

Sulfur Ylide Mediated Asymmetric Epoxidations and Aziridinations

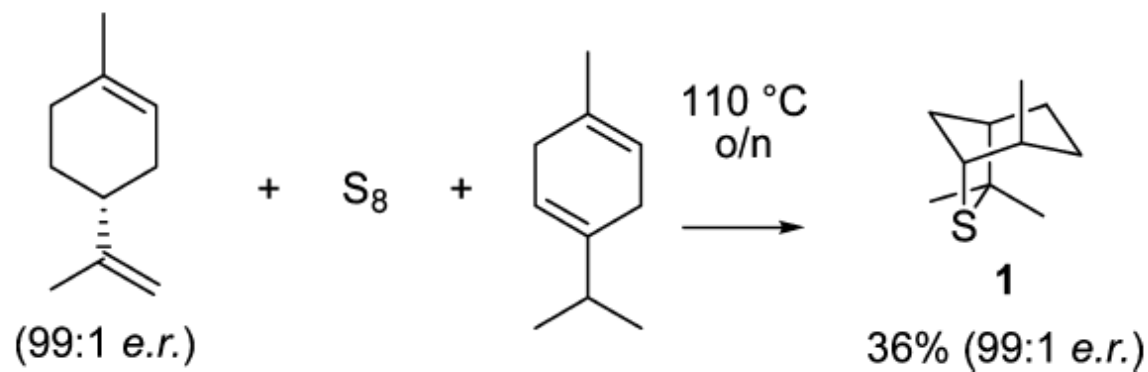
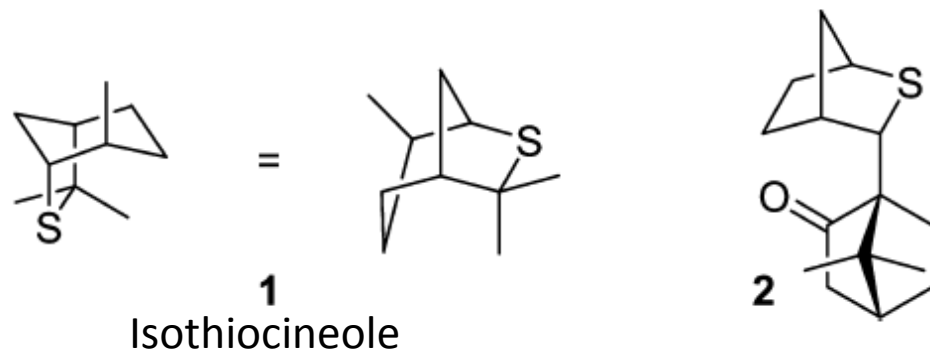
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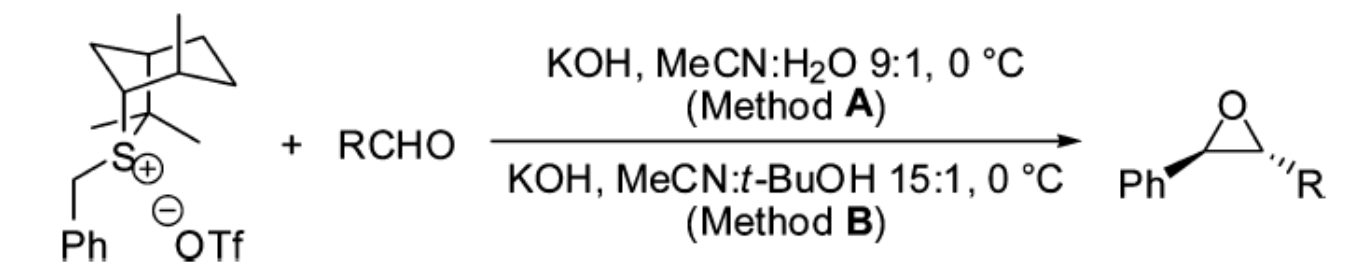
Limitations of Sulfur Ylide Mediated Epoxidation

