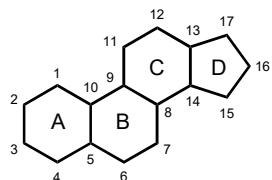


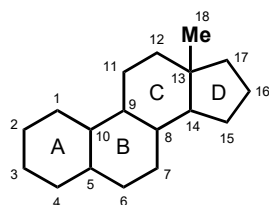
What is a Steroid?

Steroids are compounds possessing the skeleton of cyclopenta[a]phenanthrene or a skeleton derived therefrom by one or more bond scissions or ring expansions or contractions. Methyl groups are normally present at C-10 and C-13. An alkyl side chain may also be present at C-17. Sterols are steroids carrying a hydroxyl group at C-3 and most of the skeleton of cholestane. Additional carbon atoms may be present in the side chain.

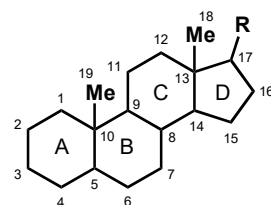
Core Scaffold:



Gonane



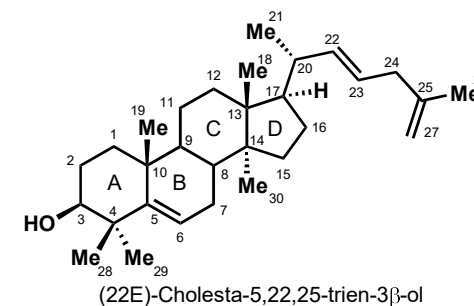
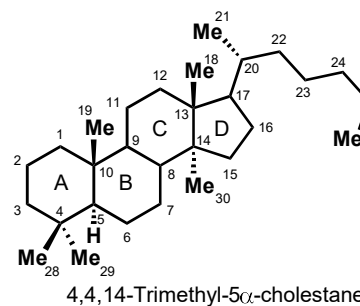
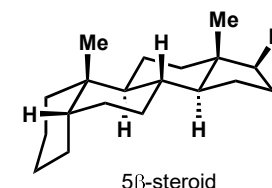
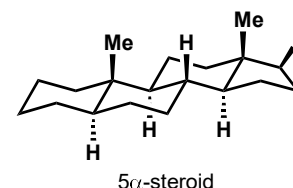
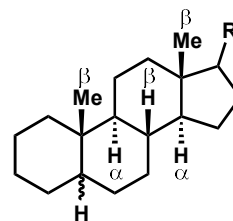
Estrane



R=H Androstane

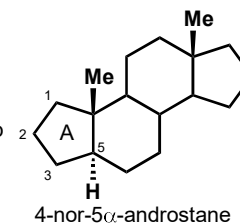
α , β nomenclature

When the rings of a steroid are denoted as projections onto the plane of the paper, the formula is normally to be oriented as depicted below. An atom or group attached to a ring depicted as in the orientation below is termed α (alpha) if it lies below the plane of the paper or β (beta) if it lies above the plane of the paper. Bonds to atoms or groups whose configuration is not known are denoted by the wavy lines (~~~~).

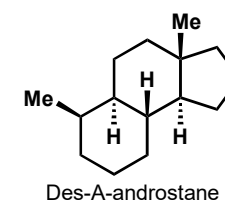


Use of nor, des, or homo

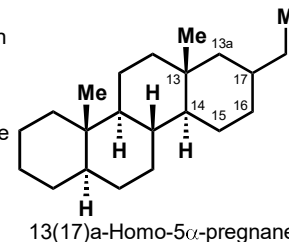
Ring contraction by loss of an unsubstituted methylene group is indicated by the prefix nor.



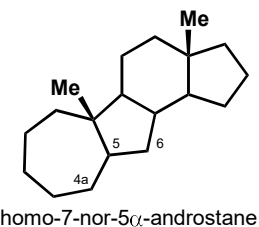
The removal of a terminal ring, with addition of a hydrogen atom at each junction with the adjacent ring, is indicated by the prefix des



Ring expansion by inclusion of one methylene group is indicated by the prefix homo.



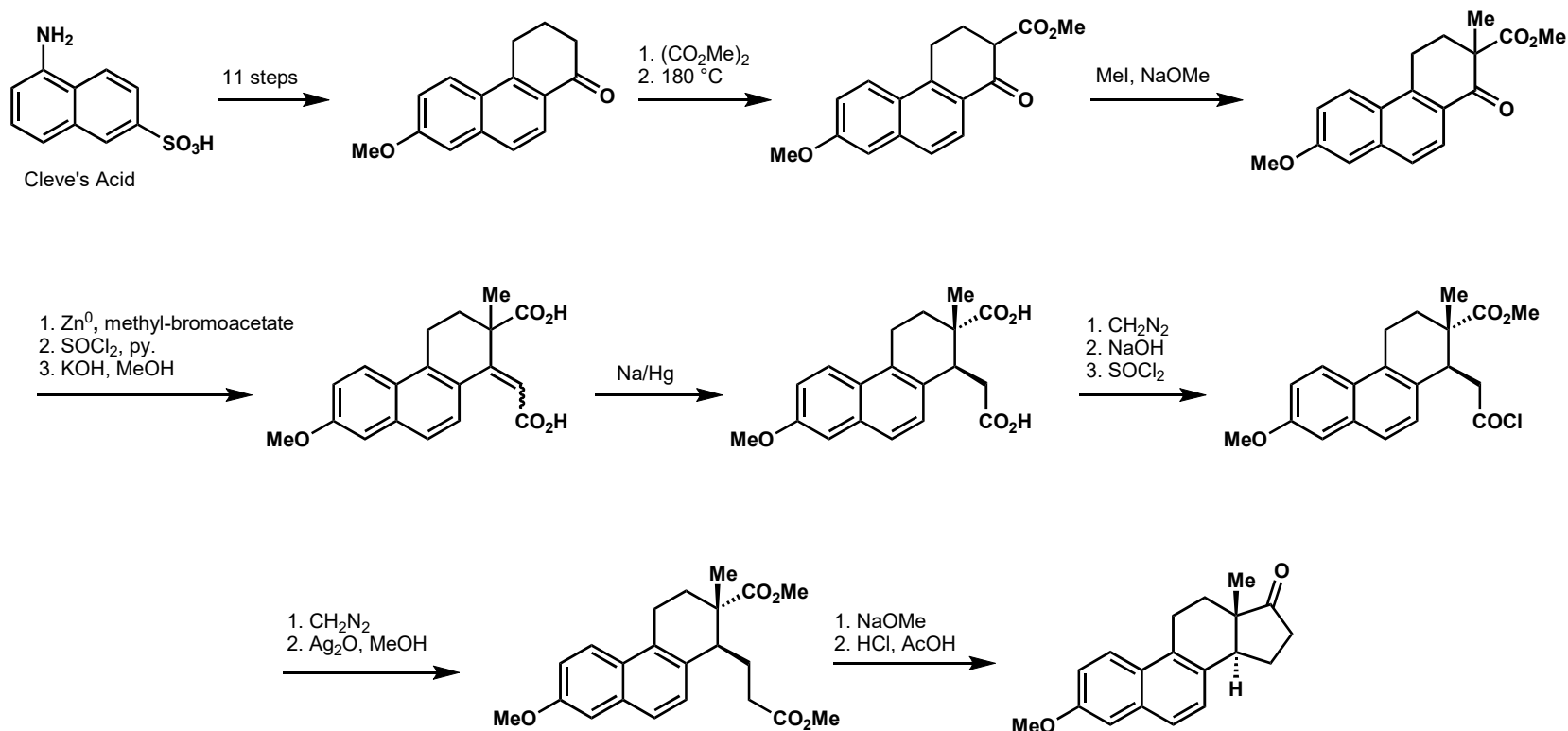
The recommendations for ring expansion and contraction may be used for modifications of two rings in the same molecule.



