OMICS GROUP

OMICS Group International through its Open Access Initiative is committed to make genuine and reliable contributions to the scientific community. OMICS Group hosts over **400** leading-edge peer reviewed Open Access Journals and organizes over **300** International Conferences annually all over the world. OMICS Publishing Group journals have over **3 million** readers and the fame and success of the same can be attributed to the strong editorial board which contains over **30000** eminent personalities that ensure a rapid, quality and quick review process. OMICS Group signed an agreement with more than **1000** International Societies to make healthcare information Open Access.

OMICS Journals are welcoming Submissions

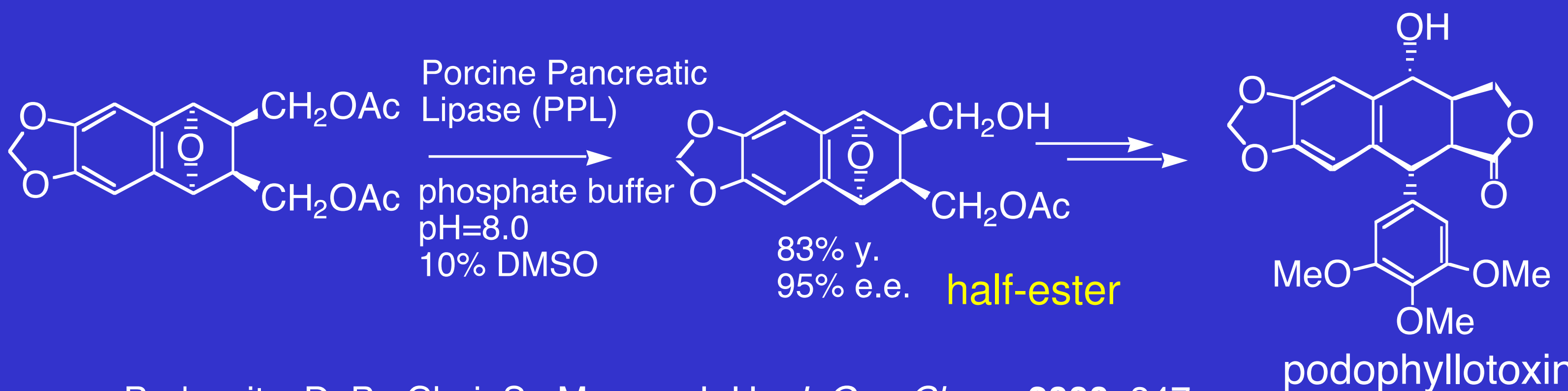
OMICS Group welcomes submissions that are original and technically so as to serve both the developing world and developed countries in the best possible way.
OMICS Journals are poised in excellence by publishing high quality research. OMICS Group follows an Editorial Manager® System peer review process and boasts of a strong and active editorial board.
Editors and reviewers are experts in their field and provide anonymous, unbiased and detailed reviews of all submissions.
The journal gives the options of multiple language translations for all the articles and all archived articles are available in HTML, XML, PDF and audio formats. Also, all the published articles are archived in repositories and indexing services like DOAJ, CAS, Google Scholar, Scientific Commons, Index Copernicus, EBSCO, HINARI and GALE.

For more details please visit our website:
http://omicsonline.org/Submitmanuscript.php

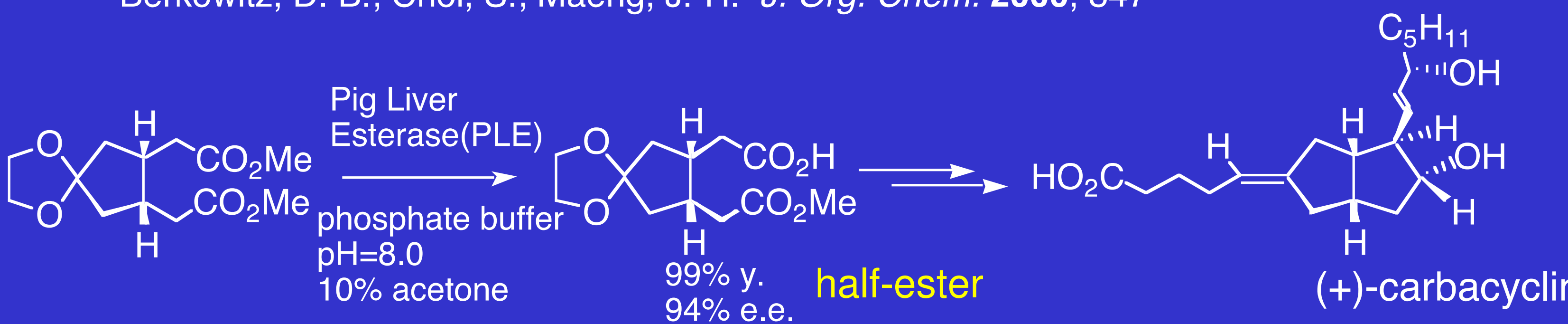
Recent Progress of Selective Monohydrolysis of Symmetric Diesters

Satomi Niwayama
Graduate School of Engineering
Muroran Institute of Technology

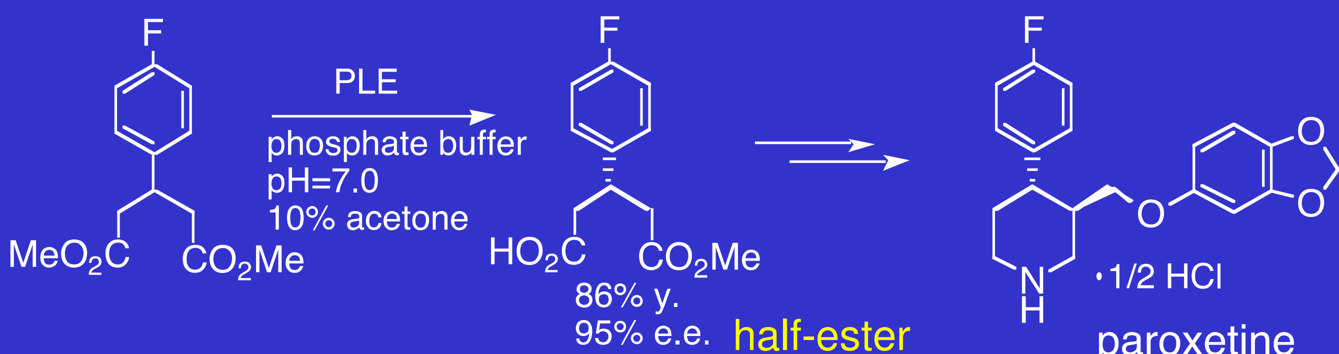
Synthesis of Pharmaceuticals with the use of half-esters



Berkowitz, D. B.; Choi, S.; Maeng, J.-H. *J. Org. Chem.* **2000**, 847



Sano, S.; Ushirogochi, H.; Morimoto, K.; Tamai, S. Nagao, Y. *Chem. Commun*. **1996**, 1775

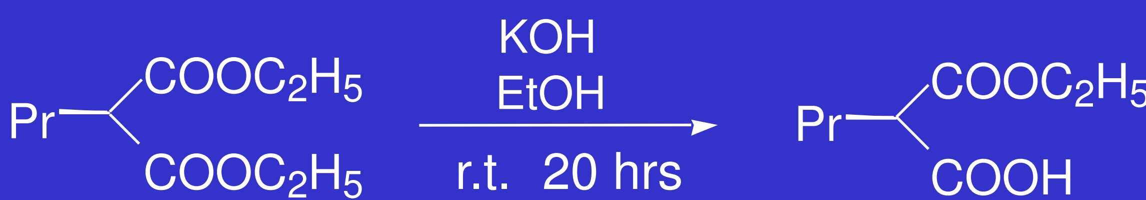


Yu, M. S.; Lantos, I.; Peng, Z-Q.; Yu, J.; Cacchio, T. J. *Tetrahedron Lett.* **2000**, 5647