- Limited scope – only 1,2 diaryl epoxides formed with high dr and er ratio
- Lack of availability - sulfides require multistep syntheses

Structure of Sulfide Catalysts



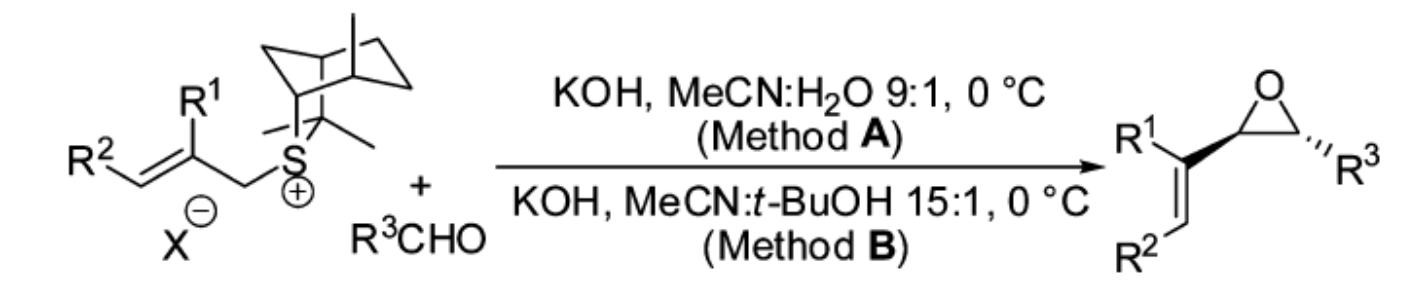
Reactions of Benzyl Sulfonium Salt with Aldehydes



entry	aldehyde	method	yield (%)	<i>d.r.</i> ^a	<i>e.r.</i> ^b
1	benzaldehyde	A	77	>95:5	99:1
2	(<i>E</i>)-PhCH=C(Me)CHO	A	84 ^c	>95:5	98:2
3	(<i>E</i>)-cinnamaldehyde	A	88 ^c	>95:5	99:1
4	(<i>E</i>)-crotonaldehyde	A	86 ^c	>95:5	97:3
5	<i>c</i> -C ₆ H ₁₁ CHO	B	62	93:7	99:1
6	<i>n</i> -C ₄ H ₉ CHO	B	56	91:9	99:1

^a *Trans/cis*. ^b Determined by chiral HPLC; see Supporting Information (SI) for details. ^c Determined by ¹H NMR with an internal standard.

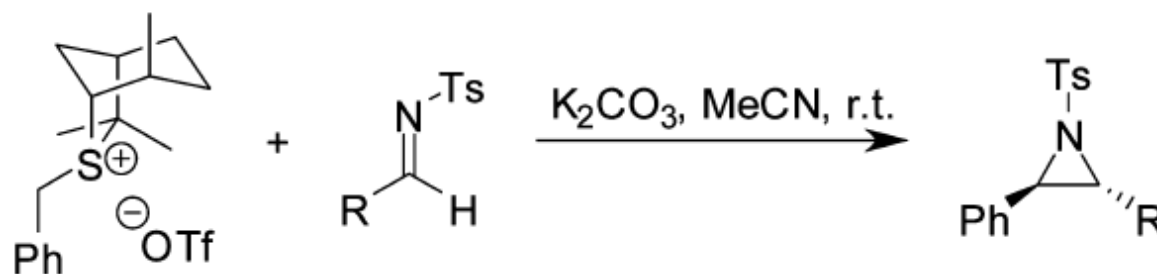
Reactions of Allylic Sulfonium Salts with Aldehydes



R ¹	R ²	R ³	method	yield (%) ^a	<i>d.r.</i> ^b	<i>e.r.</i>
H ^c	Ph	Ph	A	65	80:20	85:15 ^d
Me ^c	Ph	Ph	A	97	>95:5	99:1 ^d
Me ^e	H	Ph	A	80	>95:5	99:1 ^d
Me ^c	Ph	<i>c</i> -C ₆ H ₁₁	B	77	>95:5	98:2 ^d
Me ^e	H	<i>c</i> -C ₆ H ₁₁	B	77	>95:5	97:3 ^f

^a Determined by ¹H NMR with an internal standard. ^b *Trans/cis*. ^c X = BF₄. ^d Determined by chiral HPLC. ^e X = OTf. ^f Determined by chiral GC; see SI for details.