C ₁₇ Side Chain	Configuration	Name
	-	pregnane
	20R	cholane
	20R	cholestane
	20R, 24S	ergostane
	20R, 24R	campestane
	20R, 24S	poriferastane
	20R, 24R	stigmastane
	20S, 22,R, 23R, 24R	gorgostane

The First Total Synthesis of a Steroid

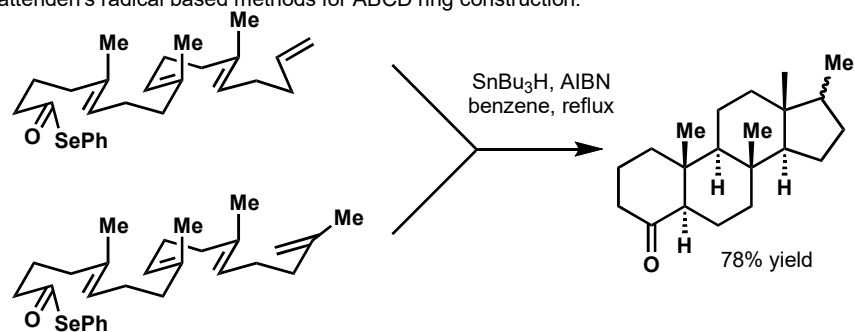
Bachmann's Synthesis of Equilenin (1939):



Although certain sex hormones such as estrone have been prepared from other naturally occurring compounds possessing similarities in structure, the total synthesis of none of them has yet been reported. We have now succeeded in accomplishing the total synthesis of the sex hormone equilenin, and in view of Marker's conversion of equilenin to estrone by reduction [THIS JOURNAL, 60, 1897 (1938)] it follows that the total synthesis of both equilenin and estrone has been accomplished. *The reactions which were used are fairly obvious ones and the successful preparation of the hormone depended principally on developing the proper conditions for making the reactions proceed.* As a matter of fact, some features of the method had been explored by other investigators without success.

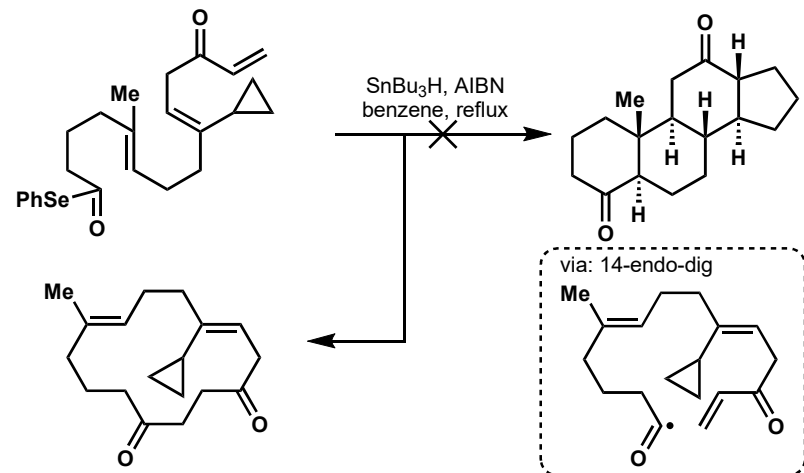
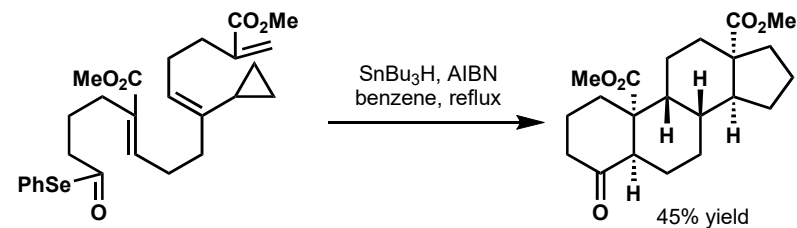
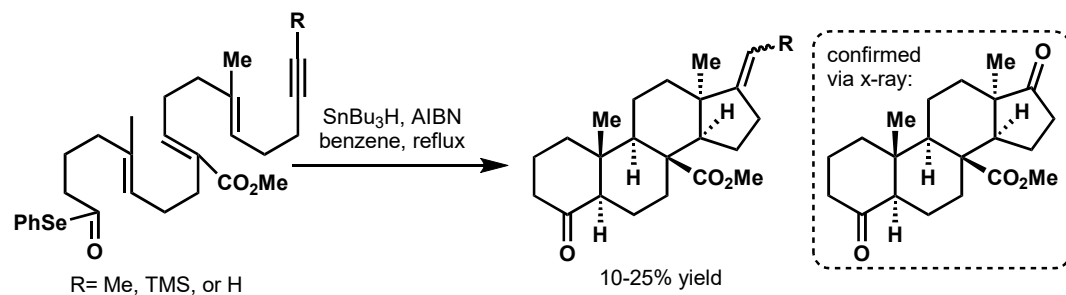
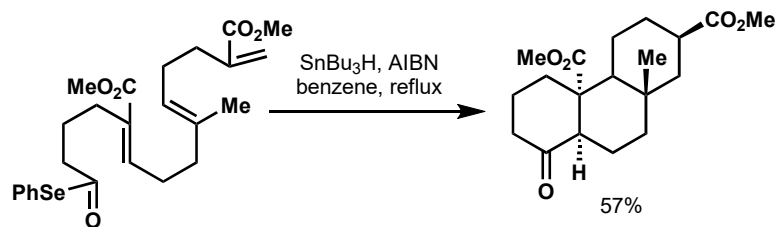
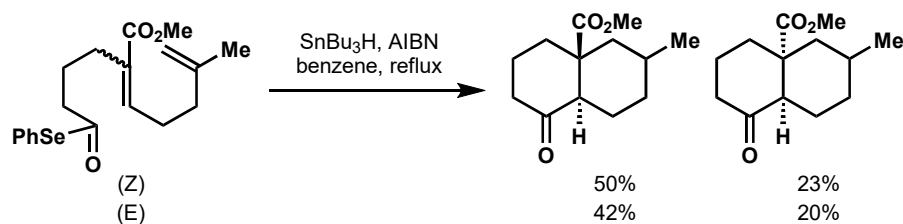
Radical Approaches for ABCD Ring Construction

Pattenden's radical based methods for ABCD ring construction:

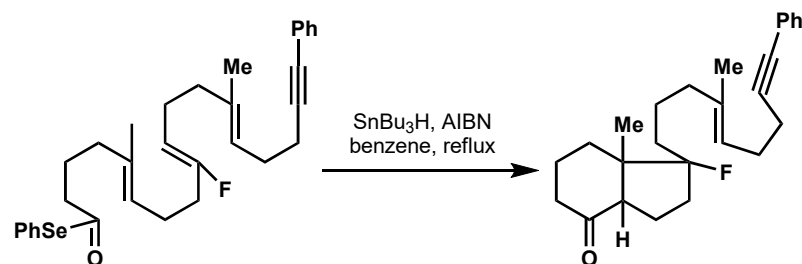


J. Chem. Soc., Perkin Trans. 1, 1996, 31-43
J. Chem. Soc., Perkin Trans. 1, 1996, 45-55

Pattenden's studies on the stereochemical outcomes of radical cascades:



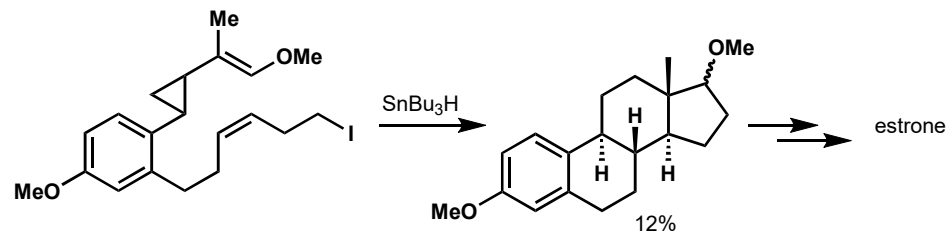
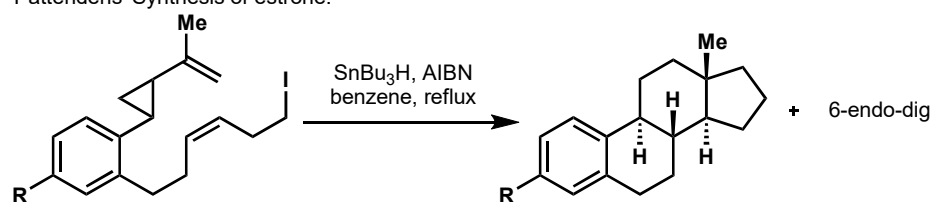
Chem. Commun., 1998,0, 311-312



J. Chem. Soc., Perkin Trans. 1, 2000,0, 3522-3538

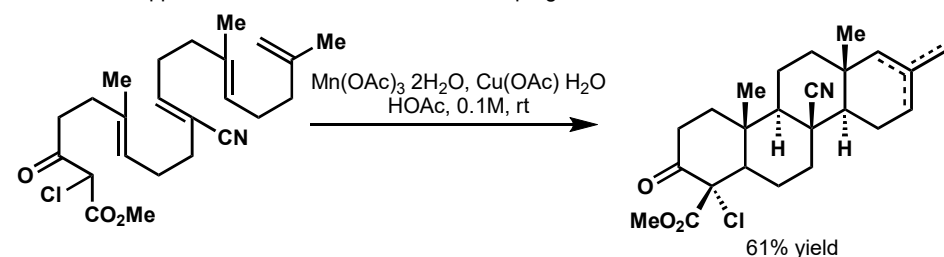
Radical Approaches for ABCD Ring Construction cont.

Pattenders' Synthesis of estrone:



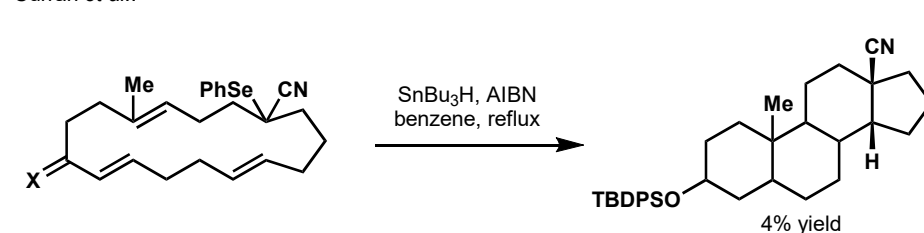
PNAS, 2004, 101 (33) 12024-12029

Zoretic *et al.* application of radical cascades towards pregnanes:



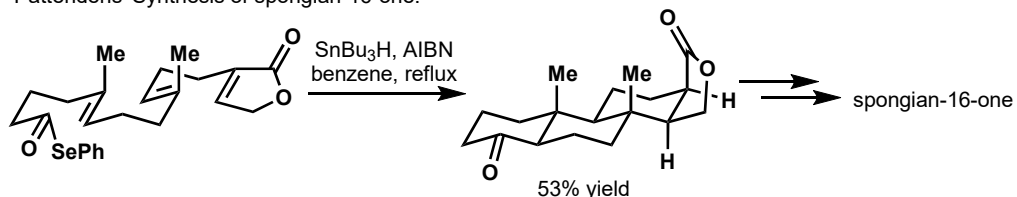
J. Org. Chem. 1998, 63, 7213-7217

Curran *et al.*:



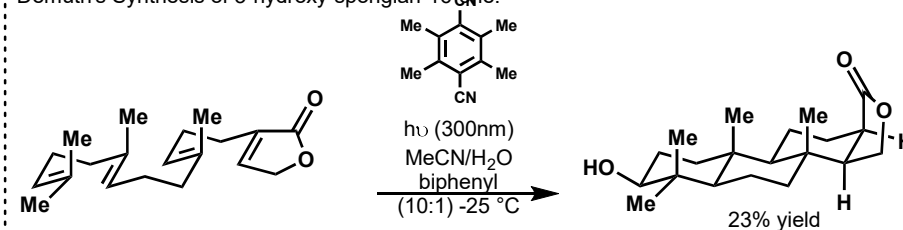
Tet. Lett., Vol. 35, No. 46, pp. 8601-8604, 1994

Pattenders' Synthesis of spongian-16-one:



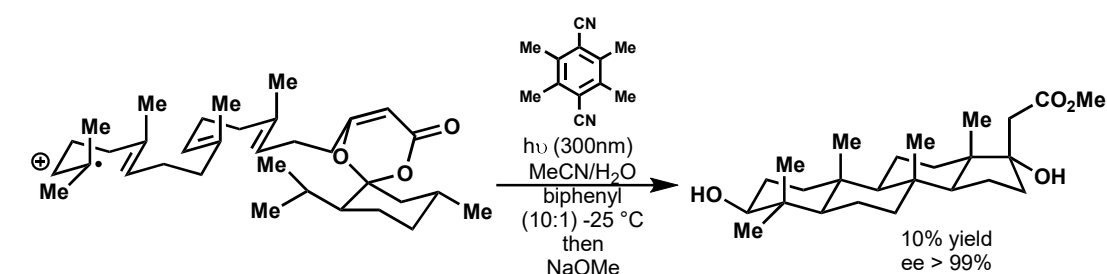
J. Chem. Soc., Perkin Trans. 1, 1998,0, 863-868

Demuth's Synthesis of 3-hydroxy-spongian-16-one:



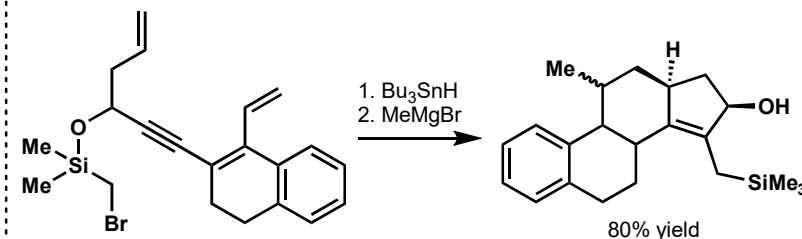
Synthesis 2001(8): 1114-1116

Synthesis of ABCD core via PET:



J. Am. Chem. Soc. 1999, 121, 4894-4895

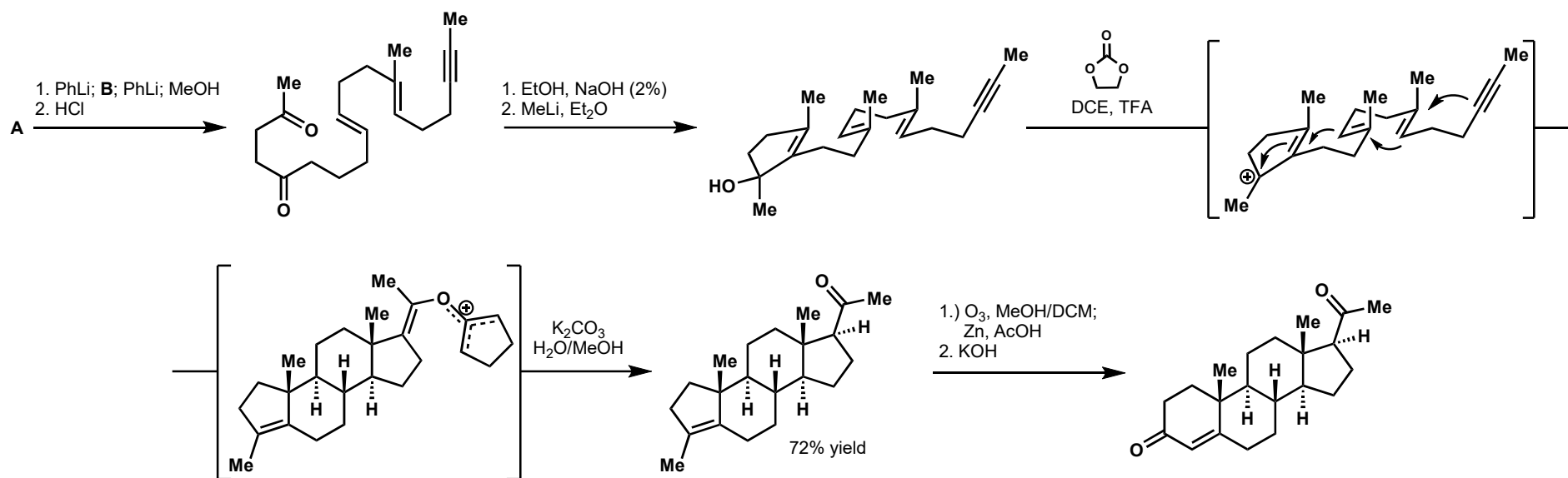
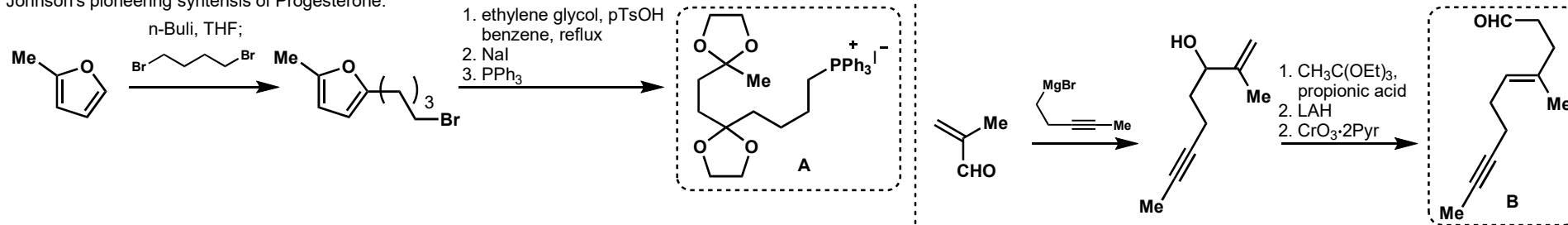
Synthesis of the CD ring via a radical cascade



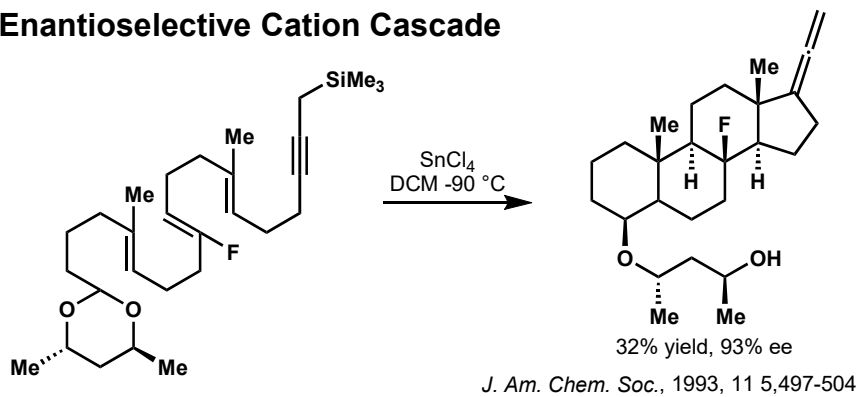
Tet. Lett., Vol. 36, No. 49, pp. 8921-8924, 1995

Total Synthesis of Progesterone via a Cation Cascade

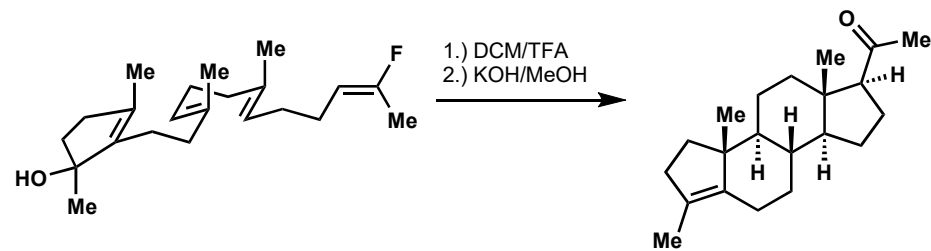
Johnson's pioneering synthesis of Progesterone:



Enantioselective Cation Cascade



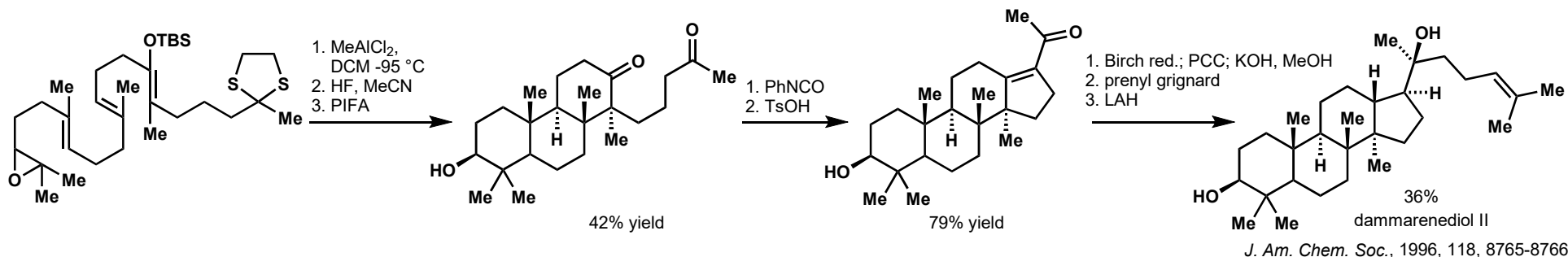
Vinyl Fluoride Effect



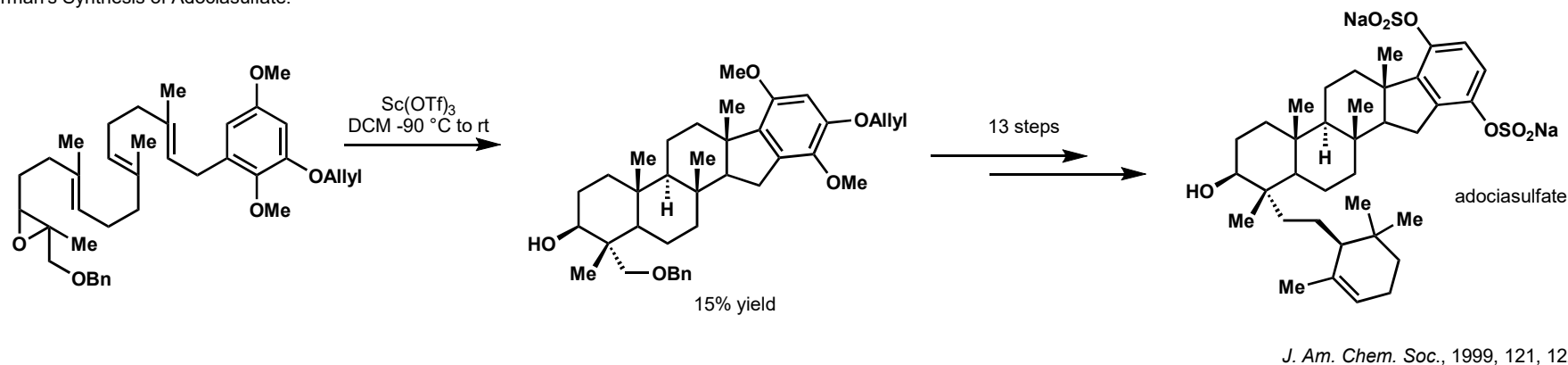
more stereoselective for the trans isomer and prevents formation of the homo steroid

