

Fieser and Fieser's

# Reagents for Organic Synthesis

VOLUME FIFTEEN

**Fieser and Fieser's**  
**Reagents for**  
**Organic Synthesis**

**VOLUME FIFTEEN**

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Harvard University



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## PREFACE

This volume of Reagents includes reports on synthetic uses of reagents published for the most part in 1988 and during the early months of 1989. The manuscript had the benefit of careful review by James R. Gage and Scott Virgil; their advice has been invaluable. In addition, both the galleys and page proofs have been scrutinized carefully by the advisors for this volume. Greg Fu drew the formula for the dustcover. Tarek Sammakia (Dr. T) is the photographer for the picture of some of the advisors.

MARY FIESER

*Cambridge, Mass.  
February 11, 1990*



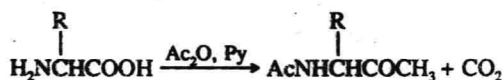
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# A

## Acetic anhydride–Pyridine.

**Dakin–West reaction.**<sup>1</sup> This reaction involves conversion of an  $\alpha$ -amino acid to an  $\alpha$ -acetyl aminoalkyl methyl ketone by reaction with an acid anhydride and a base at 25–135°. When catalyzed by DMAP, the reaction takes place at room

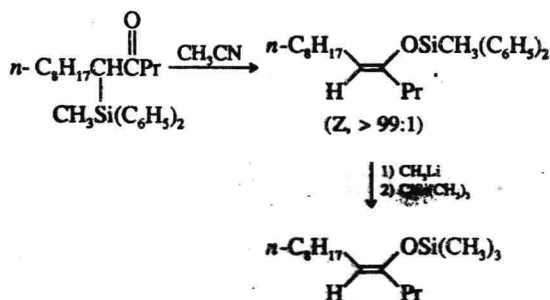


temperature. Secondary amino acids also can undergo this reaction as well as acids that lack an amino group. The review deals mainly with the preparative scope (64 references):

<sup>1</sup> G. L. Buchanan, *Chem. Soc. Rev.*, **17**, 91 (1988).

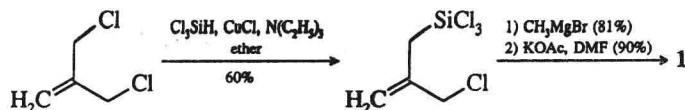
## Acetonitrile.

**Rearrangement of ( $\alpha$ -methyldiphenylsilyl)alkyl ketones.**<sup>1</sup> These  $\alpha$ -silyl ketones rearrange thermally to a mixture of (Z)- and (E)-enol silyl ethers. However, rearrangement in acetonitrile results in only the (Z)-enol silyl ethers (>99:1). These enol silyl ethers are useful precursors to (Z)-lithium enolates.



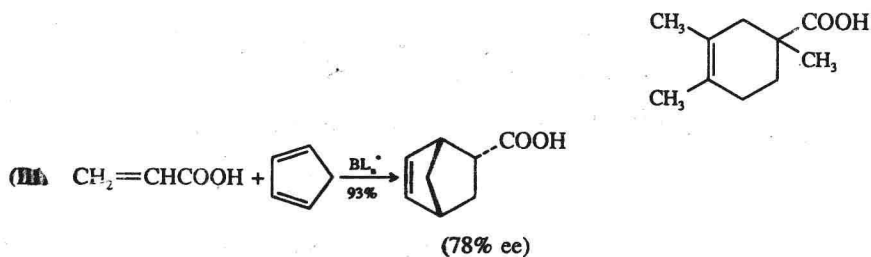
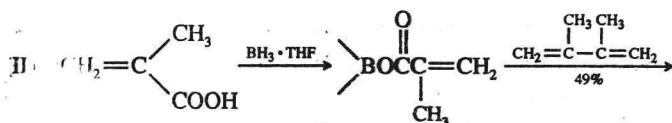
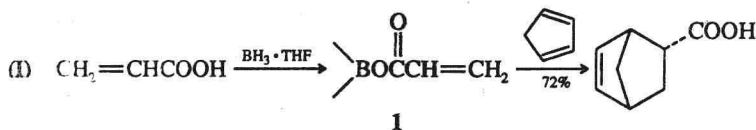
<sup>1</sup> G. L. Larson, R. Berrios, and J. A. Prieto, *Tetrahedron Letters*, **30**, 283 (1989).

