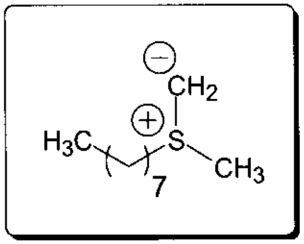
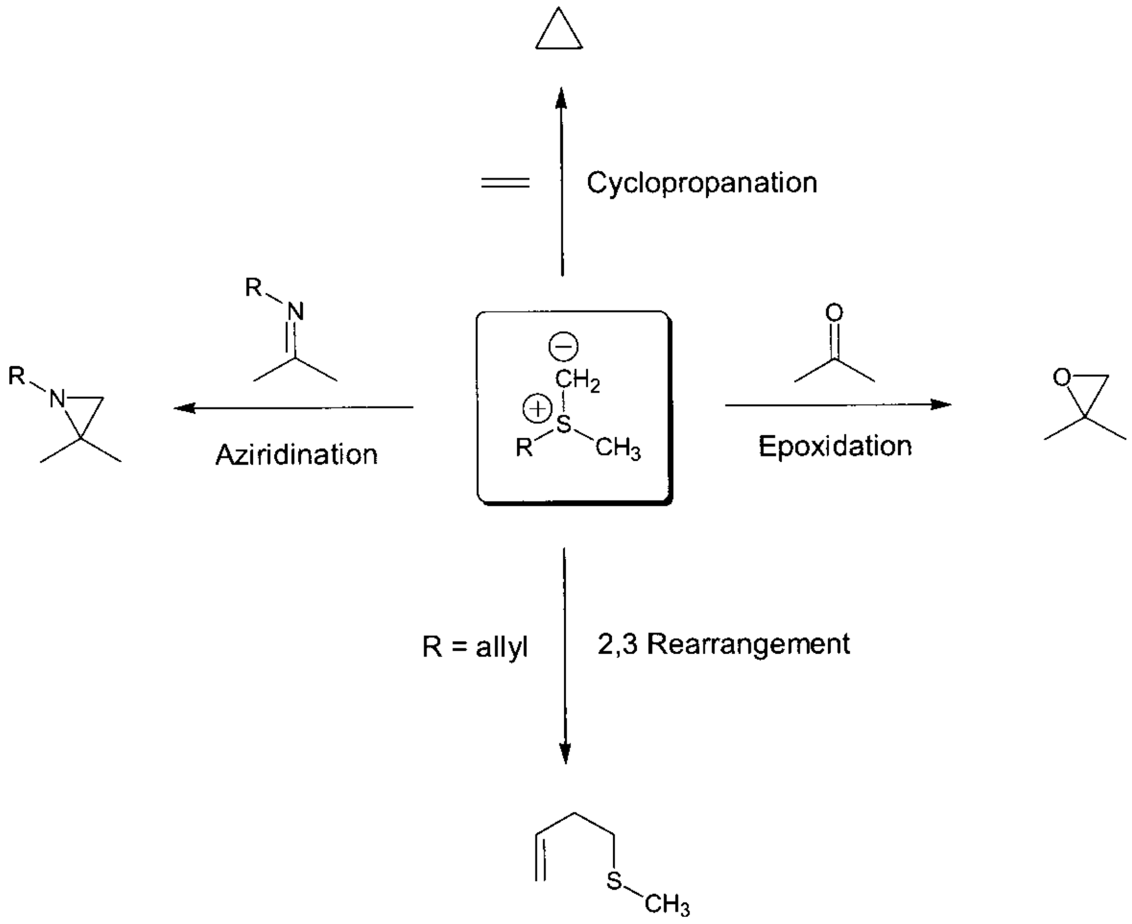
Sulfur Ylides via Decarboxylation of Carboxymethylsulfonium Betaines: A Novel and Mild Protocol for the Preparation of Oxiranes