Epoxide Opening as Cation Cascade Initiator

Corey's synthesis of dammarenediol II:

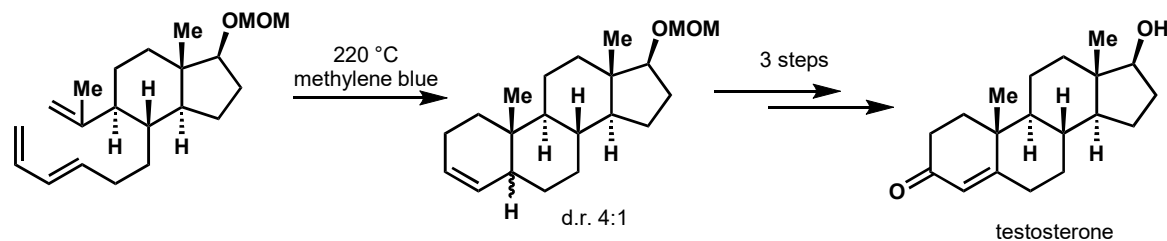
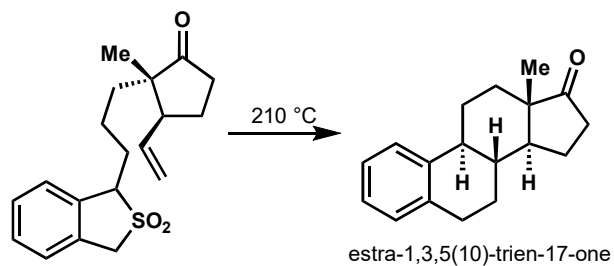


Overman's Synthesis of Adociasulfate:



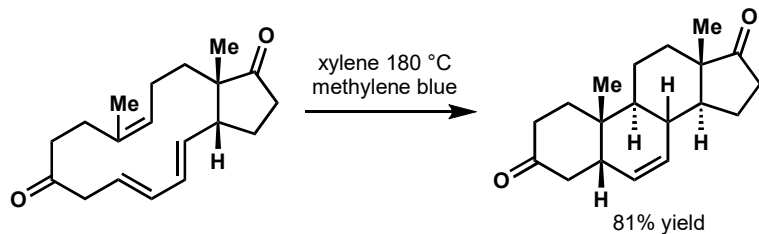
Diels-Alder Approaches to Steroids

Nicolaou *et al.* synthesis of estra-1,3,5(10)-trien-17-one:



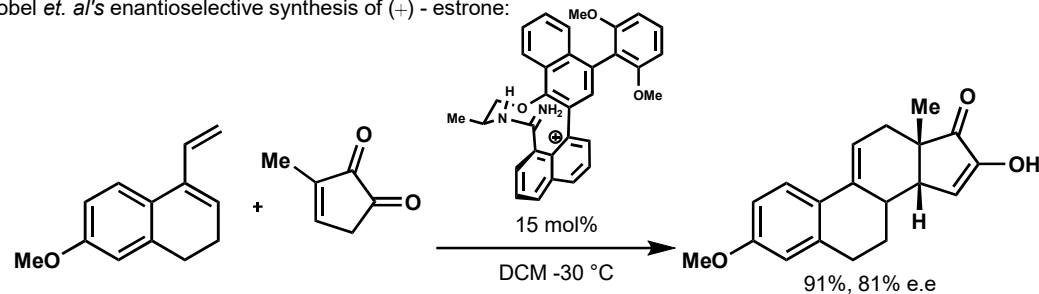
Diels-Alder Approaches to Steroids Cont.

Takashi Takahashi's transannular DA:



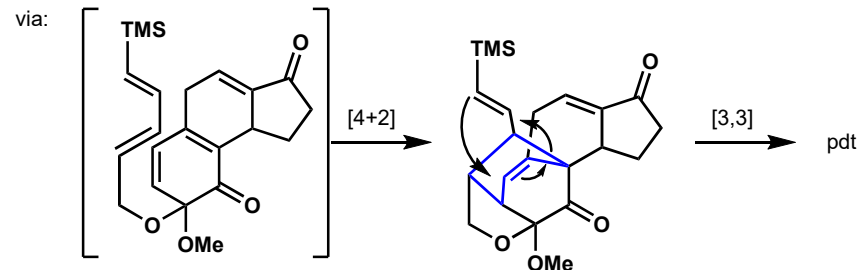
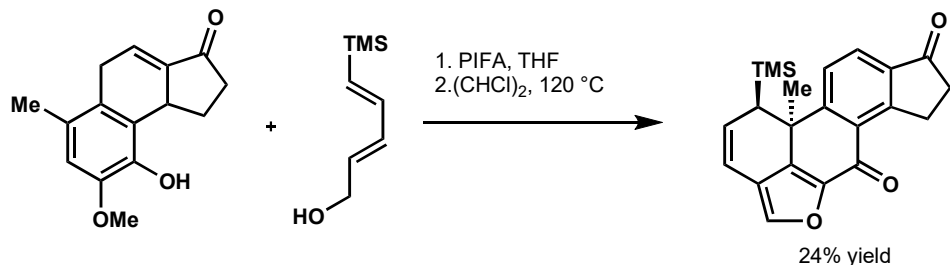
J. Am. Chem. Soc., 1988, 110, 2674-2676

Gobel *et. al's* enantioselective synthesis of (+) - estrone:



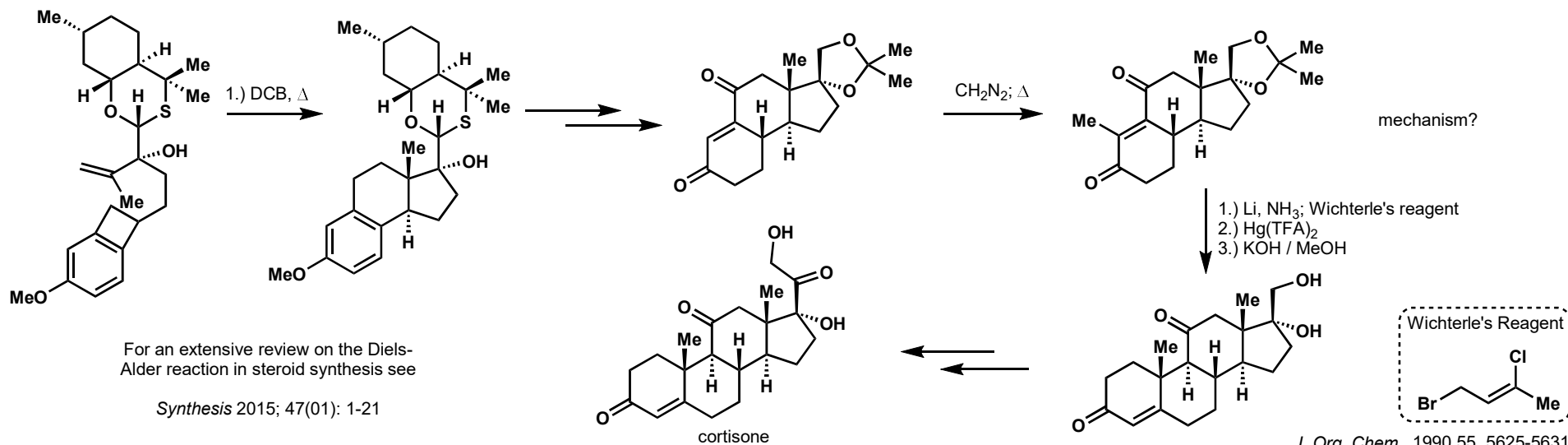
J. Org. Chem., 2010, 75, 2718-2721

Rodrigo *et als.* oxidative dearomatization cascade:



J. Org. Chem., 2009, 74 (15), pp 5429-5439

The first enantioselective synthesis of (+) - cortisone by Fukumoto *et al.*:



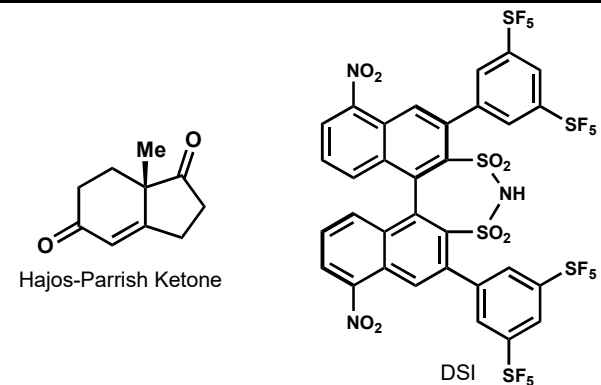
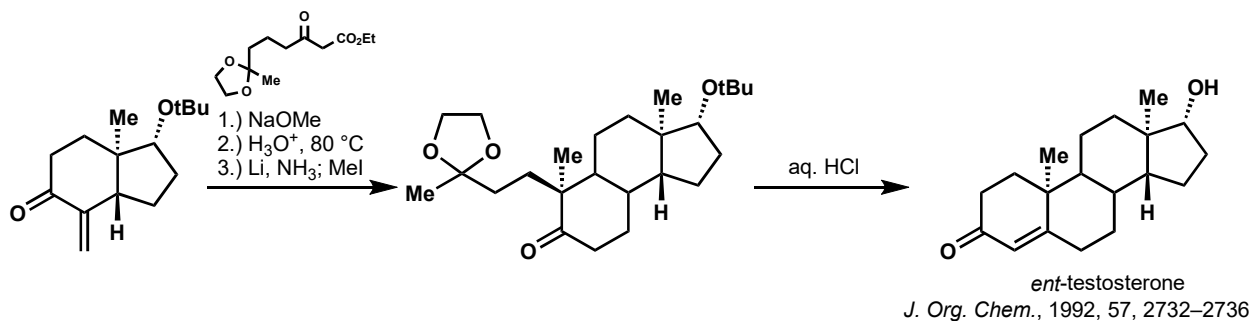
For an extensive review on the Diels-Alder reaction in steroid synthesis see

Synthesis 2015; 47(01): 1-21

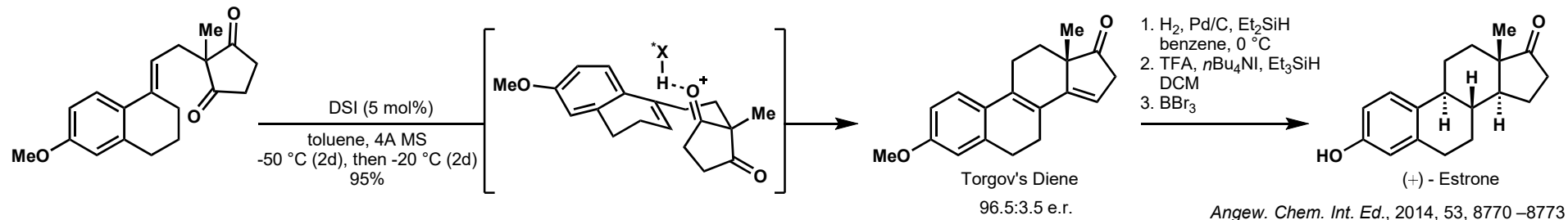
J. Org. Chem., 1990,55, 5625-5631

Annulation Methods for Steroid Construction

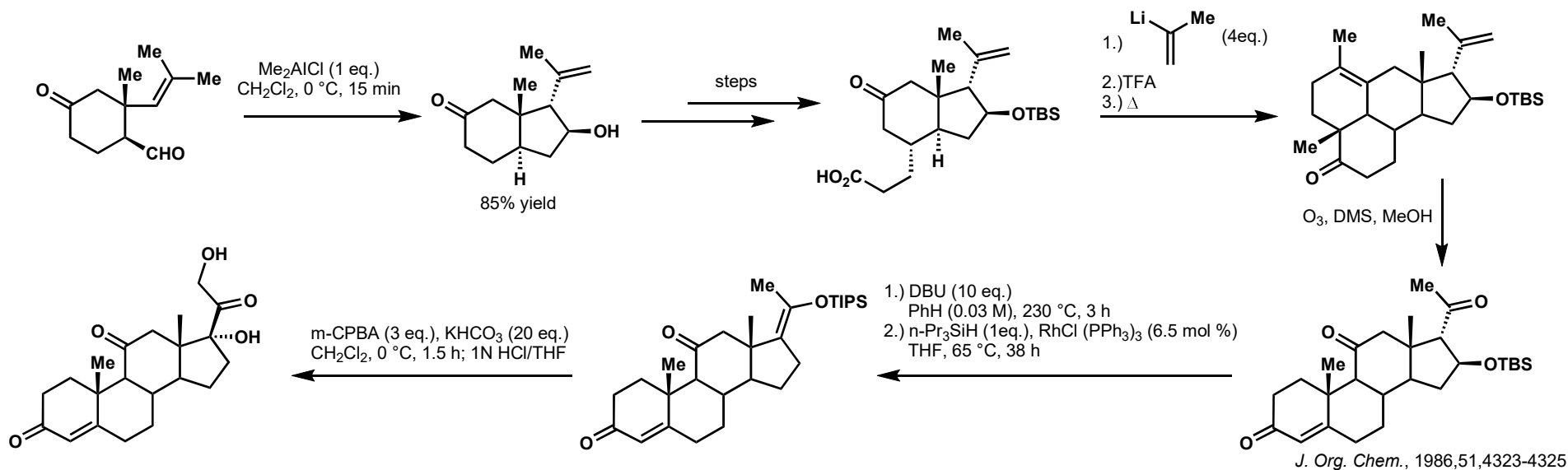
Synthesis of ent-cholesterol by Rychnovsky *et al.*



