

Supporting Information

The synthesis of cardenolide and bufadienolide aglycones, and related steroids bearing a heterocyclic subunit

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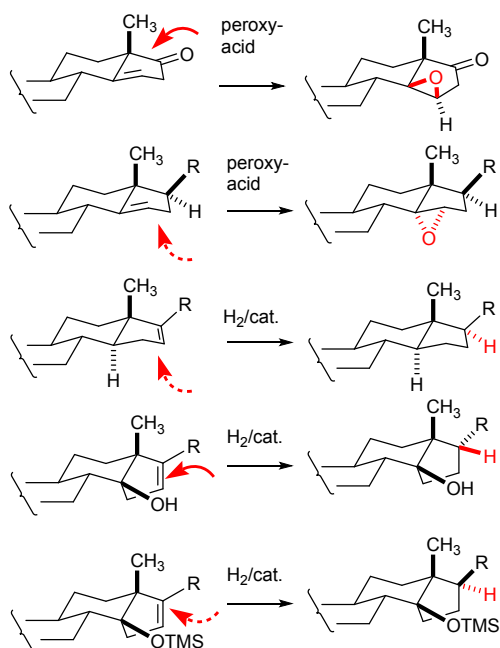
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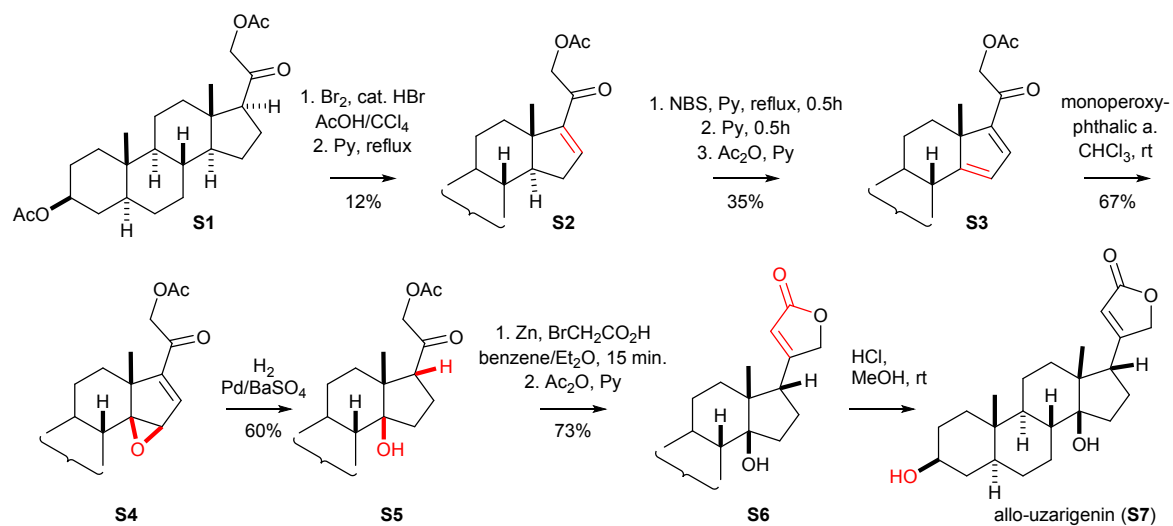
Table of contents

Graphical presentation of preferred reagent approaches to C14 and C16 double bonds in steroid ring D.....	S2
Ruzicka's synthesis of allo-uzarigenin.....	S2
Sondheimer's synthesis of digitoxigenin via the 14β-hydroxy etiocholanolic acid derivative S8.....	S3
Sondheimer's synthesis of resibufogenin and bufalin.....	S3
Deghenghi's synthesis of periplogenin (19-desoxostrophanthidin)	S4
Wiesner's synthesis of digitoxin	S4
Daniewski et al. total synthesis of 9(11)-dehydrotigitoxigenin from Wieland-Miescher dione (384) applying vinyl iodide S31 hydrogenation with diimide and Stork's radical cyanation	S5
Stork's total synthesis of (+)-digitoxigenin. Part 1. The construction of tricyclic ABC intermediate applying intramolecular Diels-Alder reaction	S6
Stork's total synthesis of (+)-digitoxigenin. Part 2. Building up ring D and construction of the lactone moiety	S6
Overman's total-synthetic approach to C19-functionalized cardenolides. Part 1. Retrosynthetic plan	S7
Overman's total-synthetic approach to cardenolides. Part 2. The synthesis of the ring A building block S55	S7
Scheme S12. Overman's synthetic approach to cardenolides. The synthesis of the CD building block S63 and the androstane derivative S69.....	S8
References	S8

