Nineteen-Step Total Synthesis of (+)-Phorbol

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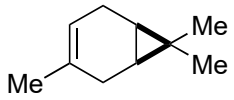


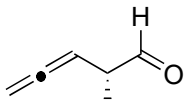
1 – 6

A

7 – 11

B

1) NCS, DMAP
2) O_3 *then* thiourea
3) LiNap *then* HMPA, MeI *then* LiHMDS, **X**
4) Ethynylmagnesium bromide
5) TBSOTf, Et_3N *then* TMSOTf, Et_3N
6) $[RhCl(CO)_2]_2$, CO



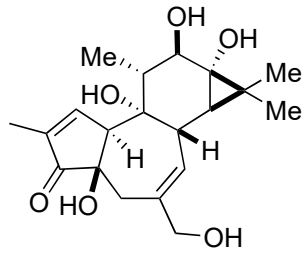
X

7) $Mn(acac)_2$, O_2, $PhSiH_3$, PPh_3 *then* TMSOTf
8) TFDO *then* ZnI_2, MgI_2
9) $Mn(acac)_2$, O_2, $PhSiH_3$, PPh_3
10) $RuCl_3$, $NaBrO_3$
11) TFAA, DMAP *then* Zn, AcOH *then* Ac_2O, DMAP *then* Et_3N

What is the name of the starting material and how would you classify it?

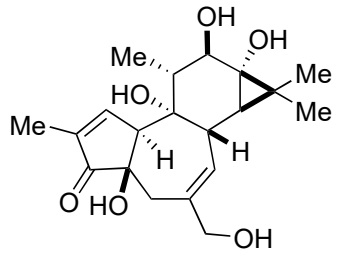
7) Name and mechanism of the reaction?

11) Hint: after addition of Ac_2O two new rings have formed



(+)-Phorbol

12-19

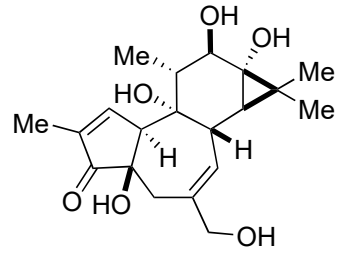


(+)-Phorbol

12) $TsNHNH_2$ *then* $NaBH_3CN$
13) CrO_3, 3,5-dimethylpyrazole
14) $TMSN_3$ then I_2, pyridine
15) Me_4Sn, $AsPh_3$, $PdCl_2(PhCN)_2$, CuI
16) HF-Py
17) Martin sulfurane *then* SeO_2
18) $NaBH_4$ *then* Ac_2O, DMAP
19) $NaBH(OAc)_3$ *then* TBAF *then* $Ba(OH)_2$

13) What is the role of 3,5-dimethylpyrazole?

17) Structure of Martin sulfurane? What name reaction is taking place in this step and what is the mechanism?



(+)-Phorbol