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A MERCURY MEDIATED ROUTE TO THE MITOSENES

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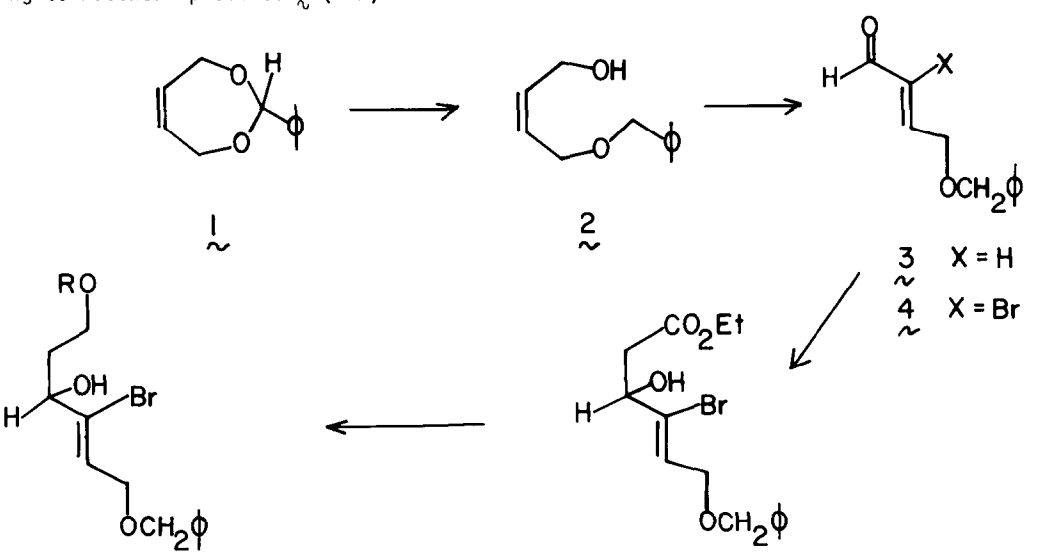
Abstract A Mitsunobu type of coupling is used to prepare a complex phenyl allyl ether which undergoes a Claisen rearrangement. A synthetic route to a mitosene is achieved.

Interest in the synthesis of the mitomycins and their derived mitosenes remains high.[2] The primary challenge lies reaching targets of such exacting functionality.[3] Furthermore, *de novo* synthesis would allow for more deep-seated structural modifications than are feasible *via* operations on the parent systems.[4] Finally, and most relevant to this Letter, this family provides a framework to probe new strategies for the orderly assemblage of polyfunctional aromatic systems. In this vein we describe a convergent route to the mitosenes.[5]

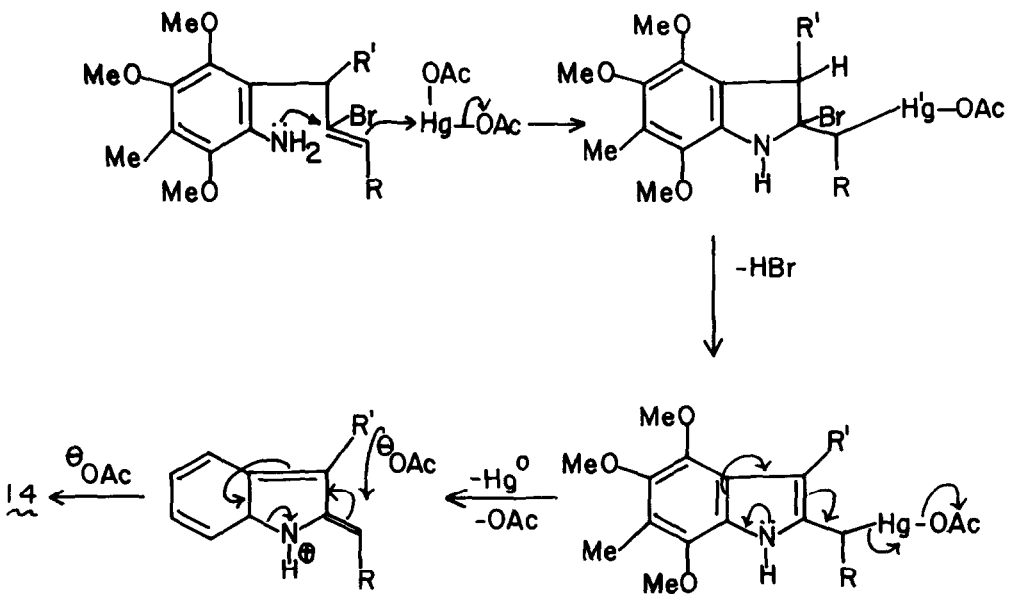
Reaction of acetal 1 with $LiAlH_4$-$AlCl_3$[6] afforded 2[7] in 83% yield. Oxidation of 2 gave 4-benzyloxycrotonaldehyde (3,[7] 56%) which was converted (i) Br_2/AcOH; (ii) KOAc/AcOH; 92%) to the bromoenal, 4.[7] Reformatsky reaction (Rathke conditions[8]) led (55%) to hydroxyester 5.[7] Reduction of 5 with lithium aluminum hydride furnished 6, which on mono tert-butyldimethysilylation according to Hassner[9] provided 7 (92%).