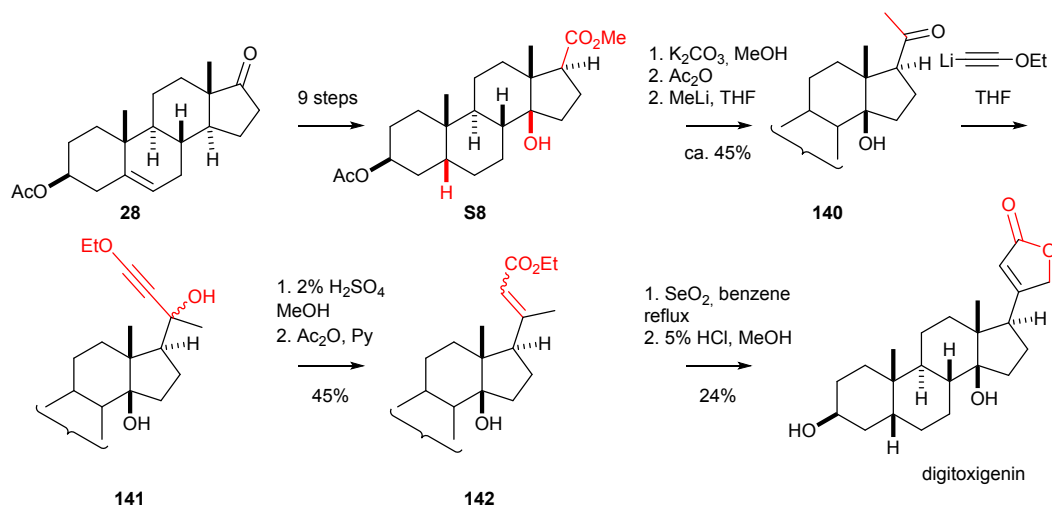
Scheme S1. Graphical presentation of preferred reagent approaches to C14 and C16 double bonds in steroid ring D.



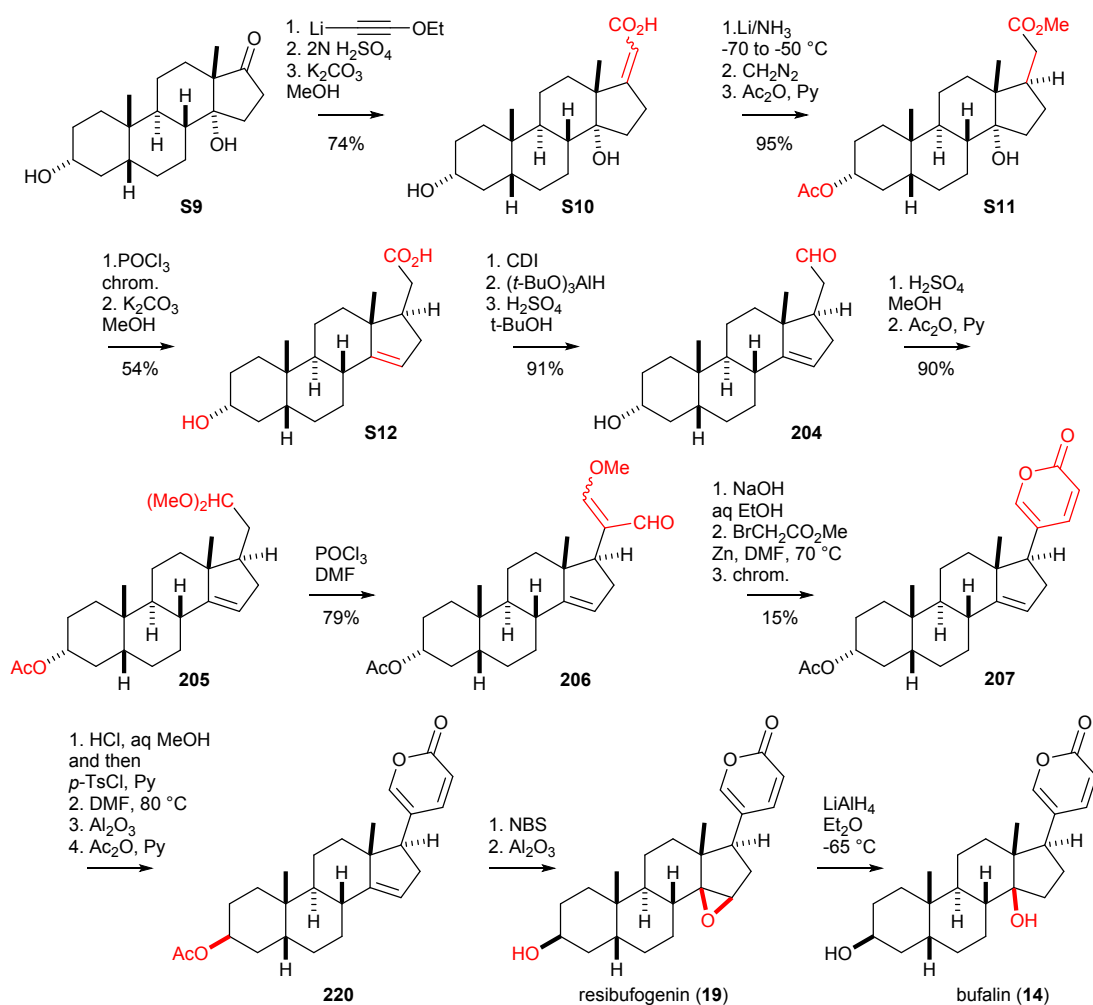
Scheme S2. Ruzicka's synthesis of allo-uzarigenin.¹⁻³



