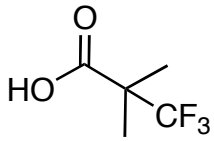
Discovery of NVP-BYL719 a potent and selective phosphatidylinositol-3 kinase alpha inhibitor selected for clinical evaluation (Heterocycles Quiz)

Furet, P.; Guagnano, V.; Fairhurst, R. A.; Imbach-Weese, P.; Bruce, I.; Knapp, M.; Fritsch, C.; Blasco, F.; Blanz, J.; Aichholz, R.; Hamon, J.; Fabbro, D.; Caravatti, G.

Bioorg. Med. Chem. Lett. **2013**, *23*, 3741ų3748.



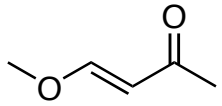
1-4

A

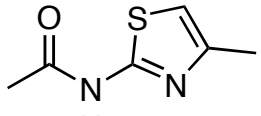
5-8

Alpelisib (NVP-BYL719)

1) oxalyl chloride
2) **1**, LiHMDS, -78 °C, *then* substrate, *then* TFA
3) NH_3 (aq.)
4) $POBr_3$



1



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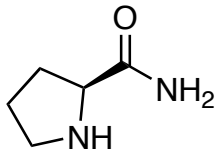


3

5) **2**, $Pd(OAc)_2$/*t*-Bu_3P^y HBF_4, Cs_2CO_3
6) 6 N HCl, EtOH
7) CDI
8) **3**, Et_3N

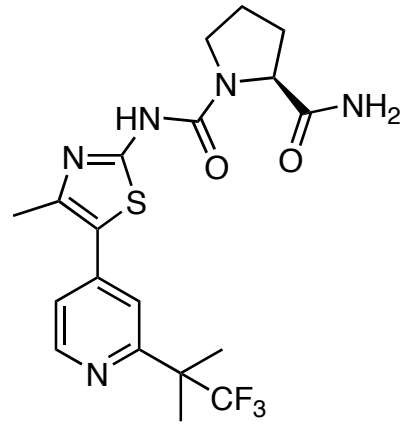
2) what heterocycle is formed? please provide a mechanism

3) what heterocycle is formed?

5) which heterocycle is introduced? How would you make **2**?

7) what is the structure of CDI? what is the heterocycle?

8) what is the amino acid analog of **3**? what heterocycle is in **3**?



Alpelisib (NVP-BYL719)

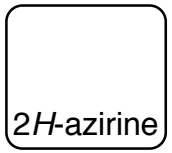
Heterocycle Quiz!

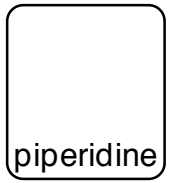
Be honest with yourself - how many can you name/draw? How long did it take you?

No cheating!

person at the board will have to draw 10 random heterocycles and answer some questions

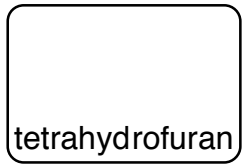

aziridine

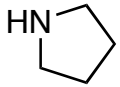

2*H*-azirine

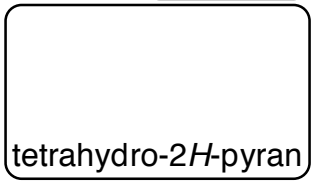

piperidine

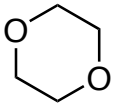

piperazine

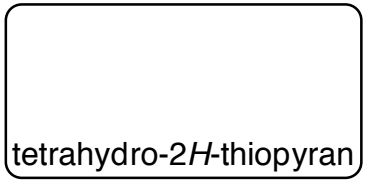

morpholine

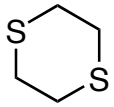

tetrahydrofuran

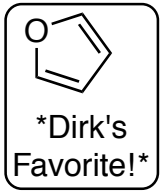


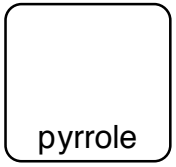

tetrahydro-2*H*-pyran

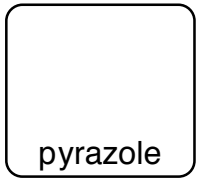



tetrahydro-2*H*-thiopyran

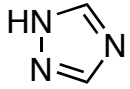


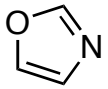

Dirk's Favorite!

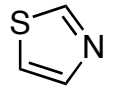

pyrrole

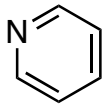

pyrazole


imidazole

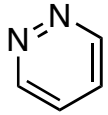


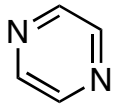


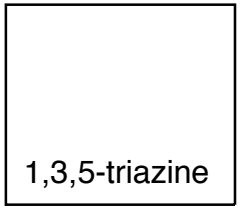


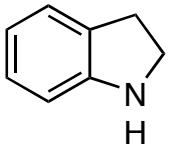


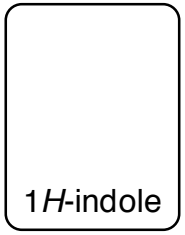

pyrimidine

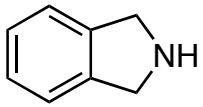


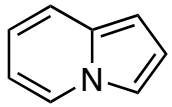



1,3,5-triazine




1*H*-indole






benzimidazole