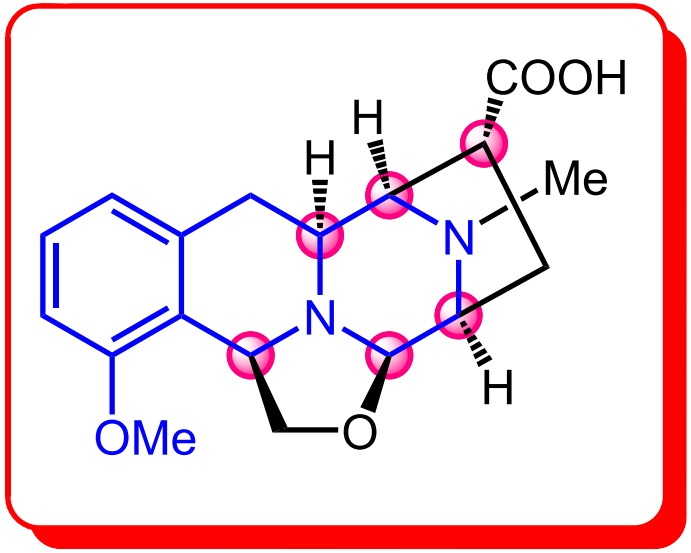
Synthesis of (-)-Quinocarcin



Synthesis of (-)-Quinocarcin



Summary



1. 反应总线性步骤为24步。总收率为3.5%
2. 主要反应：分子内的关环反应构建吡咯啉环，Mitsunobu反应，Sonogashira偶联，金催化氢胺化。

(-)-Quinocarcin is a pentacyclic tetrahydroisoquinoline alkaloid. It has attracted considerable attention from both synthetic and biological chemists interested in its intricate polycyclic architecture and potent broad-spectrum antitumor activity. After its isolation from Streptomyces melanovinaceus in 1983 by Takahashi, Tomita and co-workers, several efficient syntheses of quinocarcin have been reported by the groups of Fukuyama, Garner, Terashima, Myers, Zhu, and Stoltz. The piperizinohydroisoquinoline motif, the core structure of quinocarcin, appears in a variety of alkaloids such as tetrazomine, lemonomycin, and ecteinascidins. The development of a novel strategy that facilitates convergent assembly of this tetracyclic core unit is therefore desirable.

In conclusion, we have achieved the asymmetric total synthesis of quinocarcin. Notably, the regioselectivity of intramolecular hydroamination of **19a-d** could be completely switched by substrate control. This novel and concise construction of the tetrahydroisoquinoline core structure of quinocarcin using the combination of a Sonogashira coupling and an intramolecular hydroamination will enable the synthesis of a variety of related tetrahydroisoquinoline alkaloids.

谢谢！