**2-(Acetoxymethyl)-3-trimethylsilylpropene**,  $(\text{CH}_3)_3\text{SiCH}_2\overset{\text{CH}_2}{\underset{|}{\text{C}}}\text{CH}_2\text{OAc}$  (**1**), **11**, 259.  
Improved preparation:<sup>1</sup>



B. M. Trost, M. Buch, and M. L. Miller, *J. Org.*, **53**, 4887 (1988).

**Acyloxyboranes.** Yamamoto *et al.*<sup>1</sup> have used the known reactivity of borane with carboxylic acids to activate acrylic acids for Diels–Alder reactions. Thus addition of  $\text{BH}_3 \cdot \text{THF}$  to acrylic acids at  $0^\circ$  furnishes an acyloxyborane formulated as **1**, which undergoes cycloaddition (equations I and II). The reaction proceeds satisfactorily even when borane is used in catalytic amounts. A chiral acyloxyborane,  $\text{BL}_n^*$ , prepared from a tartaric acid derivative, can serve as a catalyst for an asymmetric Diels–Alder reaction (equation III).

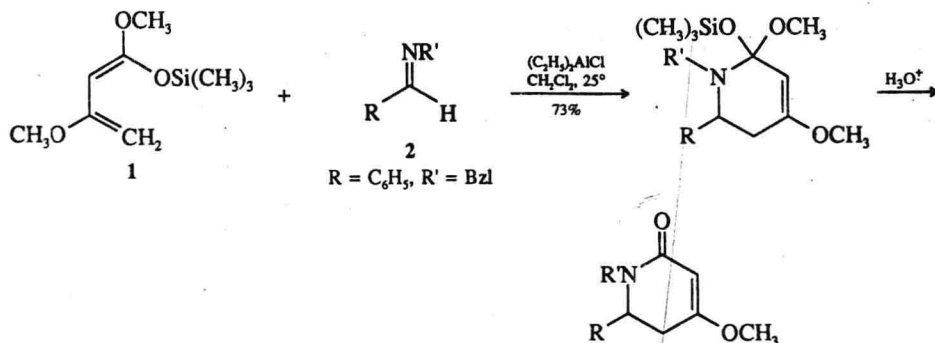


<sup>1</sup> Furuta, Y. Miwa, K. Iwanaga, and H. Yamamoto, *Am. Soc.*, **110**, 6254 (1988).

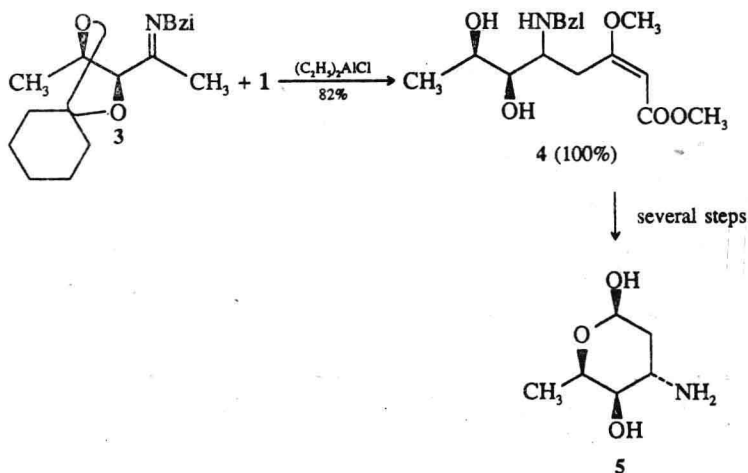
#### Alkylaluminum halides.