Previous examples of monosaponification

(yield unknown)

Vecchi, A.; Melone, G.
J. Org. Chem. **1959**, *24*, 109



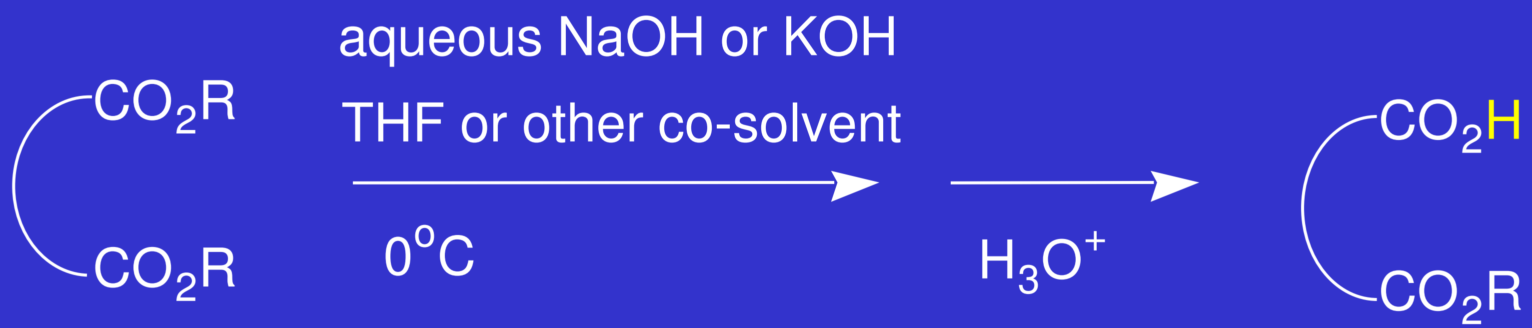
74.6 %

Corey, E. J.
J. Am. Chem. Soc. **1952**, *74*, 5897

Corey, E. J.
J. Am. Chem. Soc. **1952**, *74*, 5897

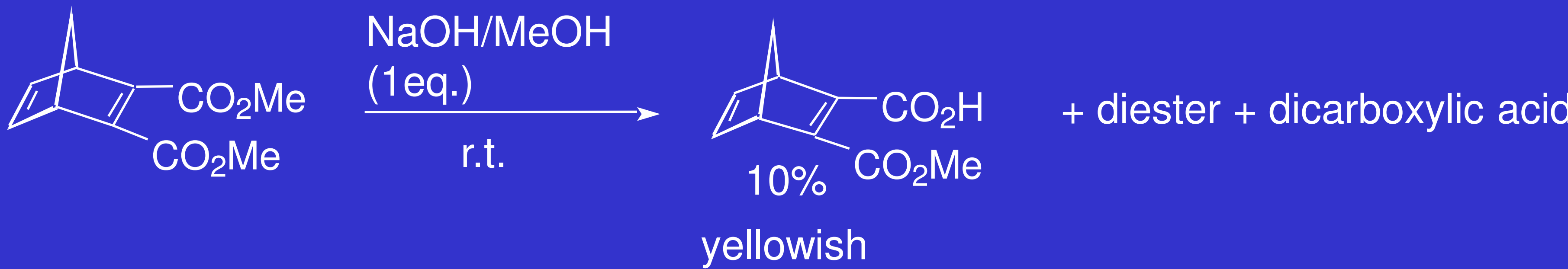
98.5 % (as a crude product)

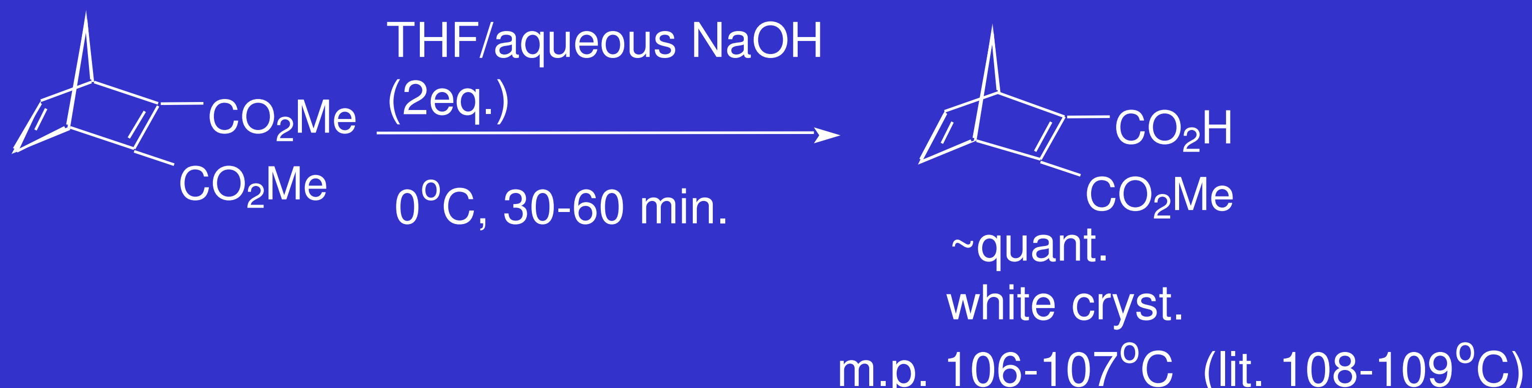
New Selective Monohydrolysis



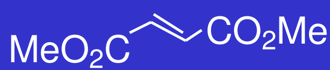
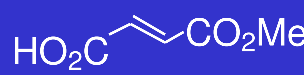
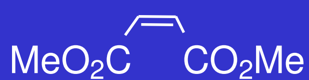
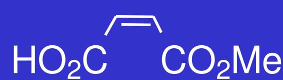
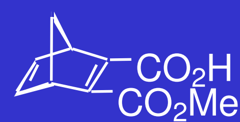
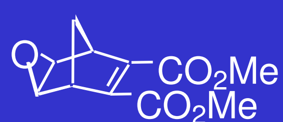
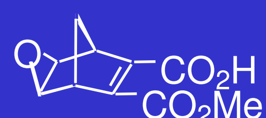
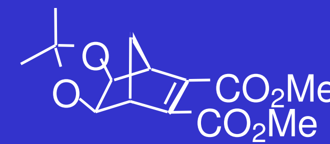
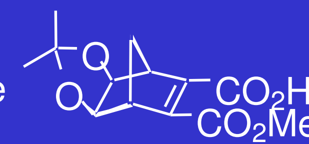
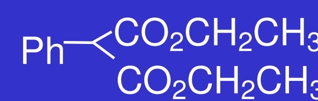
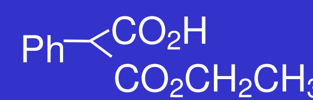
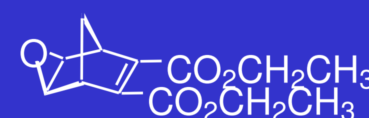
R=Me, Et