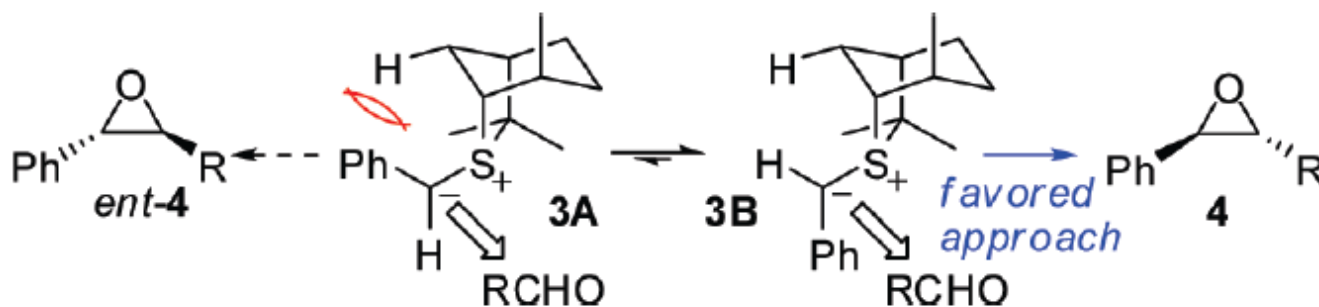
Reaction of Benzyl Sulfonium Salt with Imines



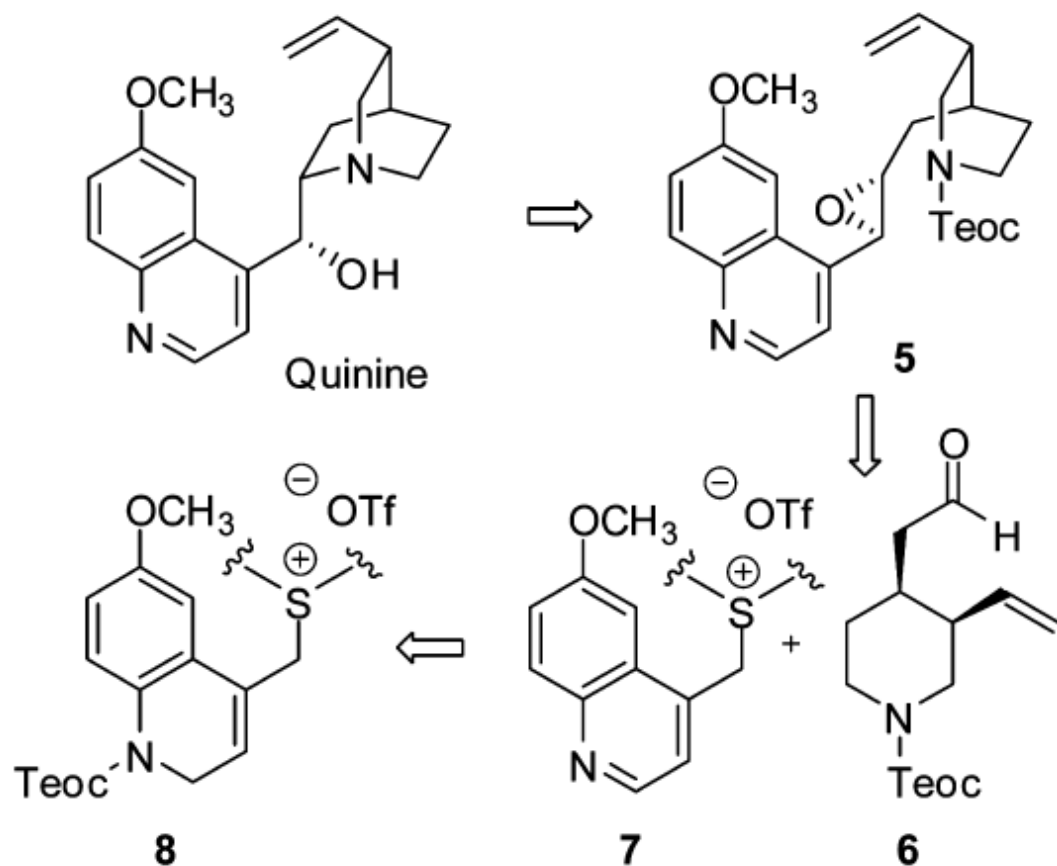
	R	yield (%)	<i>trans/cis</i>	<i>e.r.</i> ^a
1	Ph	72	85:15	99:1
2	<i>p</i> -MeC ₆ H ₄	63	86:14	99:1
3	<i>p</i> -ClC ₆ H ₄	65	75:25	99:1
4	<i>p</i> -MeOC ₆ H ₄	80	83:17	99:1
5	(<i>E</i>)-PhCH=CH	78	>99:1	98:2
6	(<i>E</i>)-TMSCH=CH	78	87:13	99:1