**[4 + 2] Cycloaddition of N-benzylimines and a diene.** Diethylaluminum chloride is the best Lewis acid for promoting addition of N-substituted imines (**2**) with the activated diene **1** (9,302–303).<sup>1</sup>

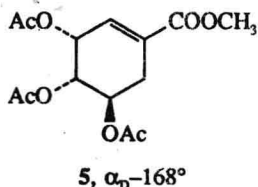
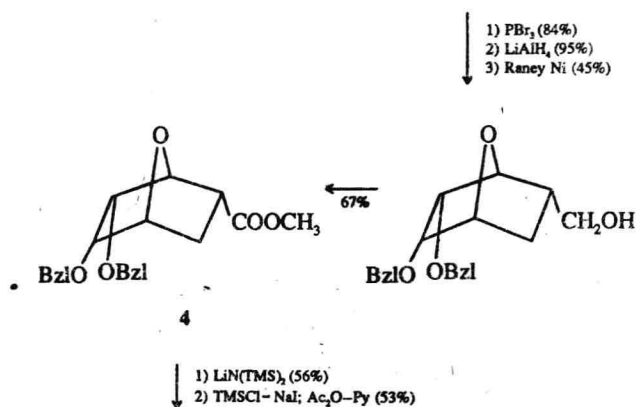
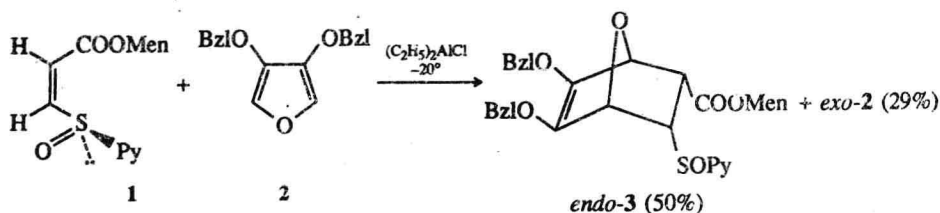




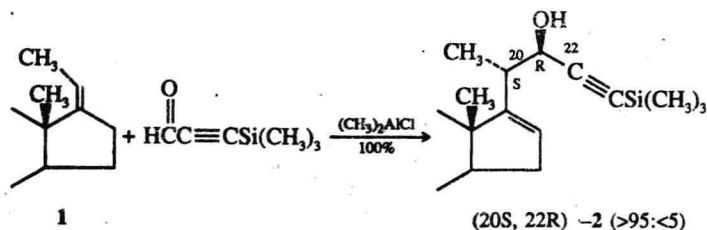
The reaction of the cyclohexylidene ketal 3 of a chiral imine, prepared from L-threonine, gives a single adduct (4), which is converted by known reactions into xylodaunosamine (5).



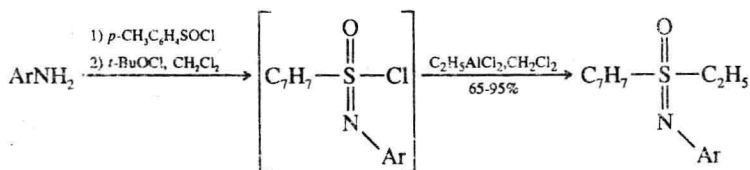
**Asymmetric Diels-Alder reaction.<sup>2</sup>** The chiral menthyl (S)-3-(2-pyridylsulfinyl)acrylate (1) undergoes [4+2]cycloaddition with the furan 2 in the presence of  $(C_2H_5)_2AlCl$  at  $-20^\circ$  to give the *endo*- and *exo*-adducts 3 in the ratio ~2:1, both in about 93% de. The *endo*-adduct (3) was converted by known reactions to 4, which is opened by lithium hexamethyldisilazide (12,257) to the unsaturated acid in 56% yield. Remaining steps to methyl (-)-triacetoxyschikimate (5) include debenzoylation and acetylation. A similar sequence with *exo*-2 should provide (+)-schikimic acid.



**Stereoselective ene reaction.<sup>3</sup>** The reaction of the  $\Delta^{17(20)}$ -steroid alkene 1 with acetylenic aldehydes catalyzed by  $(CH_3)_2AlCl$  proceeds with high diastereoselectivity (about 95:5) at both chiral centers.