Comparison to Classical Conditions



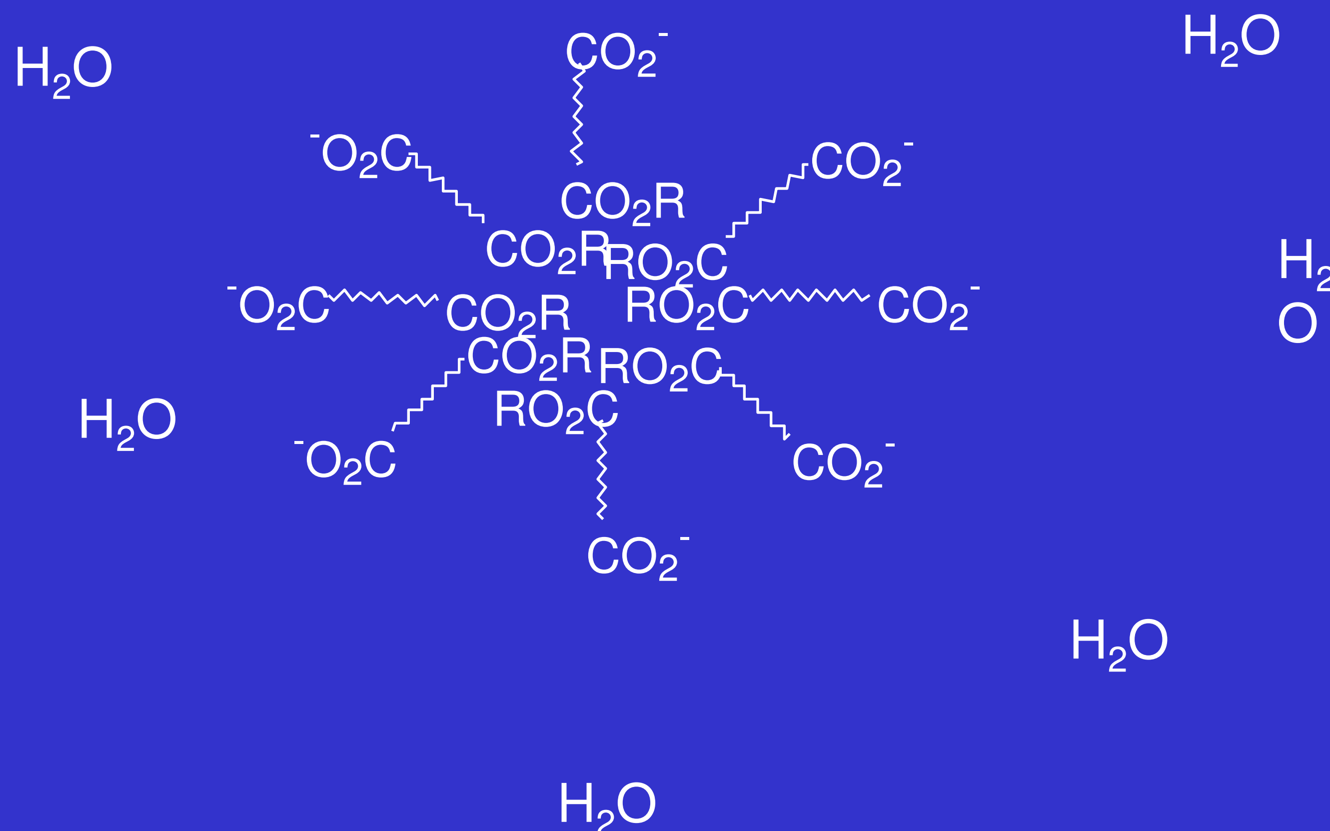


Monohydrolysis of Symmetric Diesters

entry	diester	product	yield (%)[a]
1	 **1a**	 **1b**	70%
2	 **2a**	 **2b**	79%
3	 **3a**	 **3b**	95%[b]
4	 **4a**	 **4b**	>99%
5	 **5a**	 **5b**	>99%
6	 **6a**	 **6b**	>99%
7	 **7a**	 **7b**	96%
8	 **8a**	 **8b**	>99%
9	 **9a**	 **9b**	>99%

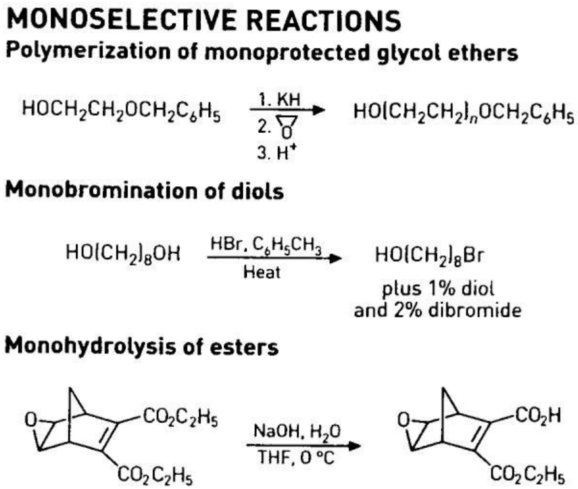
[a] Yields are isolated yields from silica gel column chromatography based on the amounts of the diesters submitted to the reaction.
[b] The yield was diminished due to the slight volatility of **3b**.

Potential Mechanism



Soap-like aggregates prohibit further hydrolysis

Chemical and Engineering News, 2001, January 22, p92-94



THREE RESEARCH GROUPS report progress in regioselective reaction of one of two identically placed functional groups in a molecule. Workers at Scripps Research Institute have succeeded in making polyethylene glycol ethers of defined molecular weights capped at one end. Chemists at the University of Waterloo in Ontario convert 1,ω-diols selectively to bromo alcohols. And investigators at Oklahoma State University hydrolyze one out of two carboxylate groups in a symmetrical structure.

Ordinarily, such selective reactions are carried out by enzymes. Often an advantage in such a case is that in prochiral substrates the product is a single isomer resulting from the enantioselectivity of the enzyme. But an enzyme offers no guarantee in advance of enantioselectivity or yield.

Chemistry professor Kim D. Janda of Scripps begins with commercially available 2-benzyloxyethanol, which he treats first with potassium hydride and then with a measured amount of ethylene oxide [*J. Org. Chem.*, **65**, 5843 (2000)]. The product is polyethylene glycol of molecular weight 1,000, 2,000, or 4,500, capped on only one end with a benzyl group. This product serves as a springboard for other interconversions. For example, reaction with *tert*-butyldimethylsilyl (TBDMS) chloride puts a TBDMS group on the other hydroxyl group. Hydrogenation of that product cleaves the benzyl group, leaving only the TBDMS group on the other end.

Organic chemistry professor J. Michael Chong of Waterloo finds that almost all of the literature methods for making bromo alcohols from diols suffer from poor yields or lack of selectivity or both. His present method is stirring a mixture of diol in toluene with 48% hydrobromic acid under reflux [*J. Org. Chem.*, **65**, 5837 (2000)]. From 1,8-octanediol, for example, he gets about 90% yield of 8-bromo-1-octanol with only 2% of dibromide and 1% of unreacted diol. He suggests that the bromo alcohol forms micellelike structures in the toluene in which polar hydroxyl groups are pointed into the center and thus kept away from exposure to the aqueous brominating agent.

A SIMILAR TWO-PHASE mechanism that protects his saponification products from further reaction is likewise suggested by organic chemistry professor Satomi Niwayama of Oklahoma State. He dissolves the diester in THF and adds that to dilute sodium hydroxide and stirs at 0 °C. Yields are high, and epoxide groups go unmolested. For example, the monoepoxide of the Diels-Alder product of cyclopentadiene and dimethyl or diethyl acetylenedicarboxylate yields monoester in greater than 99% yield.