Scheme S3. Sondheimer's synthesis of digitoxigenin⁴⁻⁵ via the 14 β -hydroxy etiocholanolic acid derivative⁶⁻⁸ **S8**.

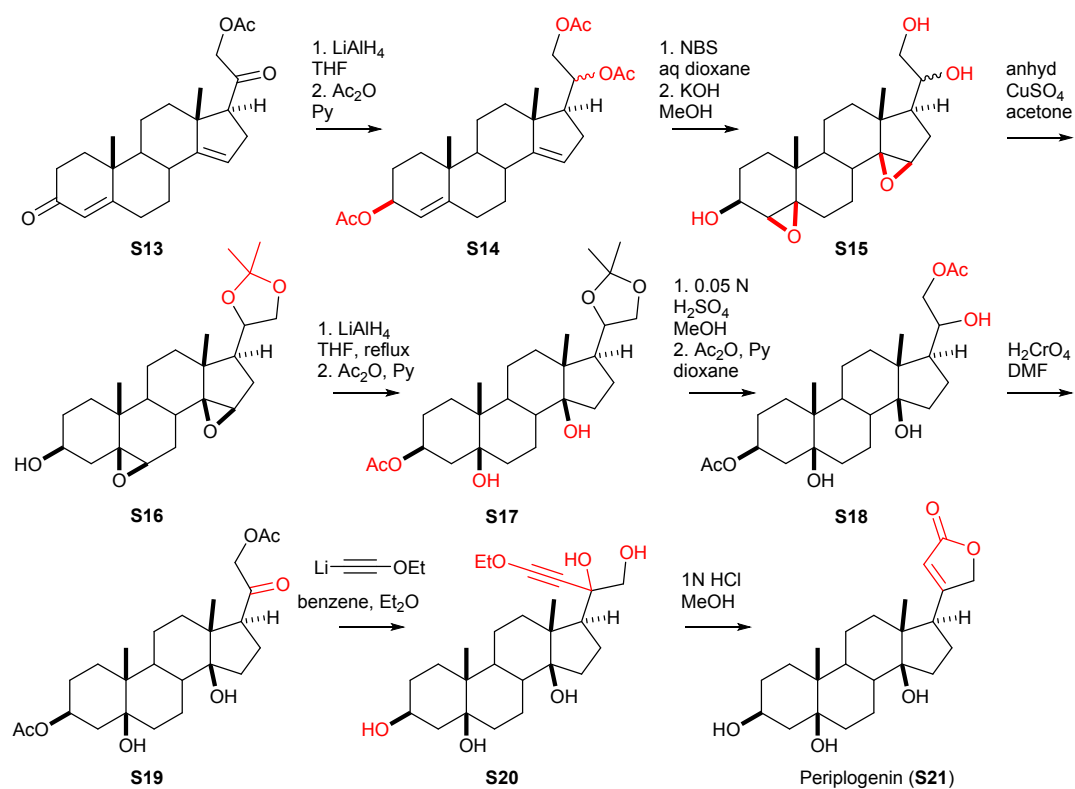