**N-Arylsulfoximines.<sup>4</sup>** These imines can be obtained in satisfactory yield by reaction of an arylamine with *p*-toluenesulfinyl chloride followed by oxidation



(*t*-butyl hypochlorite) to a sulfoxide. The resulting sulfonimidoyl chloride is then treated with  $\text{C}_2\text{H}_5\text{AlCl}_2$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ$  to provide S-ethyl sulfoximines in 65–95% overall yield.

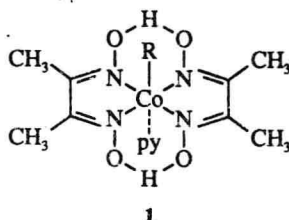
<sup>1</sup> M. M. Midland and J. I. McLoughlin, *Tetrahedron Letters*, **29**, 4653 (1988).

<sup>2</sup> T. Takahashi, T. Namiki, Y. Takeuchi, and T. Koizumi, *Chem. Pharm. Bull.*, **36**, 3213 (1988).

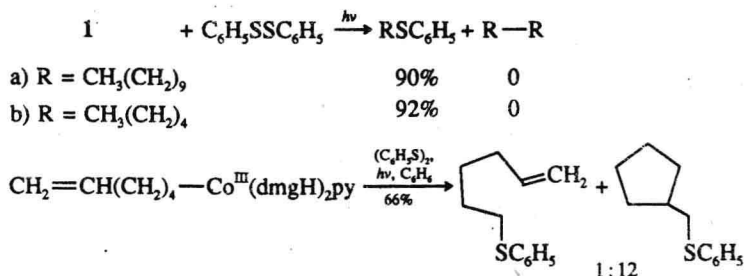
<sup>3</sup> K. Mikami, T.-P. Loh, and T. Nakai, *J.C.S. Chem. Comm.*, 1430 (1988).

<sup>4</sup> M. Harmata, *Tetrahedron Letters*, **30**, 437 (1989).

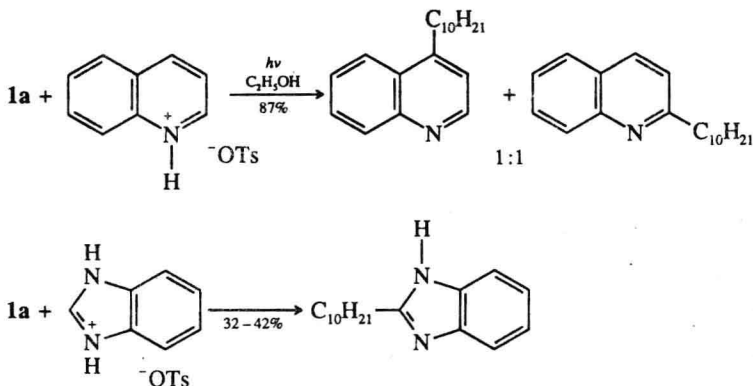
### Alkyl cobalt(III)bis(dimethylglyoxime anion)pyridine, $[\text{R-Co}^{\text{III}}(\text{dmgH})_2\text{py}, \mathbf{1}]$



These cobaloximes (**1**) are generated by reaction of alkyl halides with *in situ* generated  $\text{Co}^{\text{I}}(\text{dmgH})_2\text{py}$ . They are orange crystals that are relatively stable to air and silica gel, but on photolysis they generate  $\text{R}\cdot$ , which can be trapped in generally high yield or which cyclize in the case of alkenyl radicals.<sup>1</sup>



The  $\text{R}\cdot$  radicals can also undergo cross coupling with alkenes and with heteroarenes.<sup>2</sup>



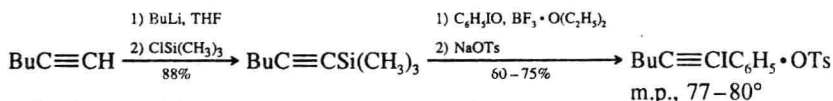
<sup>1</sup> B. P. Branchaud, M. S. Meier, and M. N. Malekzadeh, *J. Org.*, **52**, 212 (1987).