David C. Forbes, Michael C. Standen, and Derrick L. Lewis

Org. Lett. **2003**, *5*, 2283

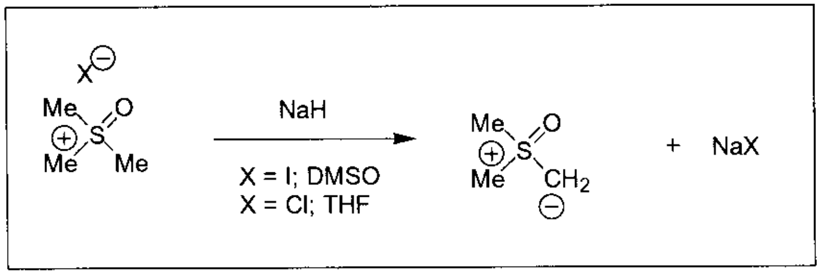


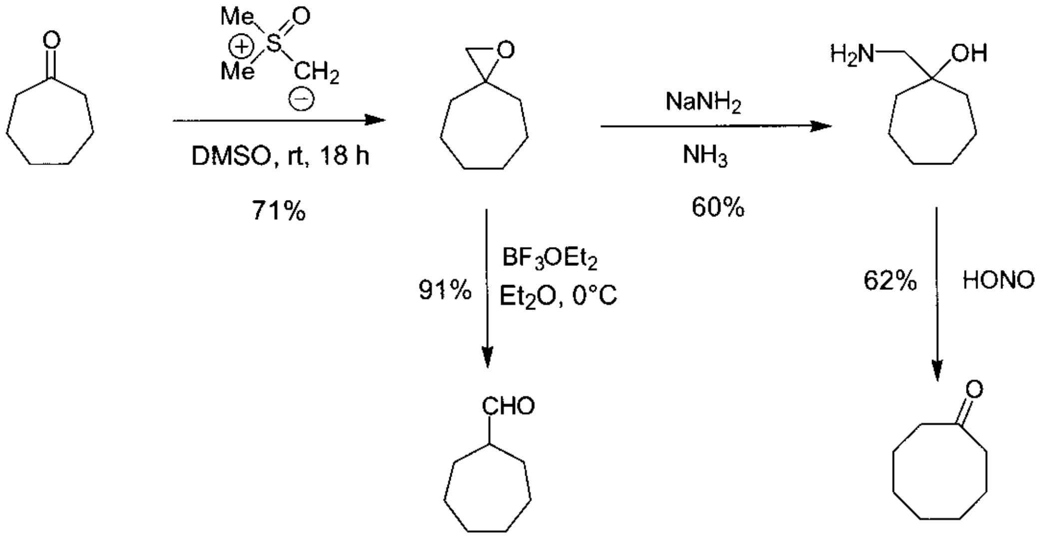
Uses for Sulfonium and Oxosulfonium Ylides



Nitrogen, Oxygen, and Sulfur Ylide Chemistry; Clark, J. S., Ed.; Oxford: New York, 2002.

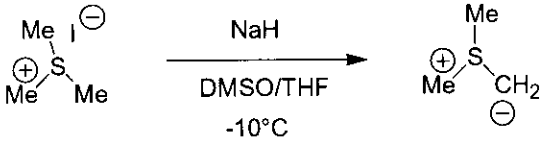
Preparation of Oxosulfonium Ylides





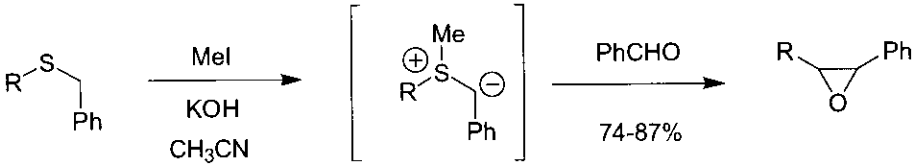
Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, *84*, 867.
Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

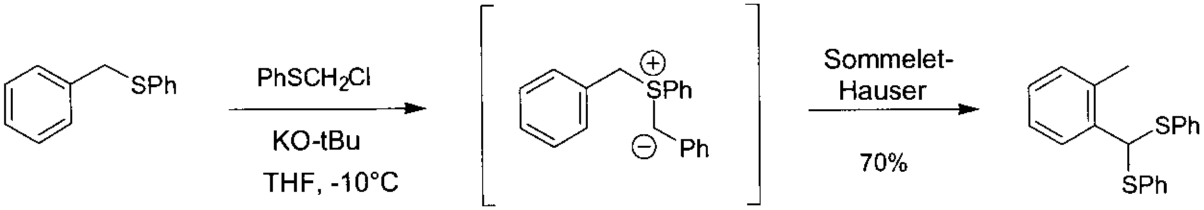
Preparation of Sulfonium Ylides



more reactive, but less stable!

