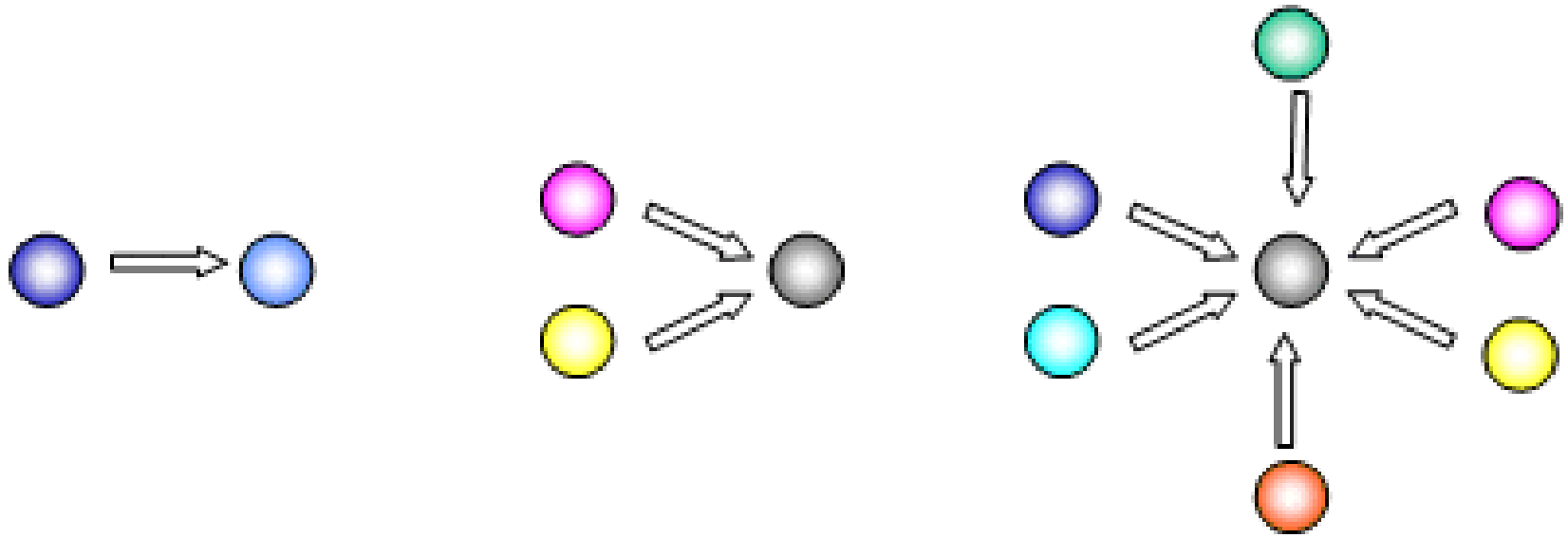
UNIVERSIDAD DE GUANAJUATO
División de Ciencias Naturales y Exactas
Departamento de Química
Campus Guanajuato

Synthesis of 1,5-disubstituted tetrazoles containing propargyl moiety

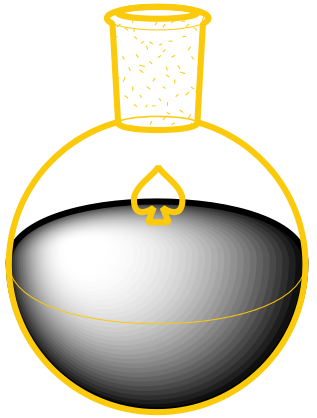
Ángel Rentería Gómez
María del Rocío Gámez Montaño*