<sup>2</sup> B. P. Branchaud and Y. L. Choi, *ibid.*, **53**, 4638 (1988).

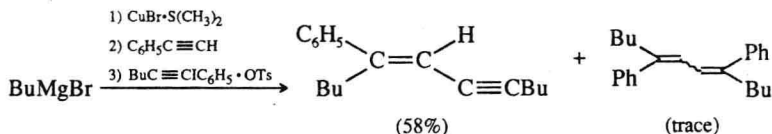
#### Alkynyl(phenyl)iodonium tosylates, $\text{RC}\equiv\text{CIC}_6\text{H}_5\cdot\text{OTs}$ , **14**, 10–11.

Full details for an improved method for preparation of these polyvalent iodine compounds are available.<sup>1</sup> The method is similar to that used to prepare vinylion-tetrafluoroborates (**13**, 151), and yields are 60–89%.

Example:



**(E)-1,3-Enyne**<sup>2</sup> These salts couple with vinylcopper reagents to give (E)-1,3-enynes in yields of 46–94%.



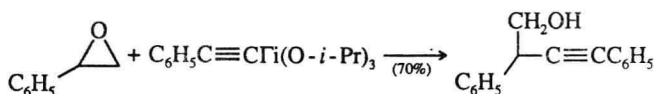
<sup>1</sup> P. J. Stang and T. Kitamura, *Org. Syn.*, submitted (1988).

<sup>2</sup> *Idem*, *Am. Soc.*, **109**, 7561 (1987).

**1-Alkynyltriisopropoxytitanium**,  $\text{RC}\equiv\text{CTi(O-}i\text{-Pr)}_3$ . These titanium acetylides are prepared by reaction of 1-alkynes with BuLi and  $\text{ClTi(O-}i\text{-Pr)}_3$ .

**Cleavage of epoxides.<sup>1</sup>** These reagents react with unsymmetrical epoxides selectively at the more-substituted carbon atom to provide 2-substituted 3-buten-1-ols in 33–79% yield. However, the cleavage requires an electron-releasing group at the epoxide, and it takes place with partial or complete retention of configuration.

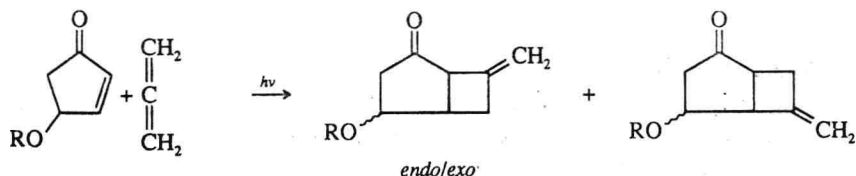
Example:



<sup>1</sup> N. Krause and D. Seebach, *Ber.*, **121**, 1315 (1988).

## Allene.

**Photochemical [2+2]cycloaddition to enones.<sup>1</sup>** This reaction has been shown to occur mainly from the less-hindered  $\alpha$ -side of steroidal enones.<sup>2</sup> Cycloaddition to the cyclopentenone (**1**) is also stereoselective, but the stereoselectivity and the yields are dependent upon the solvent. The highest yields are generally obtained in an apolar solvent (such as hexane).