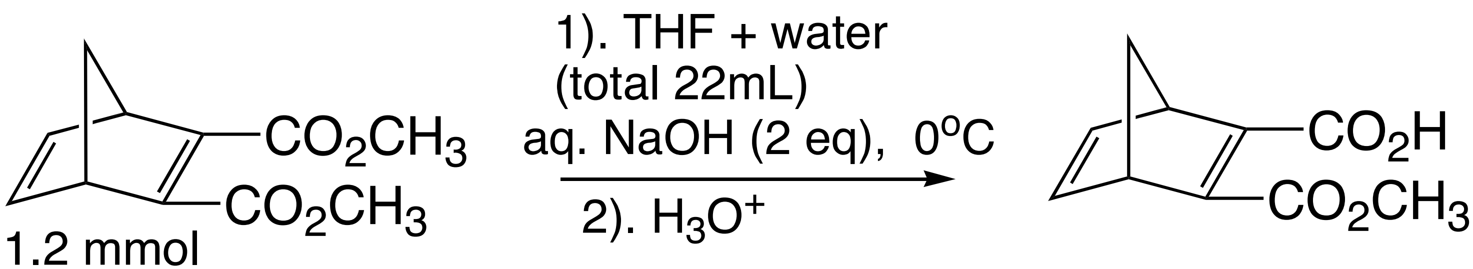
Niwayama proposes that at the low temperature the reaction mixture is a two-phase system. The already reacted carboxylate anion ties up the unreacted ester grouping in the less polar phase in such a way as to protect it from action of hydroxide ions.

Four research groups report progress in metal-mediated syntheses. These results may lead to improvements in the use of metals or to reactions that avoid metals entirely. Issues for use of metal include toxic residues in organic products and the treatment of metal wastes.

For example, researchers at the National Tsing Hua University in Hsinchu, Taiwan, have worked out a nickel-zinc replacement

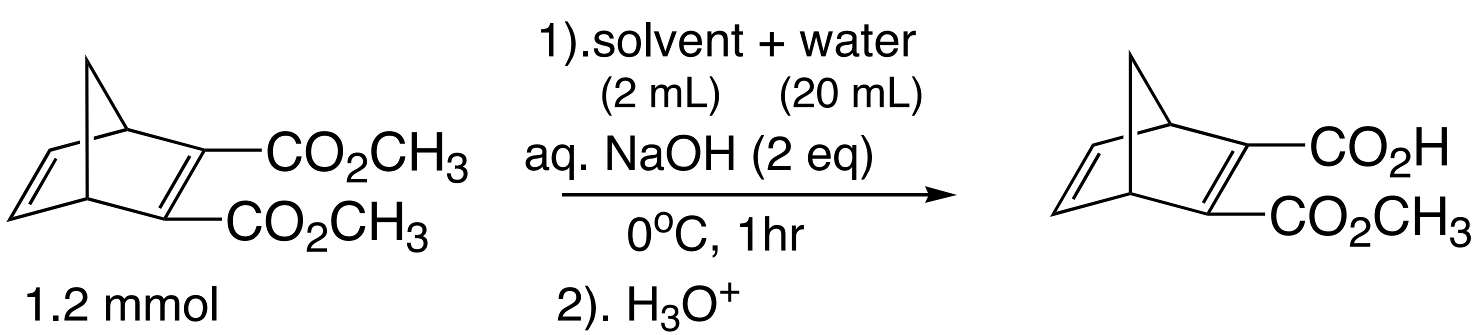
Solvent Effects

Effect of the Volume of THF



	Volume of THF (mL)	yield (%)	reaction time	rate constant($Lmol^{-1}s^{-1}$)
	22	88	8hr	3.26×10^{-3}
	18	81	6hr30min.	6.06×10^{-3}
	14	84	5hr20min.	1.10×10^{-2}
	10	90	3hr	2.06×10^{-2}
	6	93	1hr10min.	2.56×10^{-2}
initial volume ⇒	2	>99	1hr10min.	4.70×10^{-2}
	1	>99	1hr10min.	4.81×10^{-2}
	0	>99	1hr10min.	4.59×10^{-2}

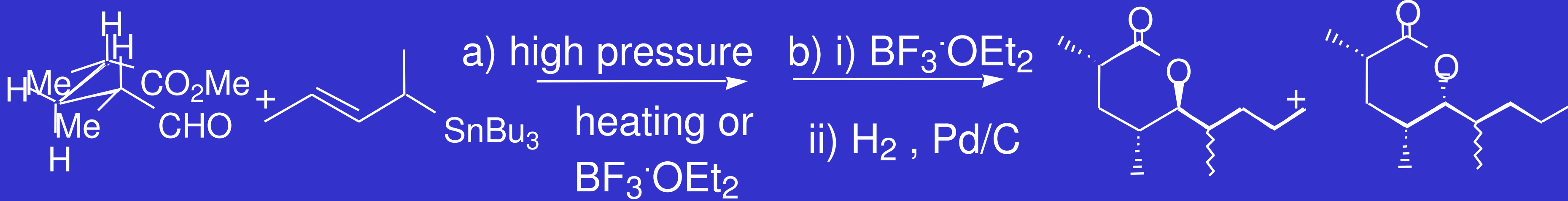
Effects of Kinds of Co-Solvent



Solvent	yield (%)	rate constant($Lmol^{-1}s^{-1}$)
THF	>99	4.70×10^{-2}
MeOH	90	3.73×10^{-2}
EtOH	86	3.48×10^{-2}
i-PrOH	88	3.29×10^{-2}
CH_3CN	>99	4.85×10^{-2}
CH_2Cl_2	trace	8.60×10^{-4}
none	>99	4.59×10^{-2}