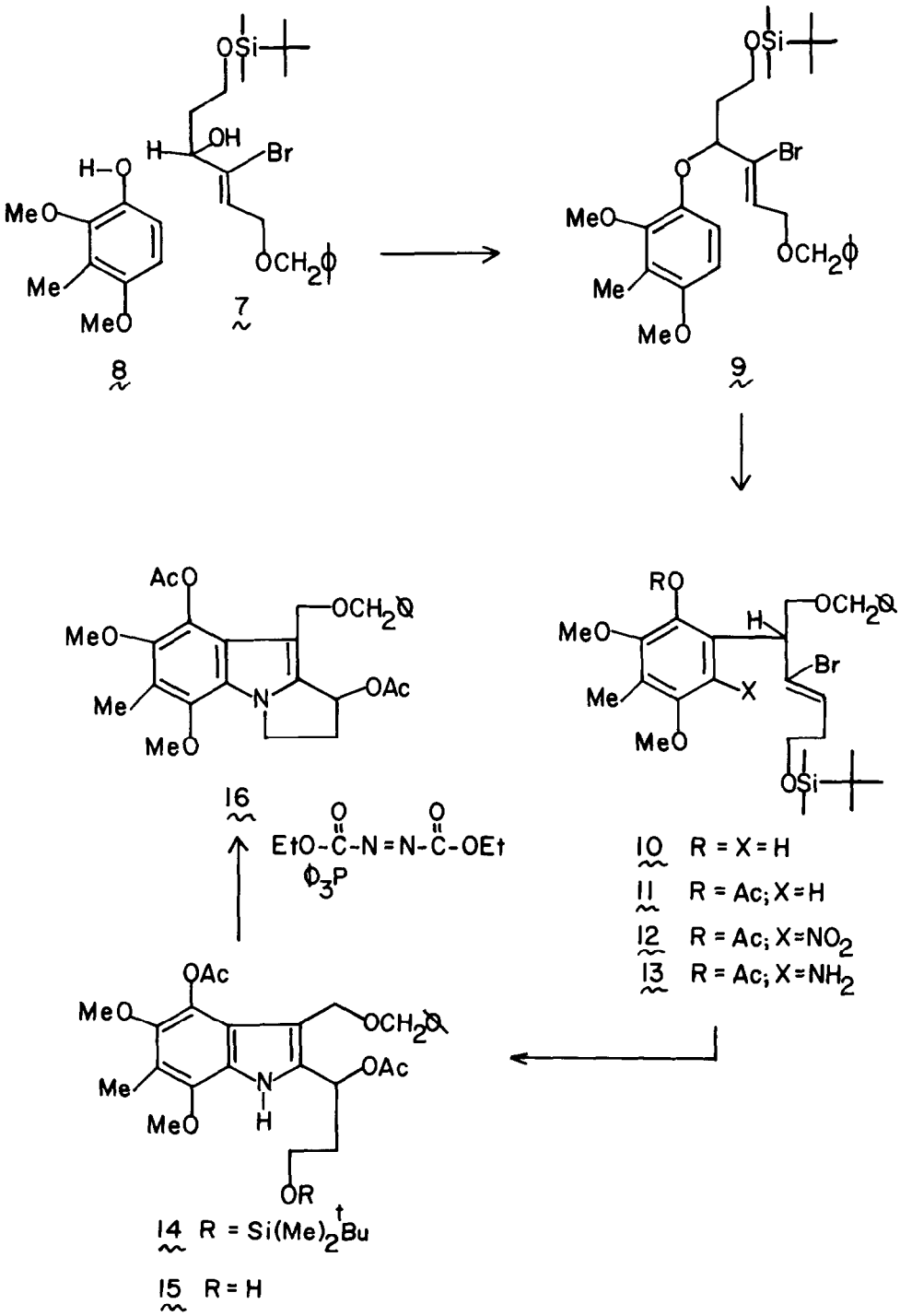


The key building blocks, phenol 8[3] and allylic alcohol 7, were coupled under Mitsunobu conditions[10] to give ether 9[7] (73%), which suffers very smooth Claisen rearrangement(N,N-dimethylaniline; 193°; 75 min.) to provide 10[7] (89%). Upon acetylation (Et_3N;AcCl) compound 10 affords (95%) the acetate 11. Nitration ($Hg(OAc)_2$[11]; 90% HNO_3; Ac_2O) followed by reduction (Zn; AcOH) affords the aniline derivative, 13.

Reaction of 13 with mercuric acetate in THF containing sodium bicarbonate gives the indole 14[7] (51% from 12).[12] Cleavage of the silyl protecting group (n-$Bu_4N^{\oplus}F^{\ominus}$) was followed by another Mitsunobu type reaction[10] to afford 15[7] (61%).

While we can offer no results which bear on the mechanism of this interesting aminomercuration process, a formal accounting of the overall result is provided. The scope and limitations of this sort of indole synthesis bear further examination. *It will be noted that this combination of reactions produces, in the case at hand, an indole (see compound 14) with differentiated oxygen functionality at each of its 2-and 3-benzylic positions.*




OSi
OH
H
Br
H–O
MeO
Me
MeO
OCH2Φ
7
8
9
AcO
OCH2Φ
OAc
N
RO
H
X
10 R = X = H
11 R = Ac; X = H
12 R = Ac; X = NO2
13 R = Ac; X = NH2
16
EtO-C-N=N-C-OEt
Φ3P
14 R = Si(Me)2tBu
15 R = H

The possibility of exploiting Mitsunobu couplings of phenols with complex allylic alcohols to prepare unusually functionalized substrates for aromatic Claisen rearrangements has been generalized in our laboratory and the results will be described in due course.

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