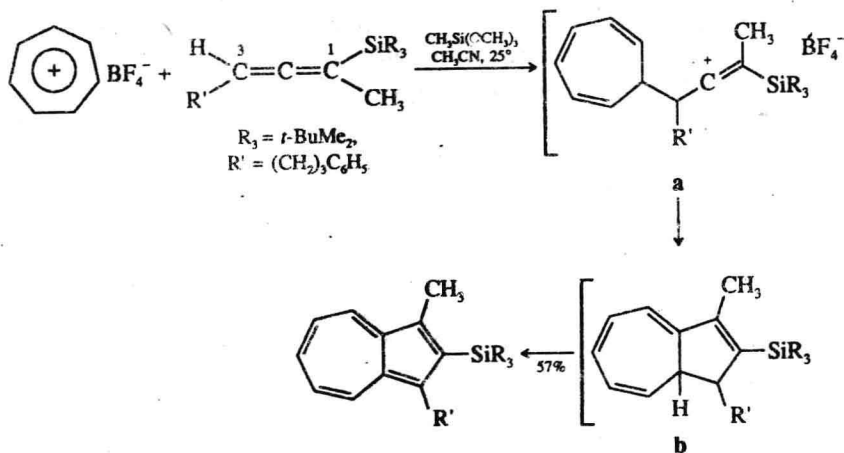
R = <i>t</i> -Bu	C <sub>6</sub> H <sub>12</sub>	76%	49:41	95:5
	CH <sub>3</sub> CN	58%	38:62	89:11
R = H	C <sub>6</sub> H <sub>12</sub>	27%	63:37	87:13
	CH <sub>3</sub> CN	45%	62:38	90:10

<sup>1</sup> W. Stensen, J. S. Svendsen, O. Hofer, and L. K. Sydnes, *Acta Chem. Scand.*, **B42**, 259 (1988).

<sup>2</sup> R. Farwaha, P. de Mayo, J. H. Schauble, and Y. C. Toong, *J. Org.*, **50**, 245 (1985).

## Allenylsilanes.

**[3+2]Annulation; azulenes.<sup>1</sup>** A new route to azulenes involves reaction of tropylium cations with allenylsilanes, which generates a vinyl cation (**a**). This cation cyclizes to a cycloheptadienyl cation, which can be converted to a dihydroazulene by elimination of H<sup>+</sup>. However, the presence of (excess) tropylium cation favors aromatization to an azulene. Protodesilylation of the allenylsilane can be effected by use of trimethoxymethylsilane as an acid scavenger. Yields are low (~25%)

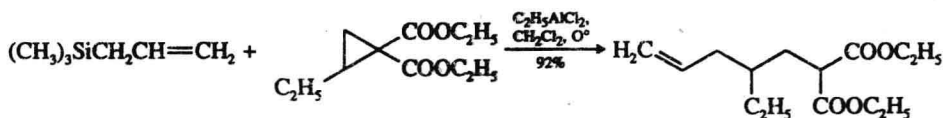


with allenylsilanes lacking an alkyl group at C<sub>3</sub>, and an alkyl group at C<sub>1</sub> is essential for this synthesis.

<sup>1</sup> D. A. Becker and R. L. Danheiser, *Am. Soc.*, **111**, 389 (1989).

### Allyltrimethylsilane.

**Conjugate addition to cyclopropanes.**<sup>1</sup> In the presence of C<sub>2</sub>H<sub>5</sub>AlCl<sub>2</sub>, allyltrimethylsilane undergoes conjugate addition to cyclopropanes substituted by *gem*-alkoxycarbonyl groups.



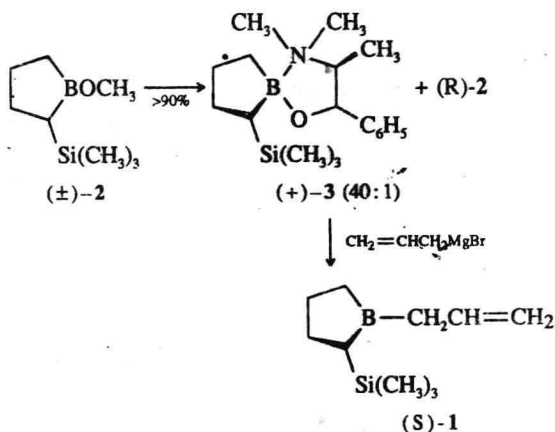
### Review.<sup>2</sup>

<sup>1</sup> R. Bambal and R. D. W. Kemmitt, *J.C.S. Chem. Comm.*, 734 (1988).

<sup>2</sup> A. Hosomi, *Accts. Chem. Res.*, **21**, 200 (1988).