Multicomponent reaction

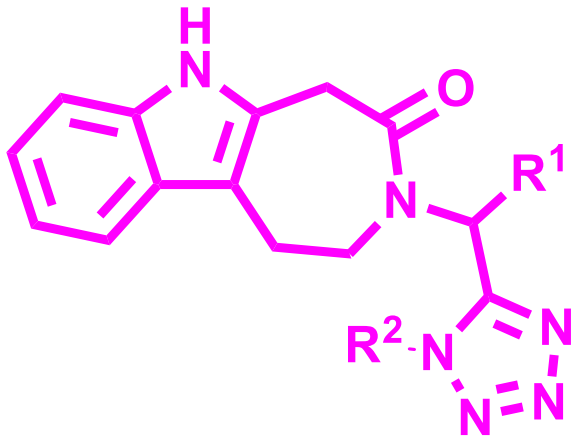


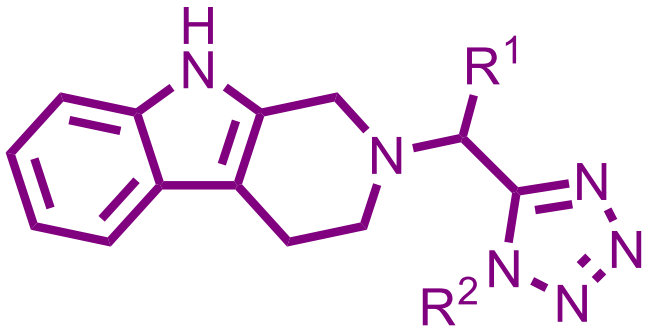
A. Dömling, I. Ugi, *Angew. Chem. Int. Ed.* **2000**, *39*, 3168.

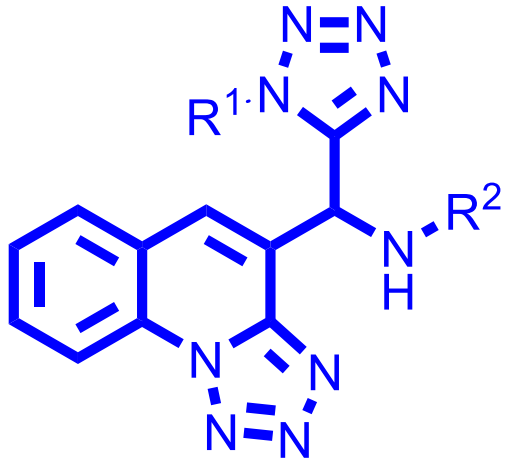
¿WHY MCR´s?



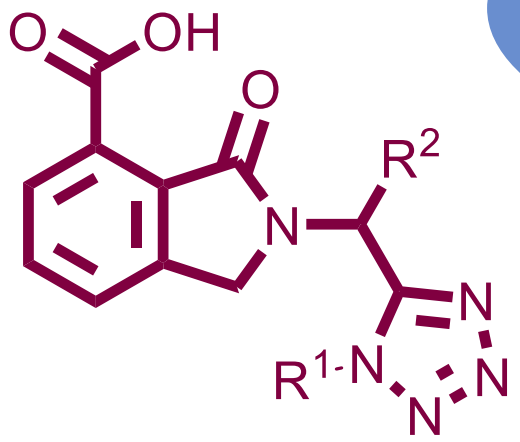
Ugi, I.; Heck, S. *Comb. Chem. High Throughput Screen.* **2001**, *4*, 1.

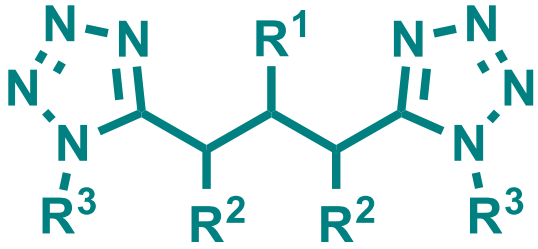






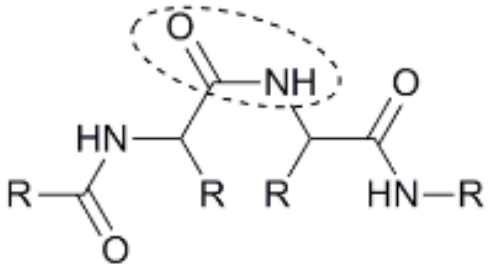
1,5-disubstituted tetrazoles





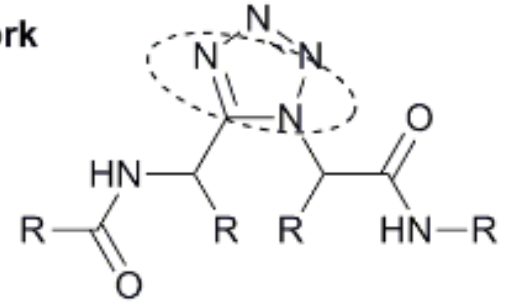
(a) Gordillo-Cruz R.; Rentería-Gómez A.; Islas-Jácome A.; Cortes-García C.; Díaz-Cervantes E.; Robles J.; Gámez-Montaño R. *Organic & Biomolecular Chemistry* **2013**, *38*, 6470. **(b)** Cárdenas-Galindo, L.E.; Islas-Jácome, A.; Alvarez-Rodríguez, N.V.; El-Kaim, L.; Gámez-Montaño, R. *Synthesis*. **2014**, *46*, 49. **(c)** Gámez-Montaño, R.; et. al. *Molecules*, **2015**, *20*, 1519. **(d)** Basavanag-Unnamatla, M. V.; Islas-Jácome, A.; Quezada-Soto, A.; Ramírez-López, S. C.; Flores-Alamo, M.; Gamez-Montano, R. *J. Org. Chem* (accepted) **DOI:** 10.1021/acs.joc.6b01576