Shortest enantioselective synthesis of estrone by List *et al.*

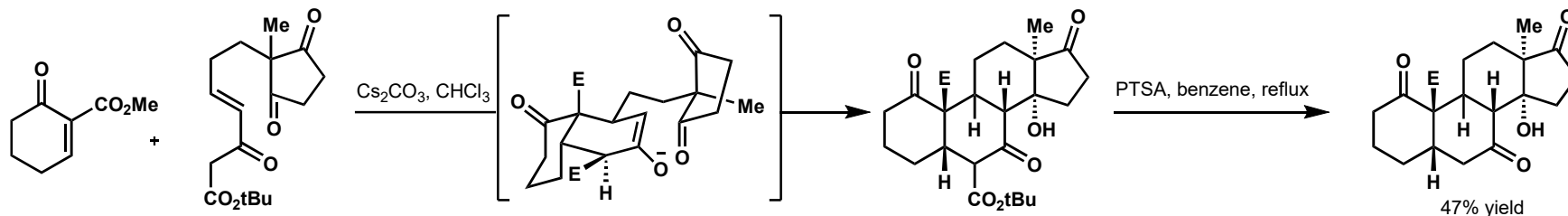


Nakamura and Kowajimas's synthesis of cortisone:



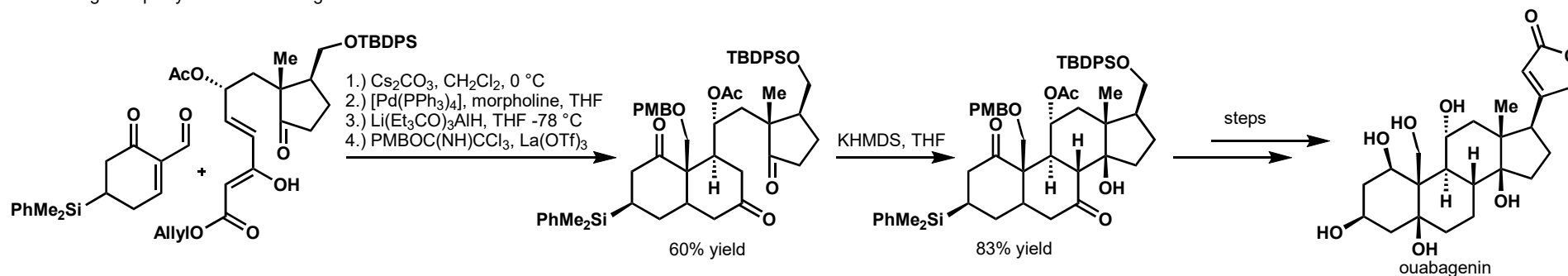
Annulation Methods for Steroid Construction Cont.

Deschlongchamps polyanionic cyclization:



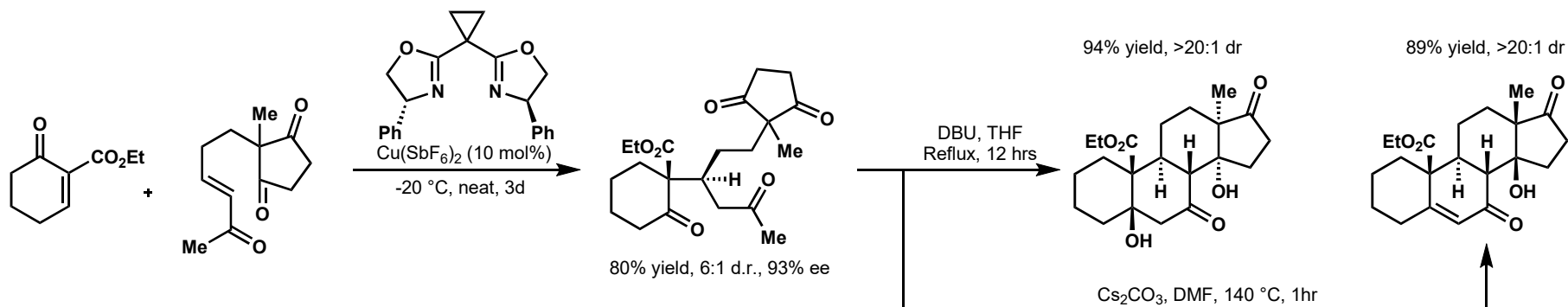
Tetrahedron Letters, Vol.29, No.47, pp. 6033-6036,1988

Deschlongchamps synthesis of ouabagenin:



Angew. Chem. Int. Ed., 2008, 47, 1272 –1275

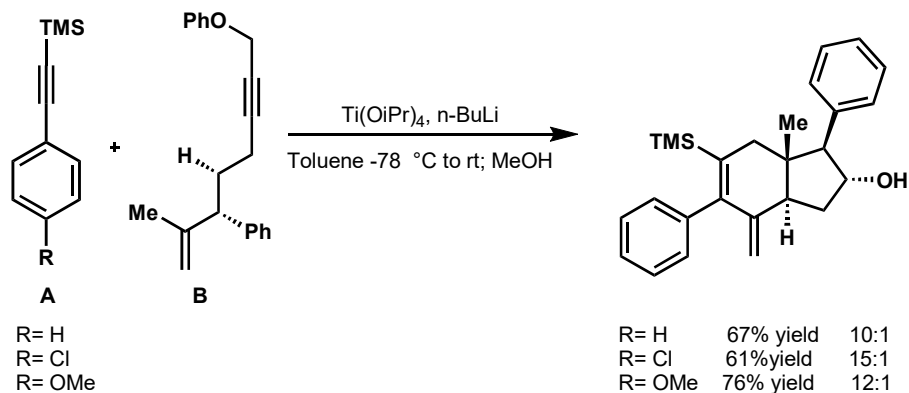
Nagorny: Enantioselective Synthesis of Oxygenated Steroids via Sequential Copper(II)-Catalyzed Michael Addition/Intramolecular Aldol Cyclization Reactions



J. Am. Chem. Soc., 2015, 137, 14341-14348

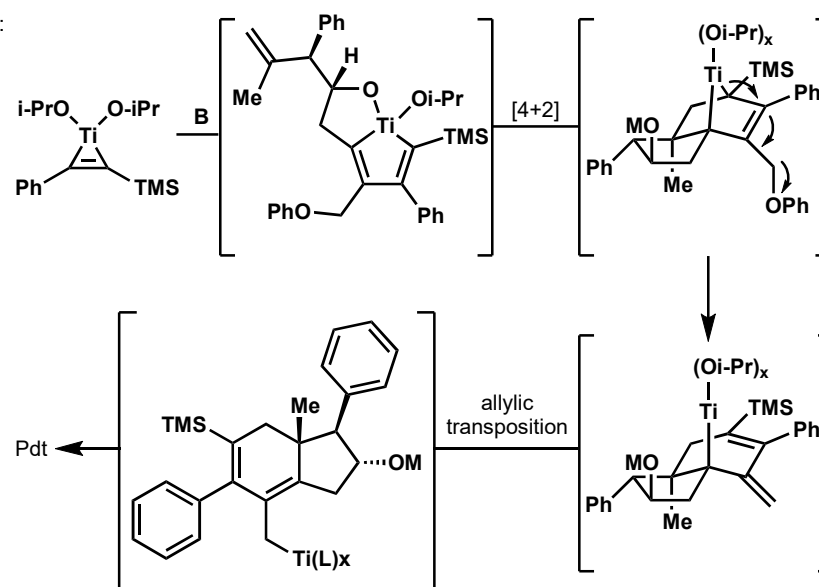
Transition Metal Mediated Approaches Towards Steroid Synthesis

Micalizio's synthesis of trans fused hydroindanes (CD rings):