### (S)-B-Allyl-2-(trimethylsilyl)borolane (1).

The borolane is prepared by kinetic resolution of (±) B-methoxy-2-trimethylsilylborolane **2** with (1S,2S)-(+)-N-methylpseudoephedrine (0.5 equiv.) to give (+)-**3**. Reaction of (+)-**3** with allylmagnesium bromide provides the borolane (S)-**1**.

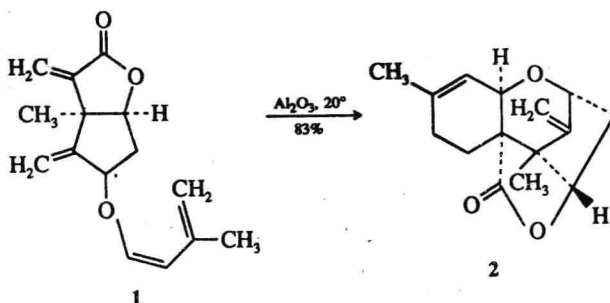


**Asymmetric allylboration of *RCHO*.<sup>1</sup>** (S)-1 reacts with aliphatic or aryl aldehydes or with  $\alpha,\beta$ -enals to form homoallylic alcohols in 92–97% ee and 80–92% chemical yield. The chemical and optical yields are higher than those obtained with B-allyldiisopinocampheylborane (14,12), with allylboronates modified with tartrates, or with B-allyltrimethylsilylboronates. The high asymmetric induction is believed to result from steric effects rather than electronic effects.

<sup>1</sup> R. P. Short and S. Masamune, *Am. Soc.*, **111**, 1892 (1989).

## Alumina

**Diels–Alder catalyst.<sup>1</sup>** Attempted purification of 1 by chromatography on neutral  $\text{Al}_2\text{O}_3$  results in an intramolecular Diels–Alder reaction at 20° in 83% yield. The product (2) is verrucarol, a typical mycotoxic sesquiterpene.

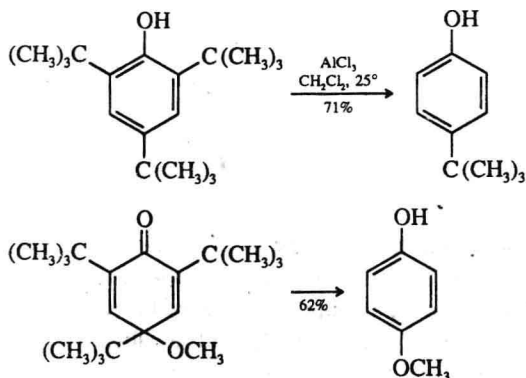


<sup>1</sup> M. Koreeda, D. J. Ricca, and J. I. Luengo, *J. Org.*, **53**, 5586 (1988).

**Aluminum chloride.**

**De-*t*-butylation of phenols.**<sup>1</sup> *t*-Butyl groups are often used for protection of various positions of arenes, and are commonly removed by a reaction involving a *t*-butyl acceptor plus a Lewis acid. Surprisingly, AlCl<sub>3</sub> alone can effect de-*t*-butylation of phenols at room temperature in nitromethane or methylene chloride. Removal of an *ortho-t*-butyl group occurs more readily than that of a *para*-group.

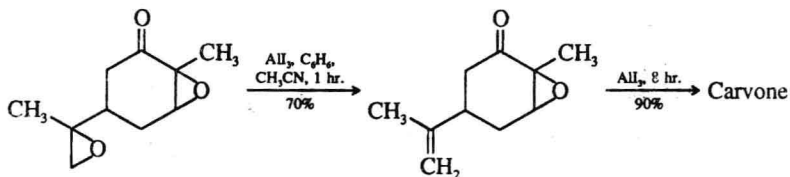
Examples:



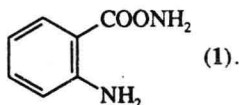
<sup>1</sup> N. Lewis and I. Morgan, *Syn. Comm.*, **18**, 1783 (1988).