Scheme S4. Sondheimer's synthesis of resibufogenin and bufalin.⁹

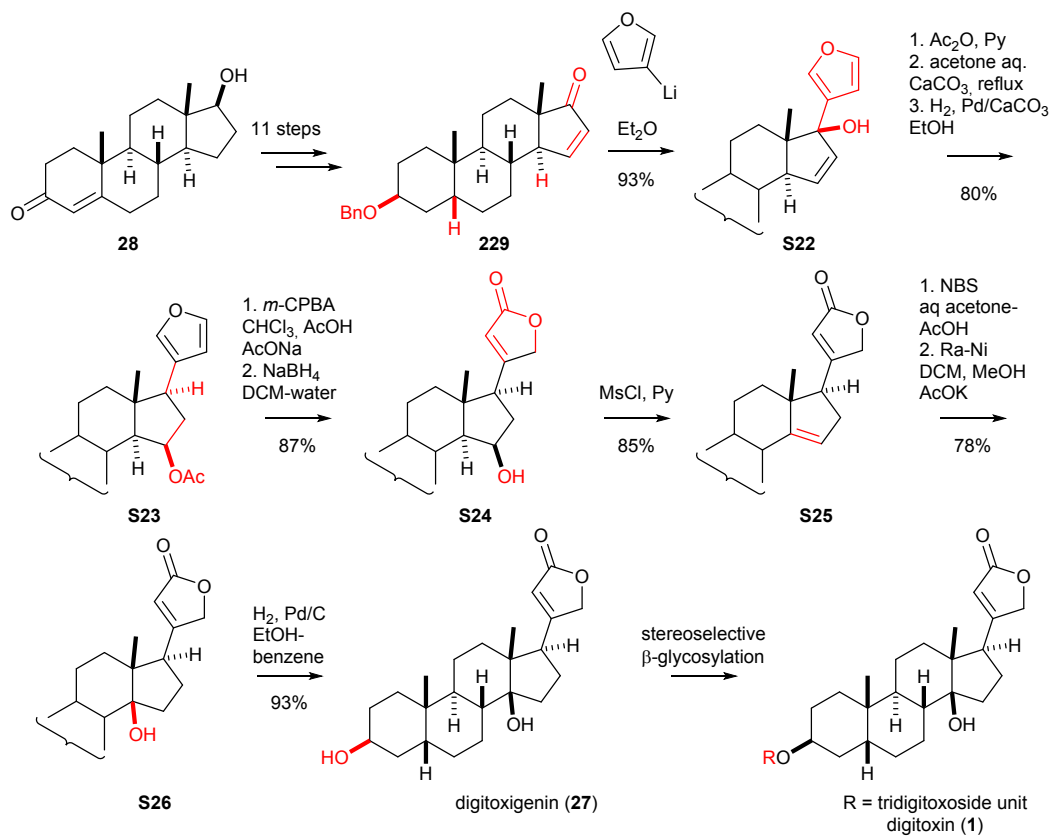


CDI - *N,N*-carbonyldiimidazole

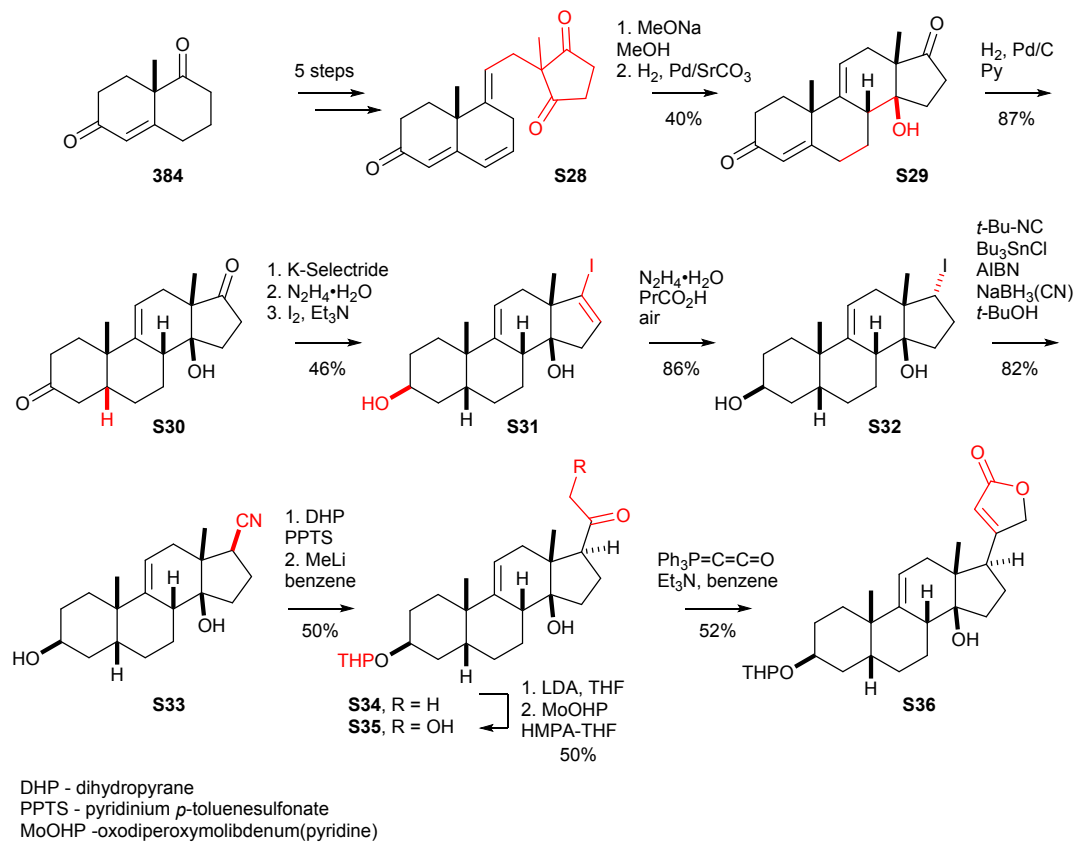