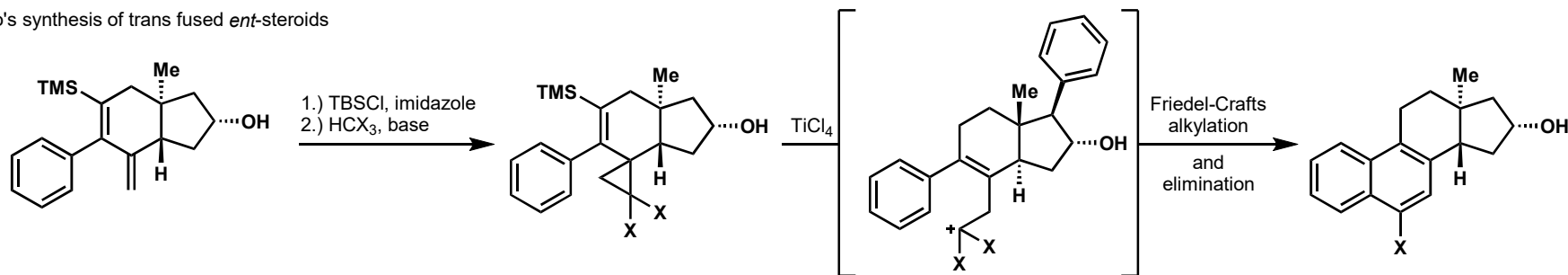


J. Am. Chem. Soc., 2012, 134, 2766-2774

via:

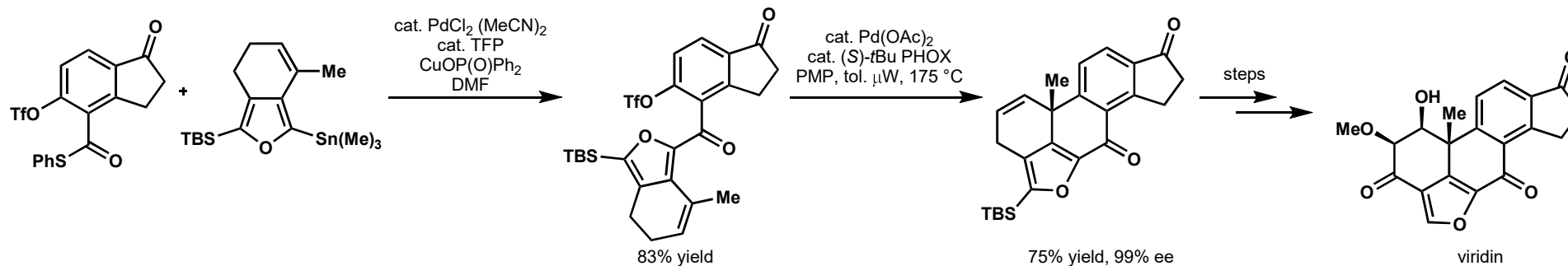


Micalizio's synthesis of trans fused *ent*-steroids



Nature Chemistry, 2018, volume 10, pages 70–77

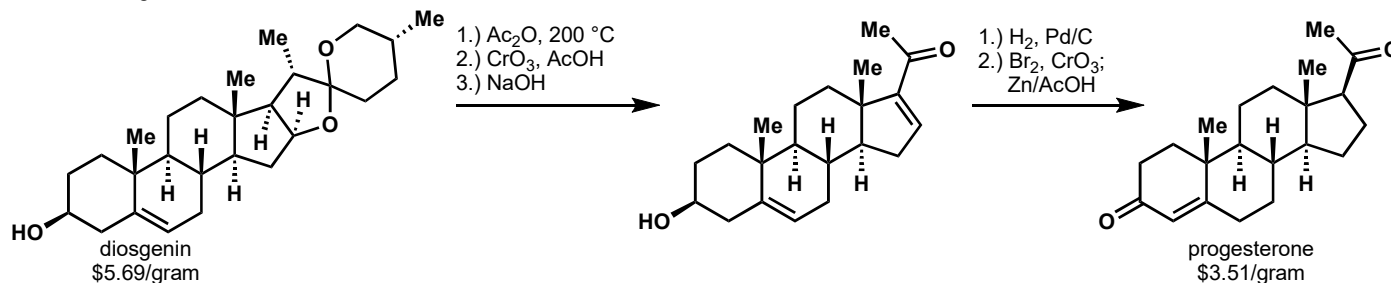
Guerrero's Heck approach to Viridin:



J. Am. Chem. Soc., 2017, 139, 6819-6822

..... Or We Just Buy Them (Semi-Synthesis)

The Marker Degradation:

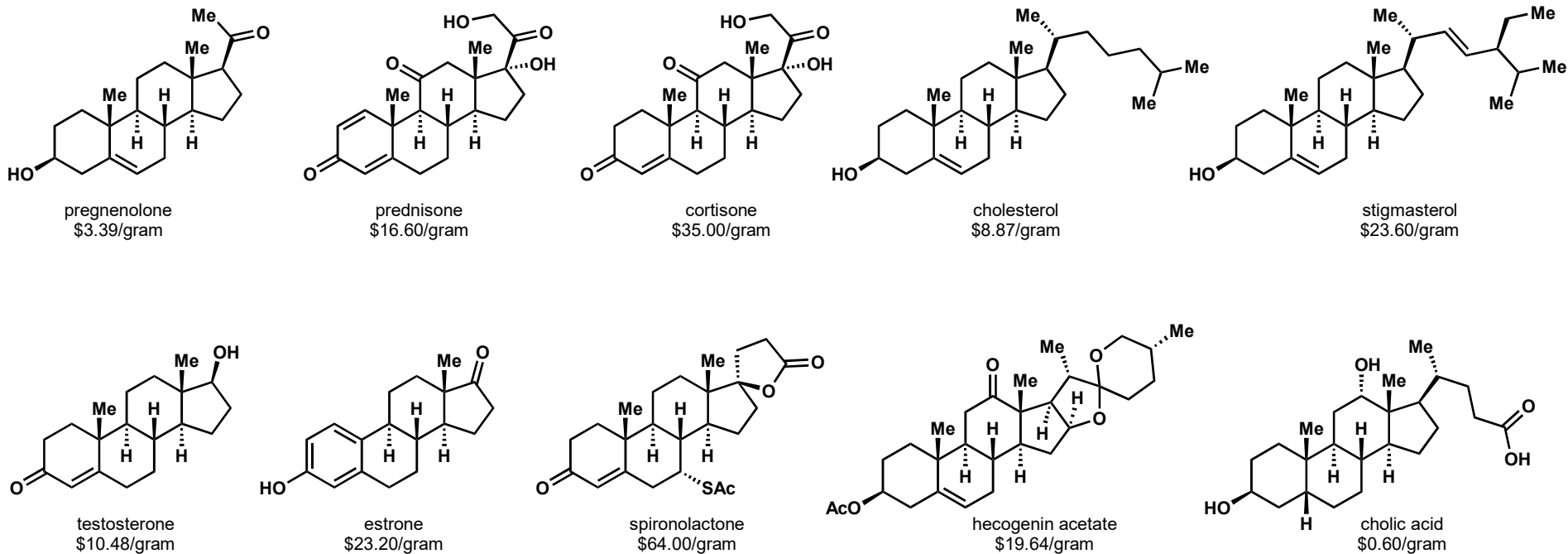


"Although Marker had no plant-collecting permit, two large roots in bags soon were loaded on top of the bus to Orizaba. When Marker got there, the bags were gone, but he recovered the larger 50-pound root by bribing a local policeman."

Due to lack of interest in this process "Marker returned to Veracruz and arranged with Moreno to collect and dry about 10 tons of *cabeza de negro*... and finished with three kilos valued at \$80 per gram, then the largest lot of progesterone ever produced."

American Chemical Society International Historic Chemical Landmarks. The "Marker Degradation" and Creation of the Mexican Steroid Hormone Industry 1938-1945

Commercial availability and prices of some steroids (sigma aldrich 4/8/2018)



The total synthesis of steroids is undoubtedly one of the most important achievements in organic chemistry. - I.V. Torgov
Pure Appl. Chem., 1963, Vol. 6, No. 4, pp. 525-544