^a Determined by chiral HPLC; see SI for details.

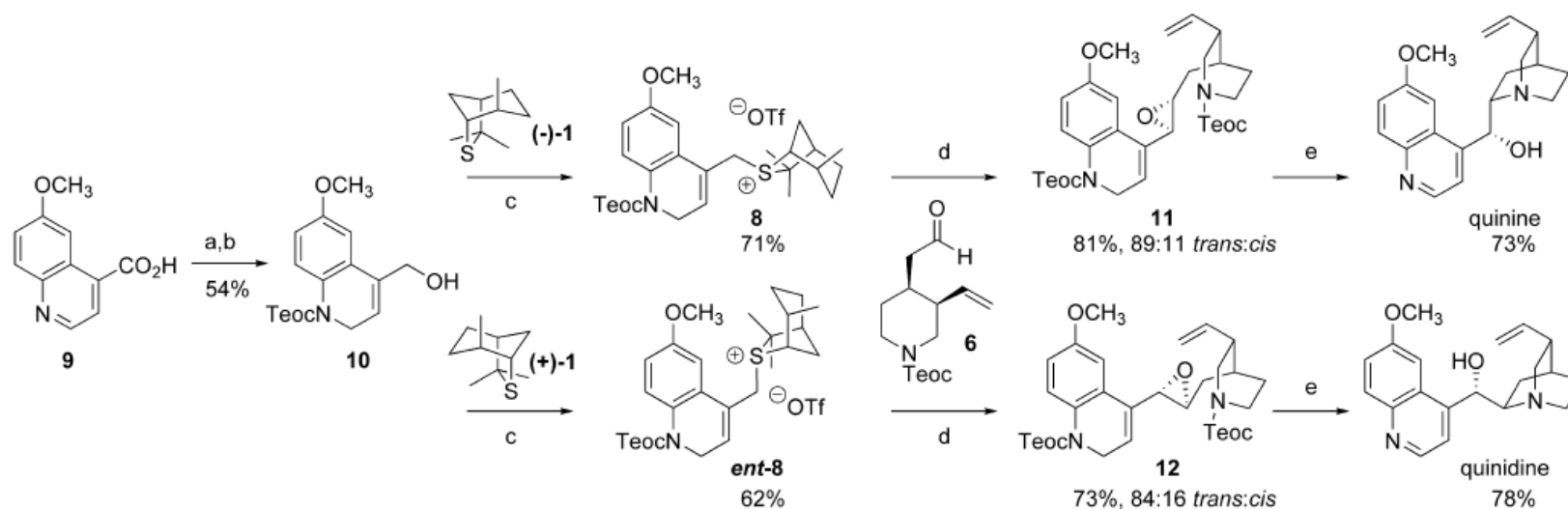
Rationalization of the Reaction Selectivity