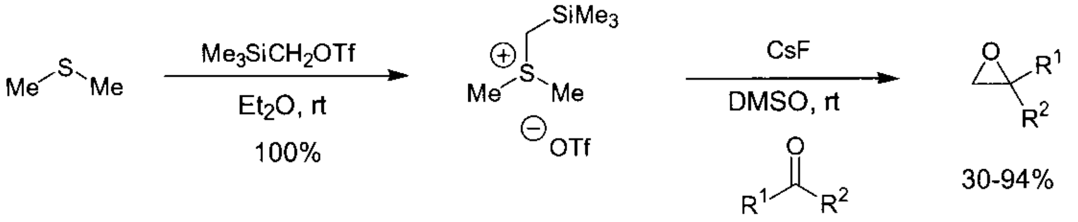
Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.



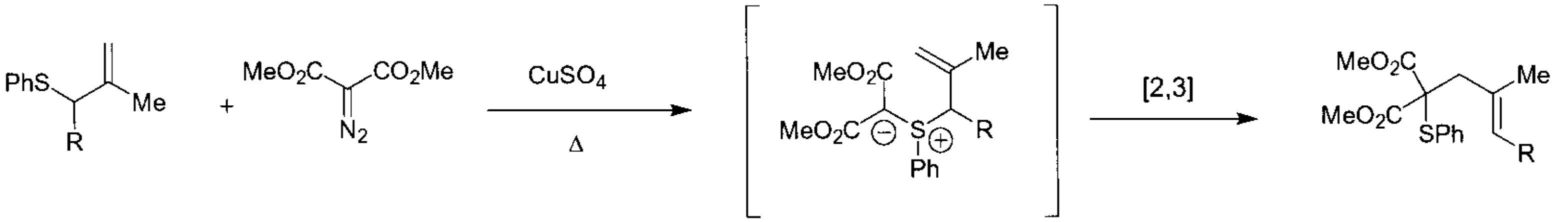


Julia, S.; Huynh, C.; Michelot, D. *Tetrahedron Lett.* **1972**, *13*, 3587.

Preparation of Sulfonium Ylides



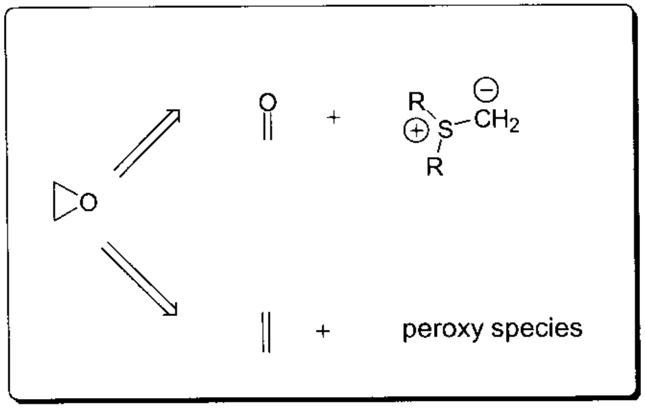
Hioki, K.; Tani, S.; Sato, Y. *Synthesis* **1995**, 649.



R = Bu; 70%
E:Z = 9:1

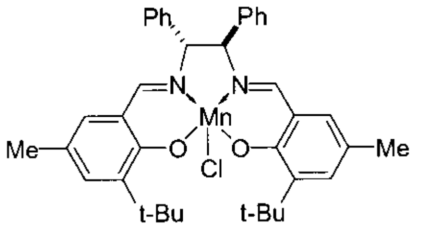
Grieco, P. A.; Boxler, D.; Hiroi, K. *J. Org. Chem.* **1973**, *38*, 2572.

Sulfur Ylides as an Alternative to Alkene Oxidation



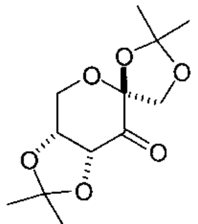
Sharpless (t-BuOOH, Ti(OiPr)$_4$, DIPT)
directed by allylic/homoallylic alcohols