Scheme S5. Deghenghi's synthesis¹⁰⁻¹¹ of periplogenin (19-desoxostrophanthidin).



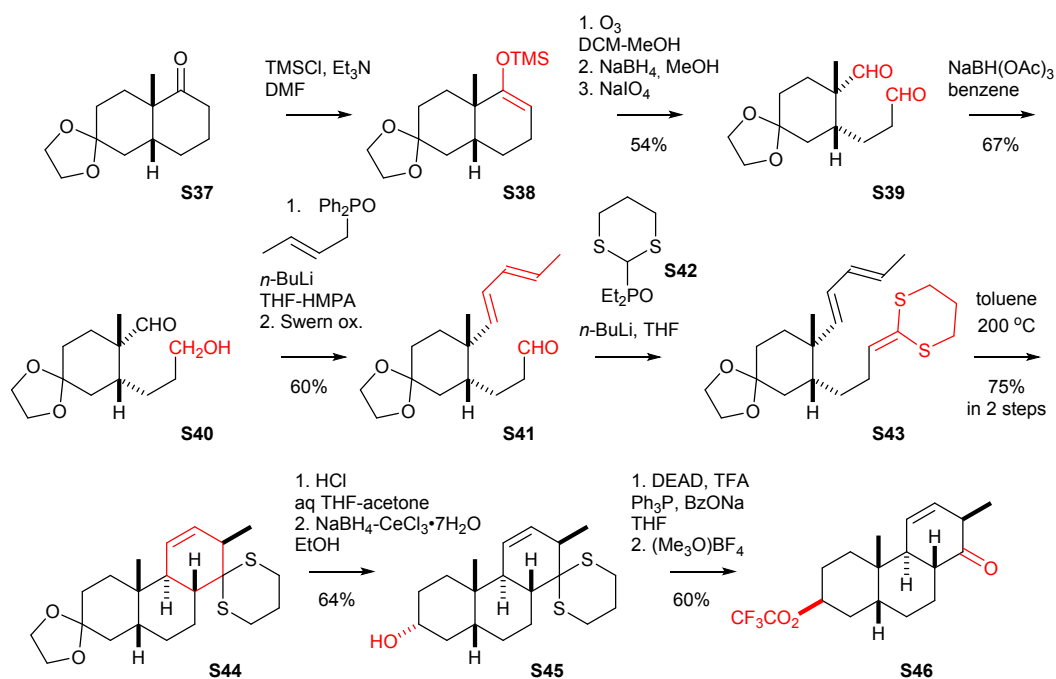
Scheme S6. Wiesner's synthesis of digitoxin.¹²⁻¹⁴