Conformational Preference of the Starting Diesters

A **B**

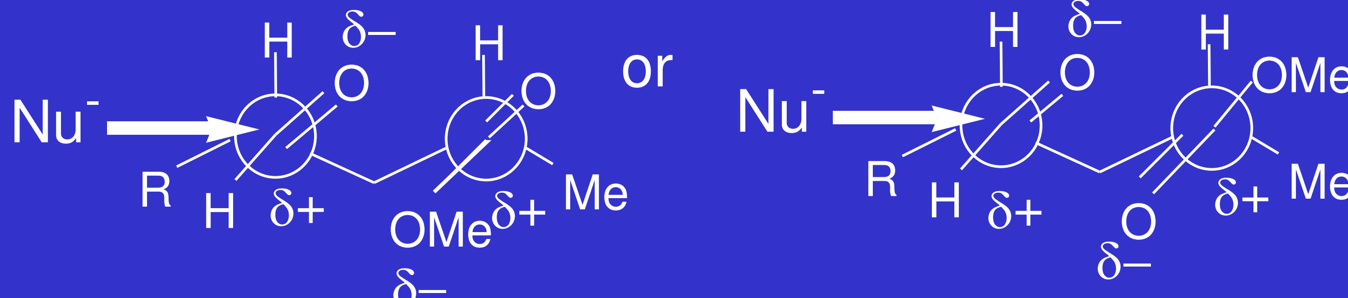


anti-Cram   Cram

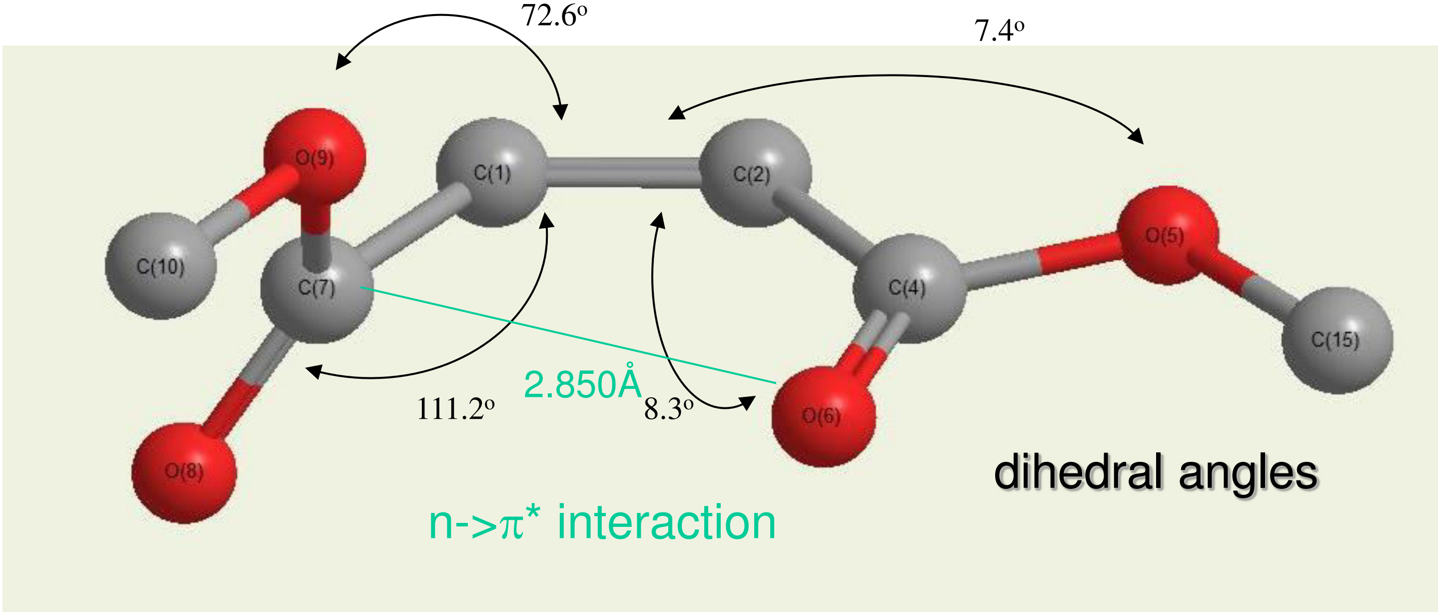
82-90 : 18-10

Yamamoto, Y. ; Nemoto, H.; Kikuchi, R.; Komatsu, H.; Suzuki, I.

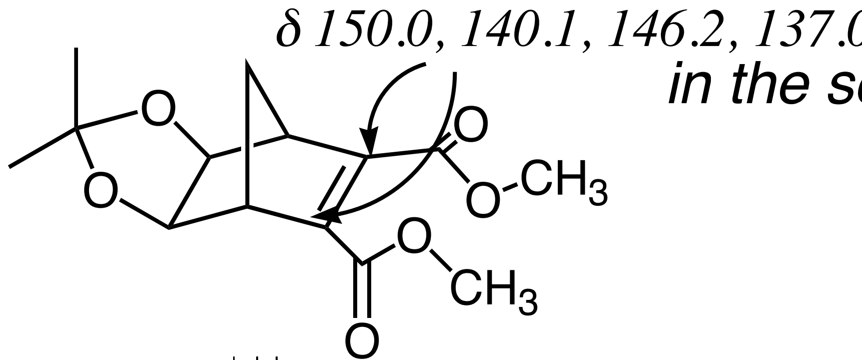
J. Am. Chem. Soc. **1990**, *112*, 8598



# The Conformer of Dimethyl Maleate with the Lowest Energy
(MP2/6-31G(d)//B3LYP/6-31G(d))

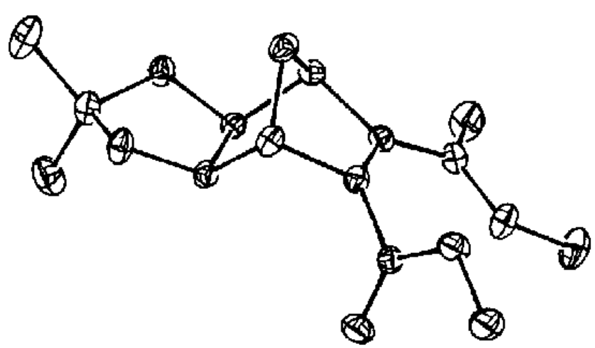


Experimental Support for the Predominant Conformation by Theoretical Studies

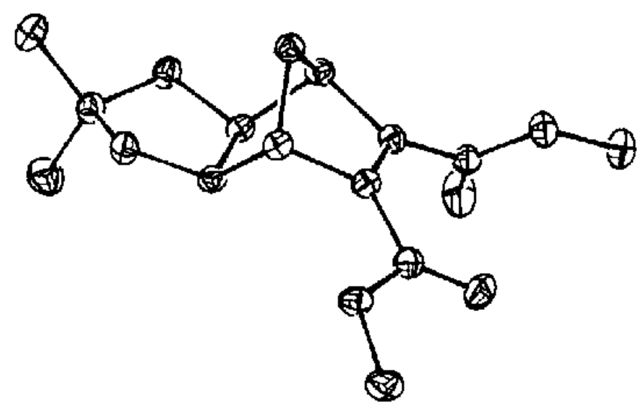


in the solid state

X-ray crystal structures

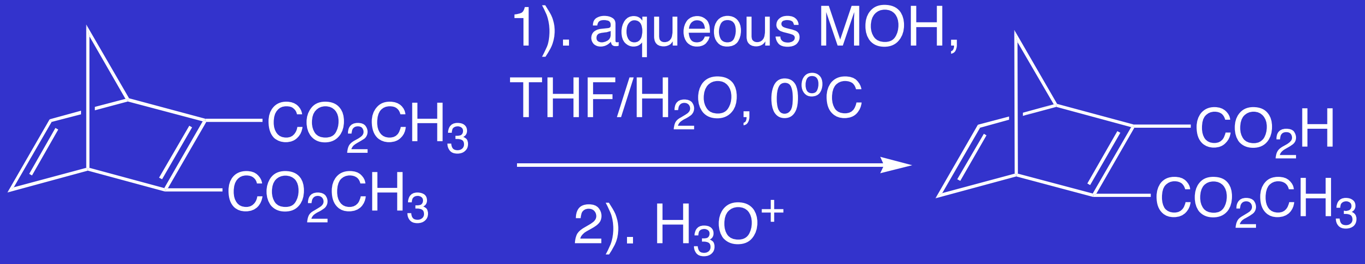


A



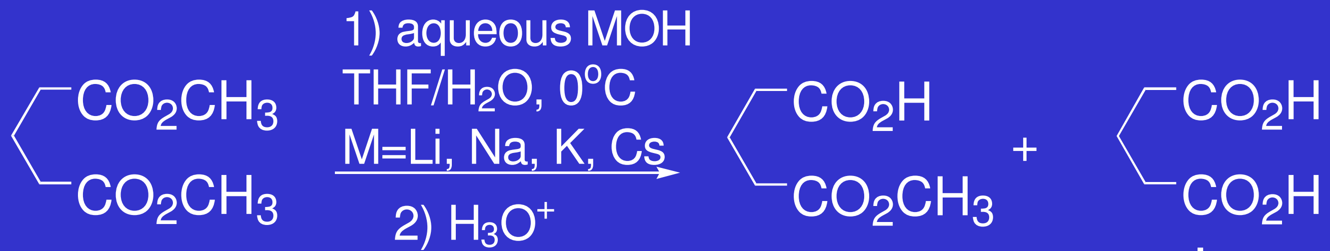
B

Effects of Counter Cations



M	reaction time/min.	yield/%
Li	60-70	>99
Na	60-70	>99
K	30-40	>99
Cs	30-40	>99

Reactivity: K≥Cs>Na≥Li



a **b**

LiOH

Reaction time/min.	**a** (%)	**b** (%)	ratio **a**:**b**
20 (diester consumed)	66.2	33.8	1.96
25	61.1	38.9	1.57
30	59.2	40.8	1.45
35	55.9	44.1	1.27

NaOH

a (%)	**b** (%)	ratio **a**:**b**
67.8	32.2	2.11
67.4	32.6	2.07
61.4	38.6	1.59
60.9	39.1	1.56