Jacobsen (m-CPBA, NMO, **A**)
useful for unactivated olefins



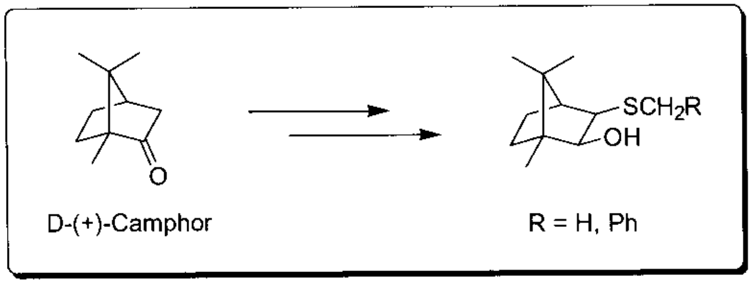
A

Shi (Oxone, NaHCO$_3$, **B**)
good for unfunctionalized trans-olefins



B

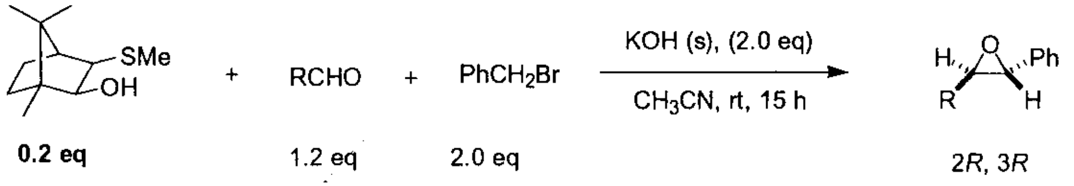
Asymmetric Epoxidation with Sulfur Ylides



R = Ph	yield = 87%	ee = 74%
R = *p*-ClC$_6$H$_4$	yield = 96%	ee = 77%
R = *p*-MeC$_6$H$_4$	yield = 89%	ee = 72%

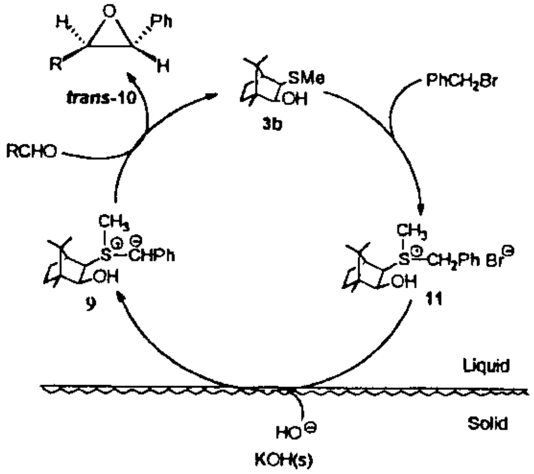
Li, A.-H.; Dai, X.; Hou, X.-L.; Huang, Y.-Z.; Li, F.-W. *J. Org. Chem.* **1996**, *61*, 489.
Dai, L.-X.; Hou, X.-L.; Zhou, Y.-G. *Pure Appl. Chem.* **1999**, *71*, 369.

Asymmetric Epoxidation with Sulfur Ylides



R = Ph	yield = 97%	ee = 42%
R = $p\text{-ClC}_6\text{H}_4$	yield = 93%	ee = 60%
R = $p\text{-MeC}_6\text{H}_4$	yield = 89%	ee = 36%

Scheme 5. Catalytic Cycle for Formation of Oxiranes

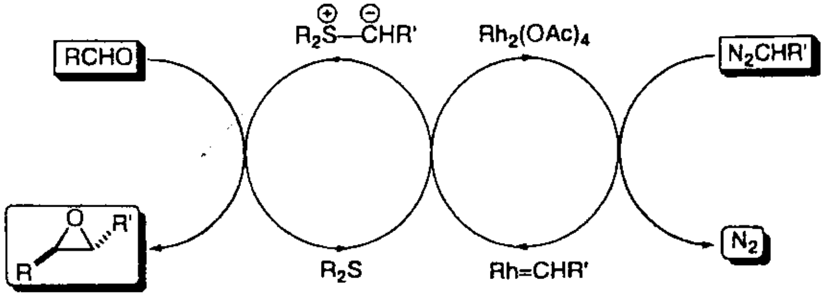


Limited scope: Only applicable to non-enolizable aldehydes and robust base stable substrates