Scheme S7. Daniewski et al.¹⁵⁻¹⁷ total synthesis of 9(11)-dehydrodigitoxigenin from Wieland-Miescher dione (**384**) applying vinyl iodide **S31** hydrogenation with diimide and Stork's radical cyanation.¹⁸

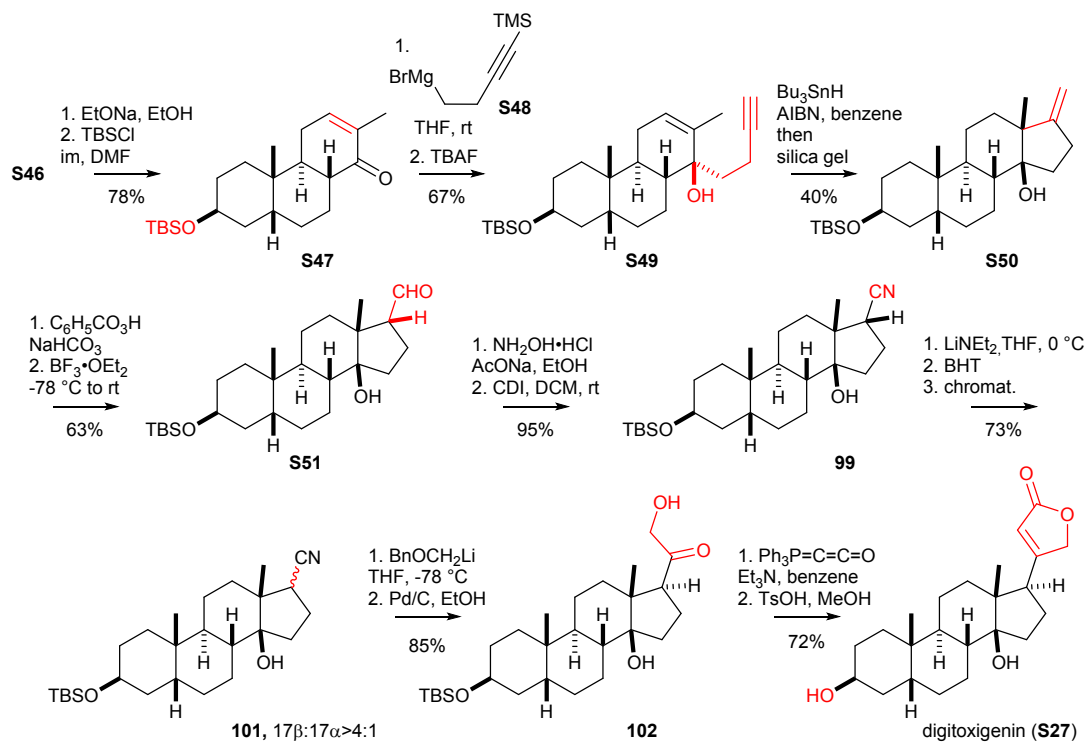


Scheme S8. Stork's¹⁹ total synthesis of (+)-digitoxigenin. Part 1. The construction of tricyclic ABC intermediate applying intramolecular Diels-Alder reaction.



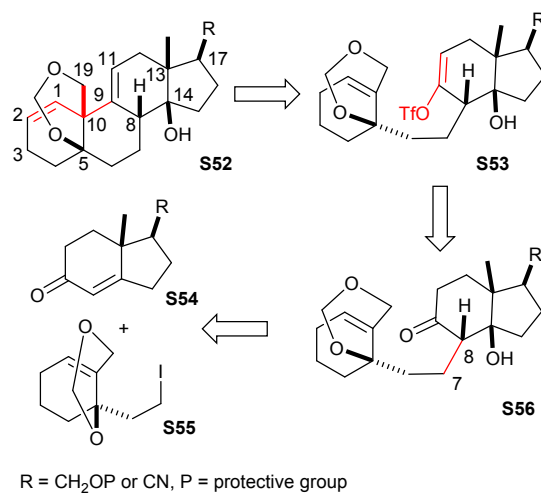
DEAD - diethyl azodicarboxylate

Scheme S9. Stork's total synthesis of (+)-digitoxigenin. Part 2. Building up ring D and construction of the lactone moiety.