KOH

Reaction time/min.	**a** (%)	**b** (%)	ratio **a**:**b**
10 (diester consumed)	86.8	13.2	6.58
15	74.5	25.5	2.92
20	69.0	31.0	2.23
25	67.9	32.1	2.12

CsOH

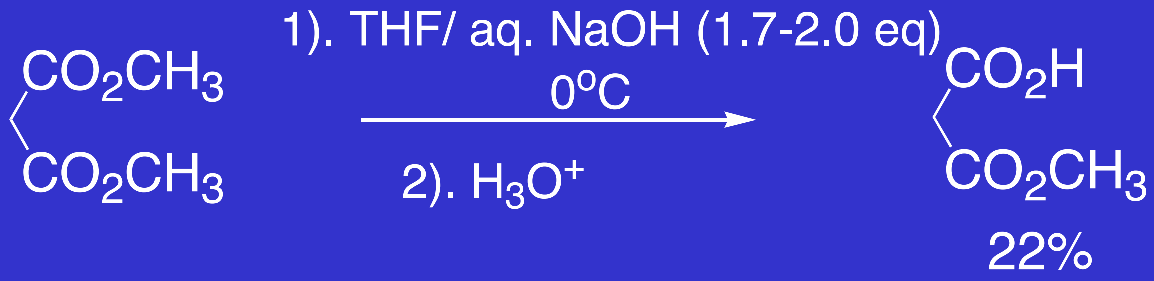
a (%)	**b** (%)	ratio **a**:**b**
82.2	17.8	4.62
67.8	32.2	2.11
64.6	35.4	1.82
51.9	48.1	1.08