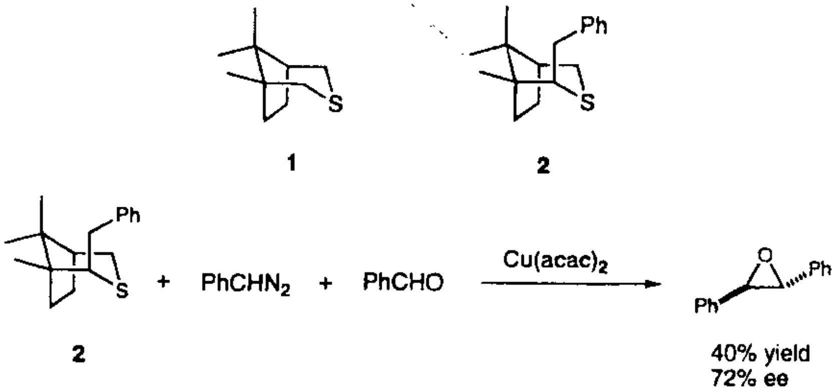
Li, A.-H.; Dai, X.; Hou, X.-L.; Huang, Y.-Z.; Li, F.-W. *J. Org. Chem.* **1996**, *61*, 489.
Dai, L.-X.; Hou, X.-L.; Zhou, Y.-G. *Pure Appl. Chem.* **1999**, *71*, 369.

Asymmetric Epoxidation with Sulfur Ylides

Scheme 1

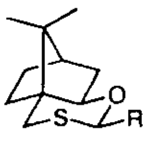


Scheme 2



Aggarwal, V. K.; Ford, J. G.; Thompson, A.; Jones, R. V. H.; Standen, M. C. H. *J. Am. Chem. Soc.* **1996**, *118*, 7004.

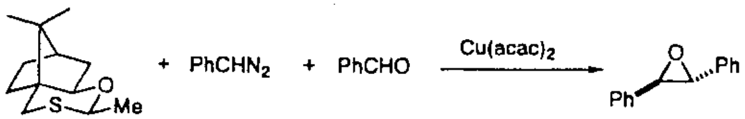
Asymmetric Epoxidation with Sulfur Ylides



3

3a R = H
3b R = Me
3c R = *i*-Pr
3d R = *t*-Bu
3e R = CH_2Ph
3f R = CH_2OPh
3g R = CH_2OMe

Table 1. Yields, Enantioselectivities, and Ratios of Stilbene Oxide Formed from Benzaldehyde Using 0.2 eq of Sulfides **3a–g**

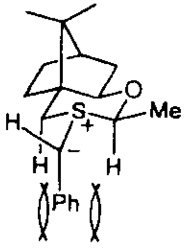


entry	sulfide	yield %	ee %[a]	trans: cis
1	**3a**	83	41 (*R*,*R*)[b]	>98:2
2	**3b**	73	93 (*R*,*R*)[b]	>98:2
3	**3c**	45	93 (*R*,*R*)[b]	>98:2
4	**3d**	0		
5	**3e**	56	88 (*R*,*R*)[b]	>98:2
6	**3f**	43	83 (*R*,*R*)[b]	>98:2
7	**3g**	70	92 (*R*,*R*)[b]	>98:2

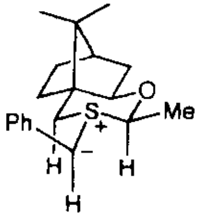
[a] Enantiomeric excess determined by chiral HPLC using a Chiralcel OD column. [b] Absolute configuration determined by comparison of $[\alpha]_D$ values with literature values.[5h]

Table 2. Yields, Enantioselectivities, and Ratios of Epoxides Formed from Aldehydes Using 0.2 eq of Sulfide **3b**

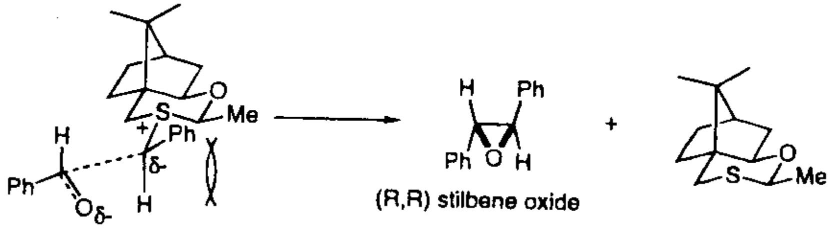
entry	aldehyde	yield %	ee %[a]	*trans*:*cis*
1	benzaldehyde	73	93 (*R*,*R*)[b]	>98:2
2	*p*-chlorobenzaldehyde	72	92(*R*,*R*)[b]	>98:2
3	*p*-tolualdehyde	64	92(*R*,*R*)[b]	>98:2
4	cinnamaldehyde	73	89[c]	>98:2
5	valeraldehyde	35	68[c]	92:8
6	cyclohexanecarboxaldehyde	32	90[c]	70:30