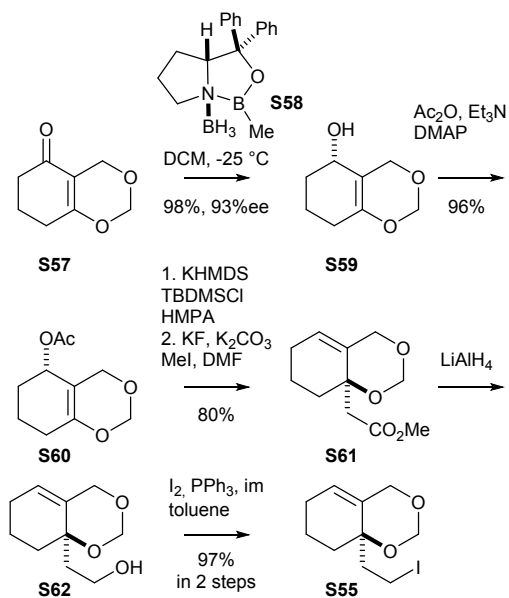


AIBN - 2,2'-azobis(2-methylpropanitrile)
 CDI - *N,N'*-carbonyldiimidazole
 BHT - 2,6-di-*tert*-butyl-4-methylphenol

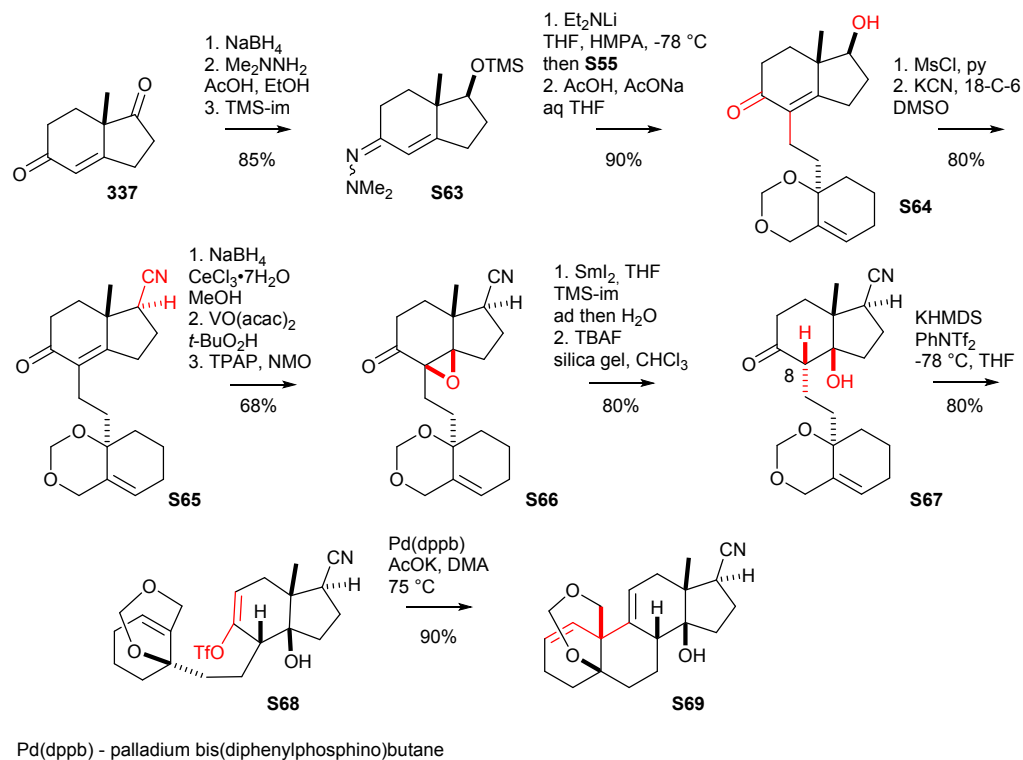
Scheme 10. Overman's total-synthetic approach to C19-functionalized cardenolides.²⁰⁻²³ Part 1. Retrosynthetic plan.



Scheme S11. Overman's total-synthetic approach to cardenolides. Part 2. The synthesis of the ring A building block **S55**.



Scheme S12. Overman's synthetic approach to cardenolides. The synthesis of the CD building block **S63** and the androstane derivative **S69**.



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