Selectivity: K>Cs>Na≥Li

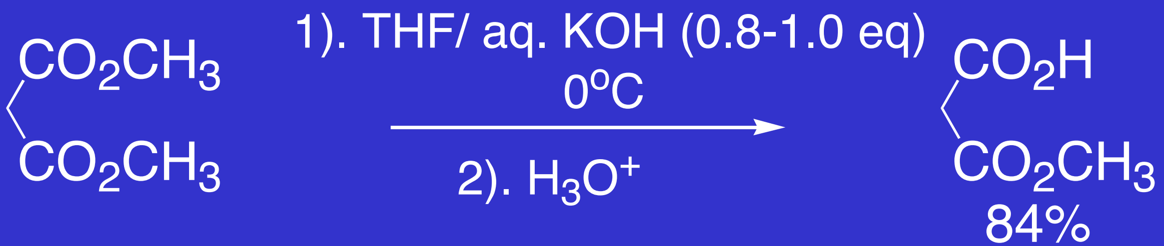
Electropositive character: Cs≥K>Na≥Li

New Conditions for Monohydrolysis of Linear Diesters

Previous Conditions

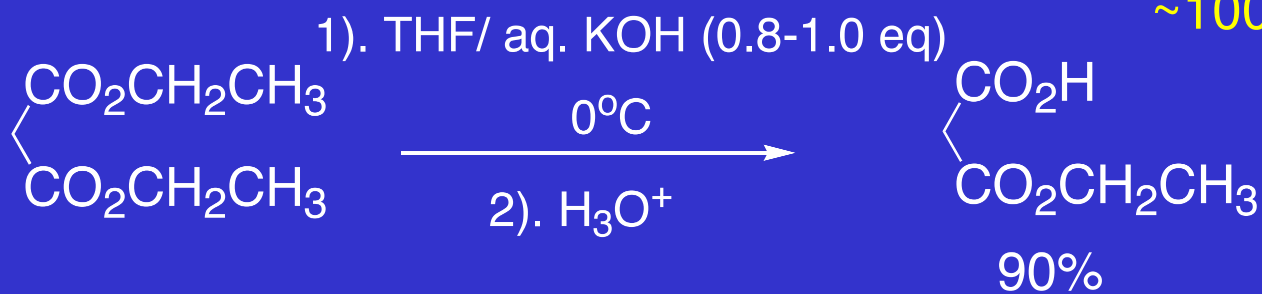


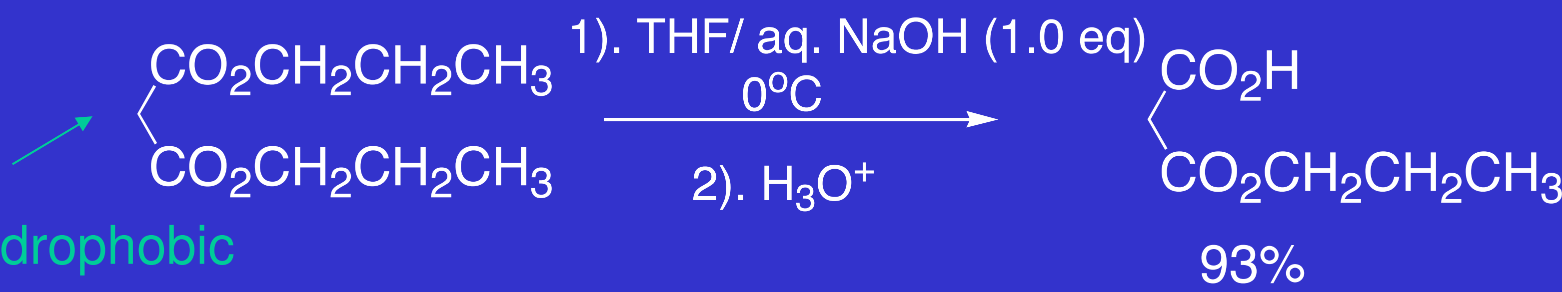
New Conditions



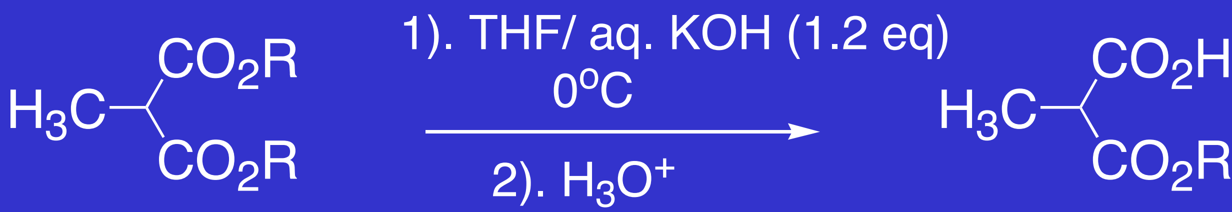
100g \$306
~96% purity

~100% purity



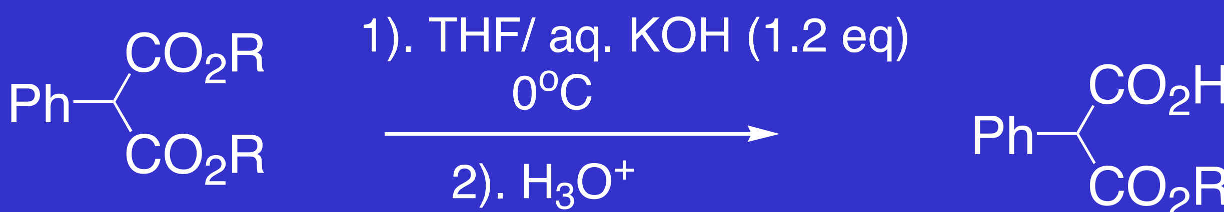


More hydrophobic

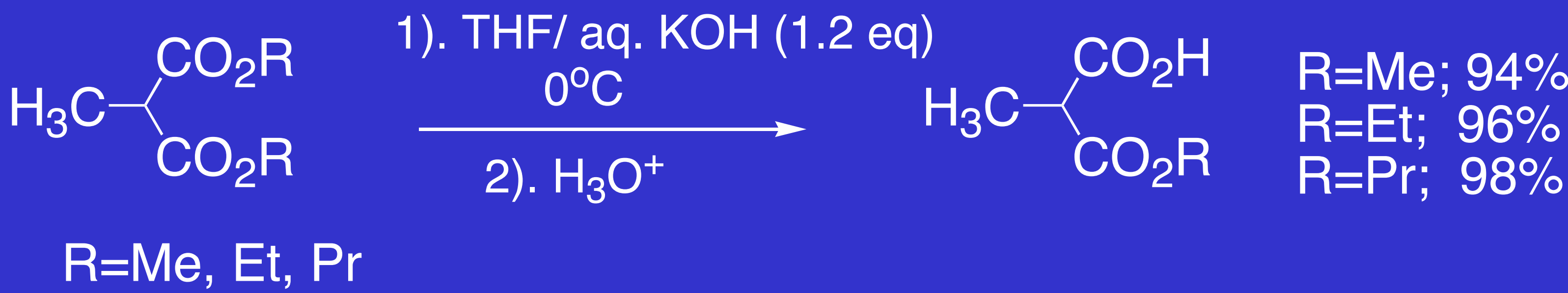


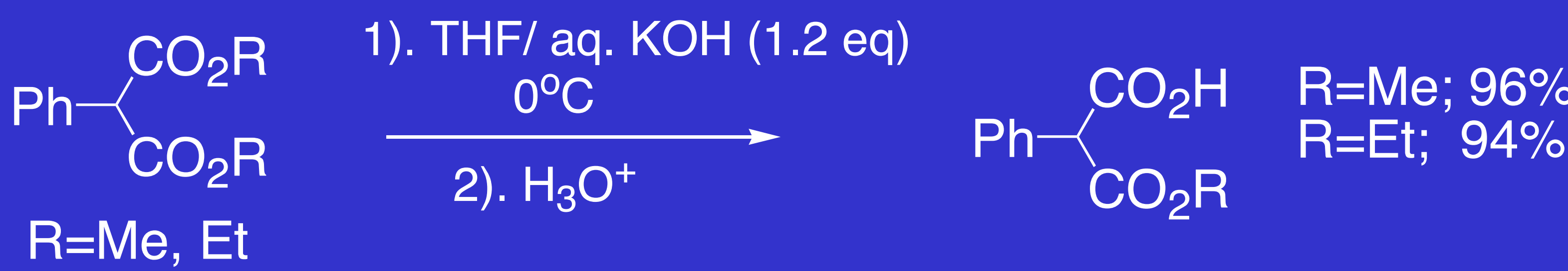
R=Me, Et, Pr

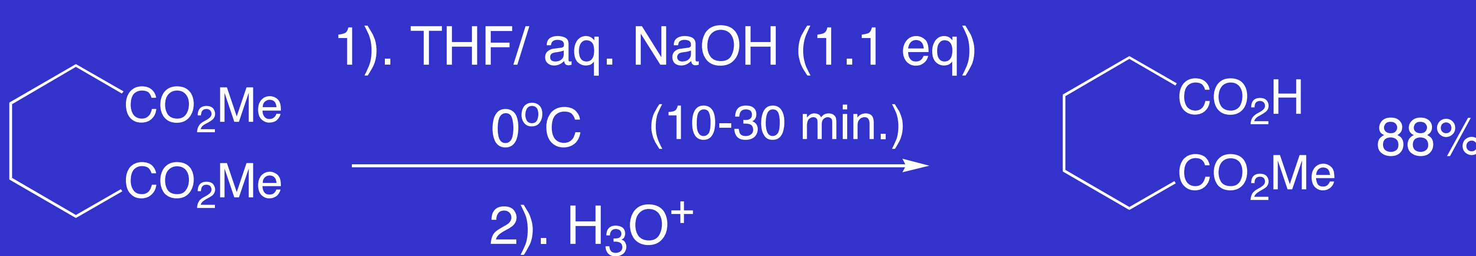
R=Me; 94%
R=Et; 96%
R=Pr; 98%

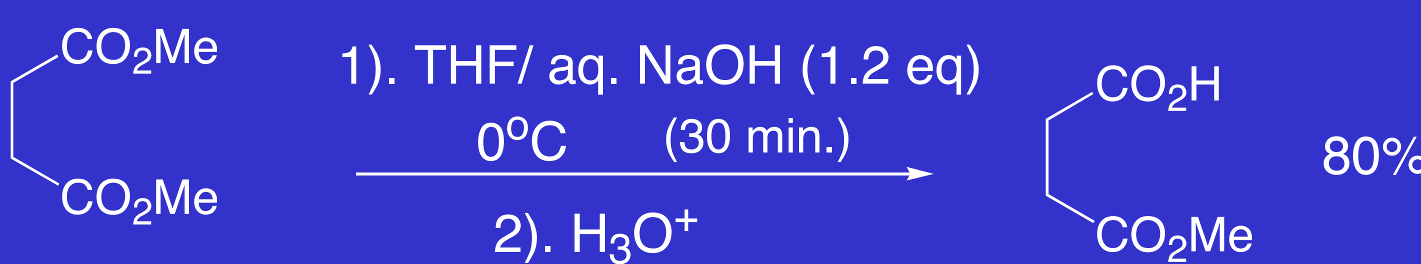


R=Me; 96%
R=Et; 94%

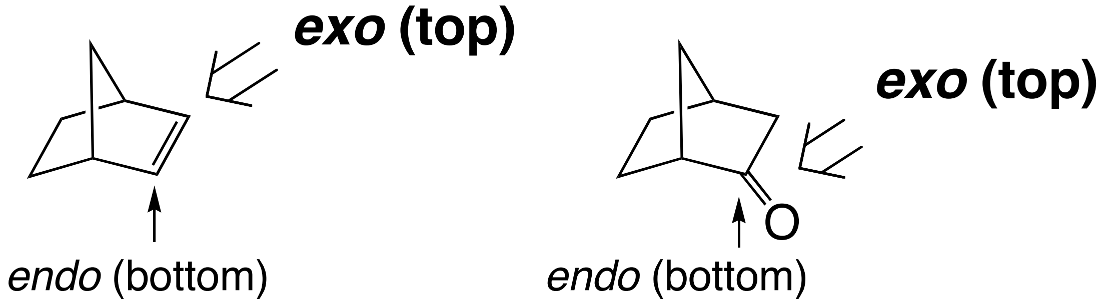

CO_2R
H_3C
CO_2R
R=Me, Et, Pr
1). THF/ aq. KOH (1.2 eq)
0^oC
2). H_3O^+
CO_2H
H_3C
CO_2R
R=Me; 94%
R=Et; 96%
R=Pr; 98%