4a



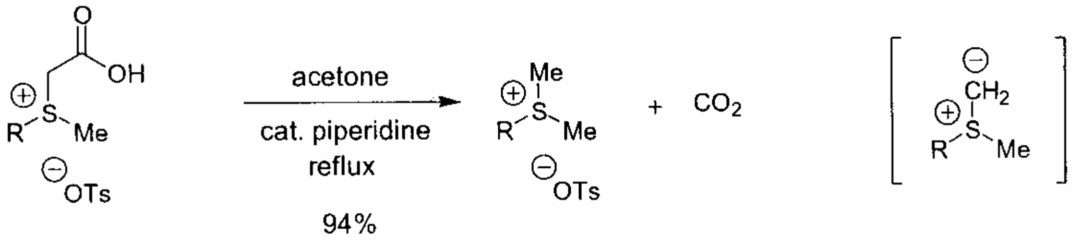
4b



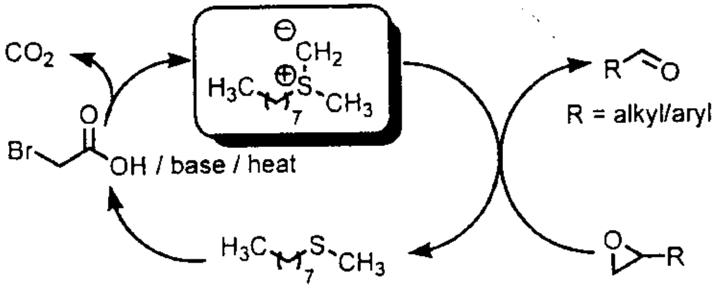
Aggarwal, V. K.; Ford, J. G.; Thompson, A.; Jones, R. V. H.; Standen, M. C. H. *J. Am. Chem. Soc.* **1996**, *118*, 7004.

A New Method for the Generation of Sulfonium Ylides

"Ylide in a bottle"



Burness, D. J. *J. Org. Chem.* **1959**, *24*, 849.



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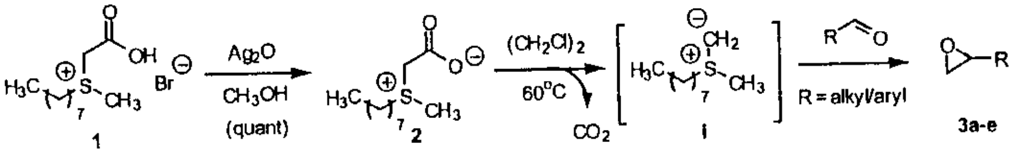
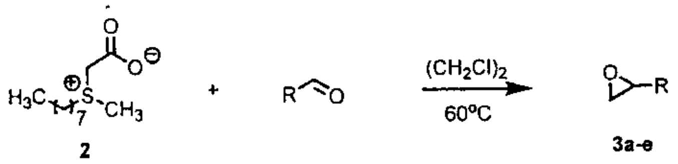
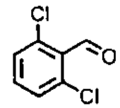
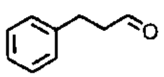
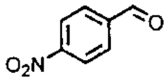
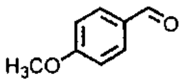
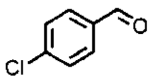
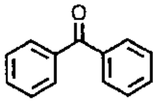
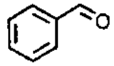




entry	carbonyl derivative	3, %[a]	entry	carbonyl derivative	3, %[a]
1, a		85	5, e		45
2, b		84	6		-[b]
3, c		62	7		-[b]
4, d		55			

[a] Isolated yields of chromatographically homogeneous spectroscopically pure products are reported. [b] Desired oxirane not isolated; carbonyl derivative recovered in >95%.

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Future Work

1. Study the effect of solvation on betaine decarboxylation
2. Use of chiral nonracemic sulfur templates to render the current methodology asymmetric
3. Optimization of the conditions to allow for catalytic quantities of sulfide to promote the reaction
4. Development of ultralabile betaines which decarboxylate at lower temperatures
5. Extension of the methodology to aziridine formation through the use of activated imines