Retrosynthesis of Quinine Molecule

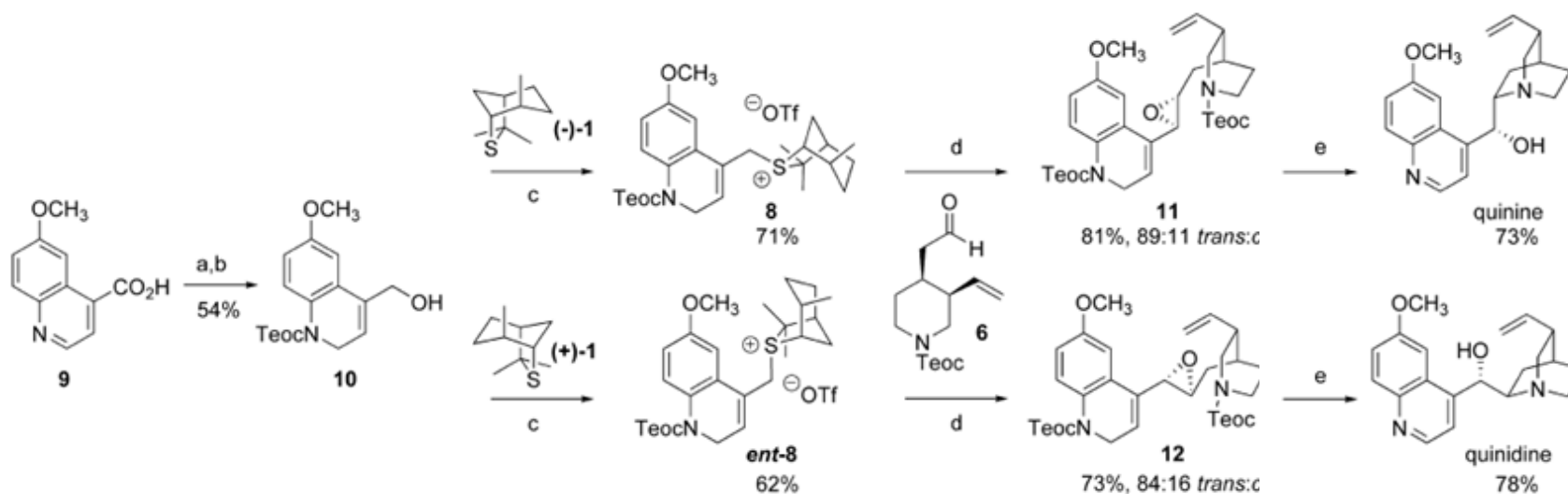


Total Synthesis of Quinine and Quinidine



^a Reagents and conditions: (a) $\text{BH}_3 \cdot \text{THF}$, THF, r.t. 16 h, 69%; (b) $\text{TMS}(\text{CH}_2)_2\text{OH}$, triphosgene, K_2CO_3 , THF, r.t. 1 h, followed by NaBH_4 , H_2O , r.t. 4 h, 79%; (c) 2,6-di-*tert*-butylpyridine, Tf_2O , sulfide **(-)-1**, CH_2Cl_2 , -45°C to r.t. 16 h, 71% (**8**), and sulfide **(+)-1**, 62% (**ent-8**); (d) KOH , $\text{CH}_3\text{CN}/t\text{-BuOH}$ 15:1, 0°C , 24 h, 81%, 89:11 *trans/cis*, (**11**), 73%, 84:16 *trans/cis* (**12**); (e) CsF , DMF, MW, 180°C , 15 min, then stir under O_2 , r.t. 24 h, 73% quinine, 78% quinidine.

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Conclusion

- Straight forward synthesis of sulfide precursor
- Broad scope of epoxidation and aziridination conditions 1,2 arylalkyl and a,b-unsaturated epoxides and aldehydes
- Limitation: stoichiometric amount of ylide