**Aluminum(III) iodide.**

**Deoxygenation of epoxides.**<sup>1</sup> The reagent effects deoxygenation of epoxides via an intermediate iodohydrin (11,30), which can be isolated as the *trans*-isomer in some cases. This reagent can effect selective reactions in the case of some diepoxides.



<sup>1</sup> P. Sarmah and N. C. Barua, *Tetrahedron Letters*, **29**, 5815 (1988).

**O-(2-Aminobenzoyl)hydroxylamine,**



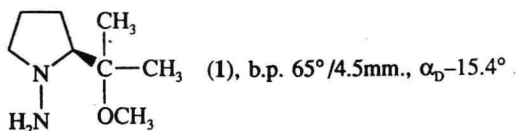
Preparation from isatoic anhydride.<sup>1</sup>

**ArCHO → ArCN.**<sup>2</sup> Reaction of aromatic aldehydes with **1** in refluxing ethanol containing  $\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2$  provides the corresponding nitrile in 78–94% yield.

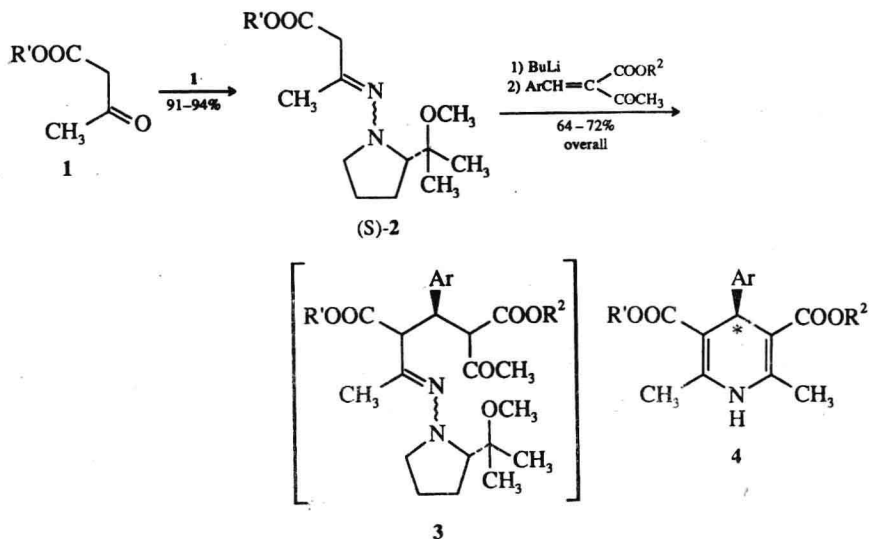
<sup>1</sup> F. D. Eddy, K. Vaughan and M. F. G. Stevens, *Canad. J. Chem.*, **56**, 1616 (1978).

<sup>2</sup> P. S. N. Reddy and P. P. Reddy, *Syn. Comm.*, **18**, 2179 (1988).

**(S)-(-)-1-Amino-2-(1-methoxy-1-methylethyl)pyrrolidine (SADP).**



**Hantzsch dihydropyridine synthesis.**<sup>1</sup> The original Hantzsch synthesis<sup>2</sup> involves condensation of two equivalents of a keto ester with an aldehyde in the presence of ammonia. In an enantioselective version,<sup>3</sup> the chirality is introduced by use of a chiral hydrazone (**2**) of an alkyl acetoacetate prepared from **1**. The anion of **2** is then treated with Michael acceptors to form adducts (**3**), which cyclize to 4-aryl-1,4-dihydropyridines (**4**), in 64–72% overall yield and in 84–98% ee.



<sup>1</sup> D. Enders, H. Kipphardt, P. Gerdes, L. J. Bréna-Valle, and V. Bhushan, *Bull. Soc. Chim. Belg.*, **97**, 691 (1988).

<sup>2</sup> A. Hantzsch, *Ann.*, **215**, 1,72 (1882); A. Singer and S. M. McElvain, *Org. Syn.*, Coll. Vol. II, 214 (1943).

<sup>3</sup> D. Enders, S. Müller, and A. S. Demir, *Tetrahedron Letters*, **29**, 6437 (1988).