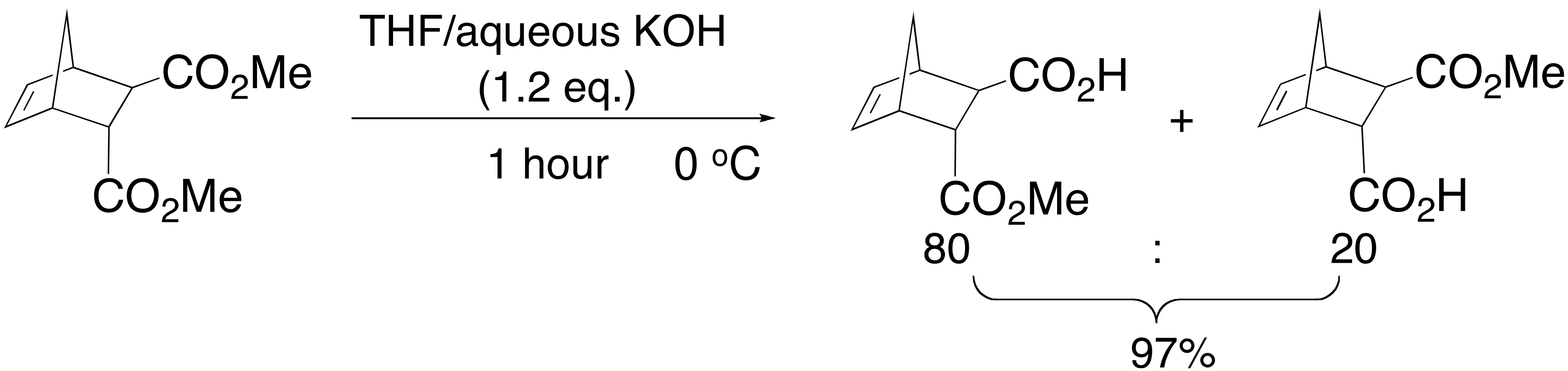

CO_2R
Ph
CO_2R
R=Me, Et
1). THF/ aq. KOH (1.2 eq)
0^oC
2). H_3O^+
CO_2H
Ph
CO_2R
R=Me; 96%
R=Et; 94%

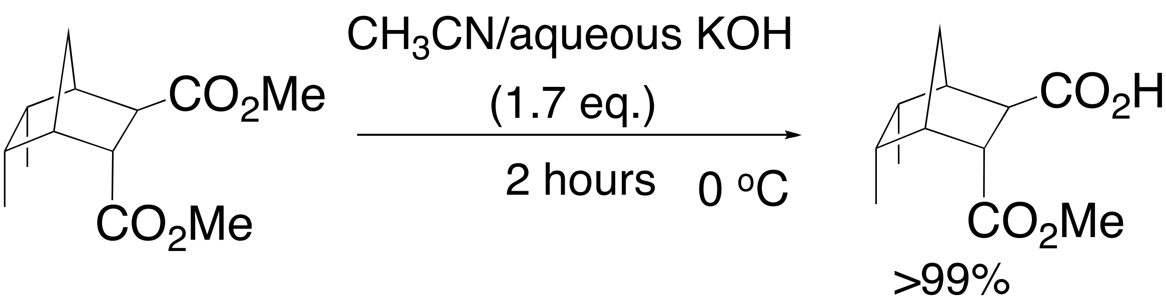

CO_2Me
CO_2Me
1). THF/ aq. NaOH (1.1 eq)
0^oC (10-30 min.)
2). H_3O^+
CO_2H
CO_2Me
88%

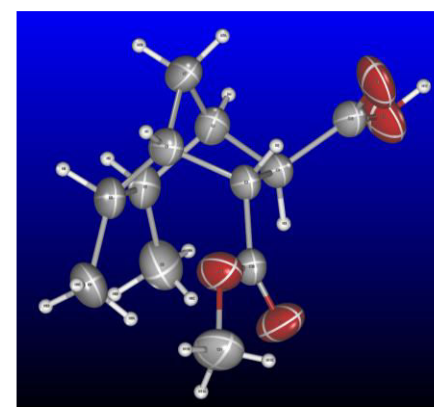

CO_2Me
CO_2Me
1). THF/ aq. NaOH (1.2 eq)
0^oC (30 min.)
2). H_3O^+
CO_2H
CO_2Me
80%

Recognition of Steric Environment

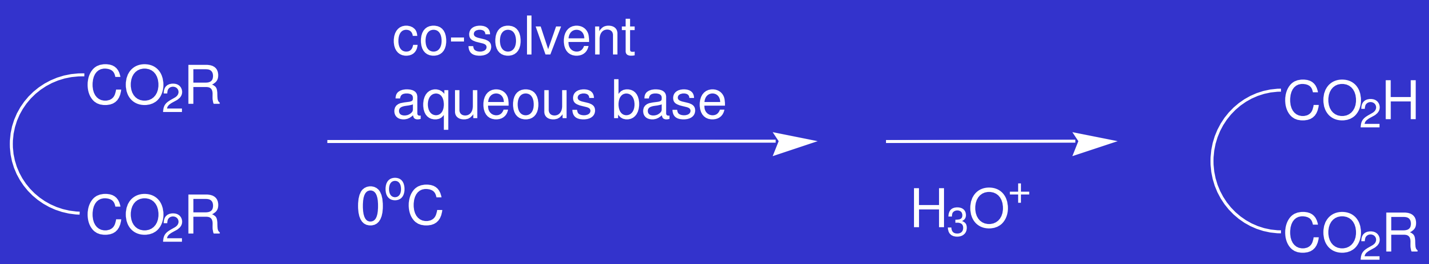








Summary



R=Me, Et

A highly efficient, mild, straightforward reaction using co-solvent-aqueous base at 0 °C was found to produce pure half-esters from symmetric diesters in high yields.

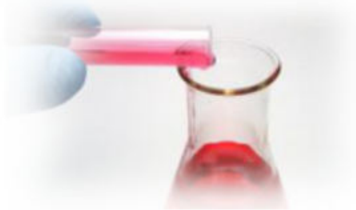
This reaction has been licensed by Kishida Chemical Co.Ltd., Japan

www.kishida.co.jp

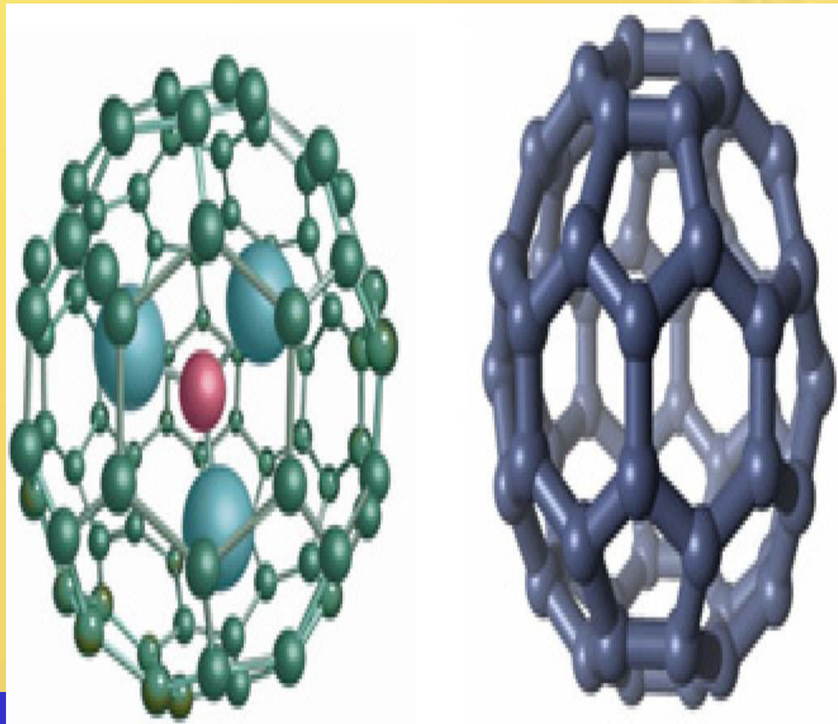
Organic Chemistry: Current Research

Open Access

ISSN: 2161-0401



- Organic Chemistry: Current Research
- Pharmaceutica Analytica Acta
- Clinical Pharmacology & Biopharmaceutics



Organic Chemistry: Current Research

Open Access

ISSN: 2161-0401

- 4th International Conference on Medicinal Chemistry & Computer Aided Drug Designing

OMICS Group **Open Access Membership**

OMICS publishing Group Open Access Membership enables academic and research institutions, funders and corporations to actively encourage open access in scholarly communication and the dissemination of research published by their authors.

For more details and benefits, click on the link below:

http://omicsonline.org/membership.php