Tetrazole rings are usually attributed to the possibility of this moiety to mimic a carboxyl group or a *cis* amide bond.

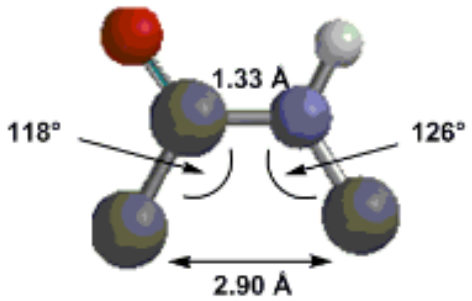


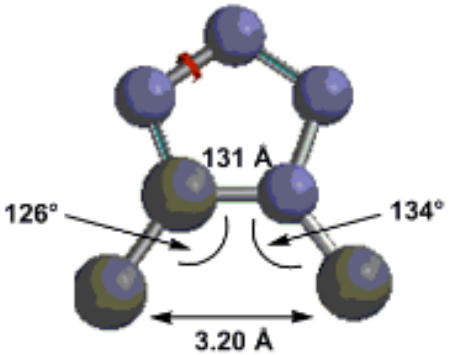
cis amide bond of peptides

Marshall's work

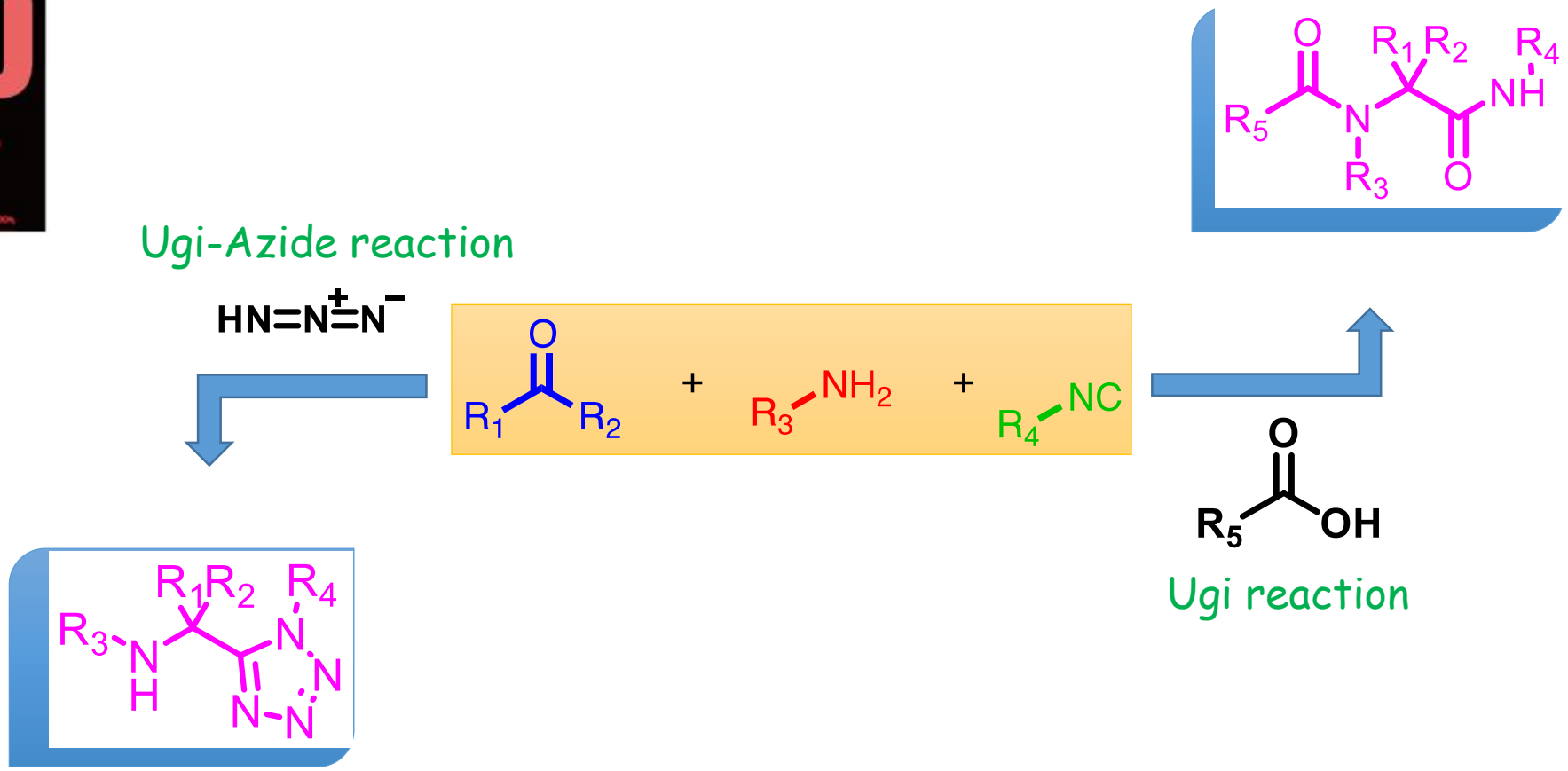


bioisosters of *cis* amides



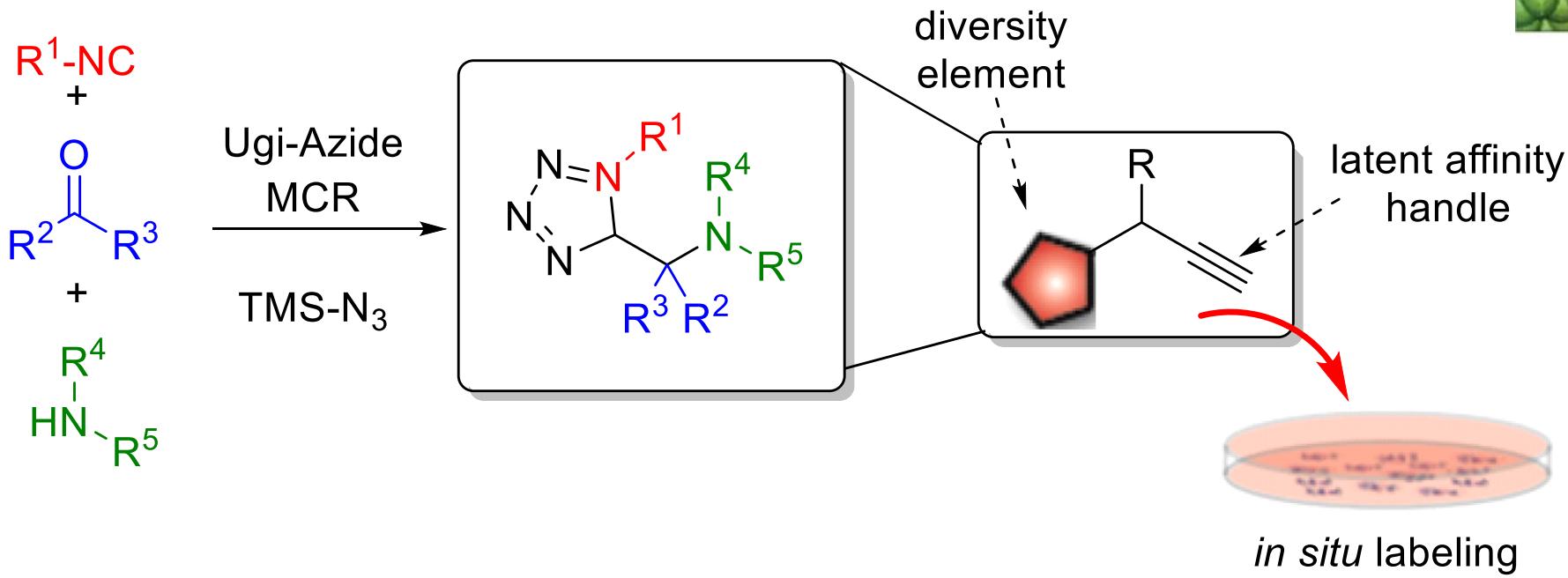


G. R. Marshall *et al. J. Am. Chem. Soc.*, 1988, **110**, 5875.



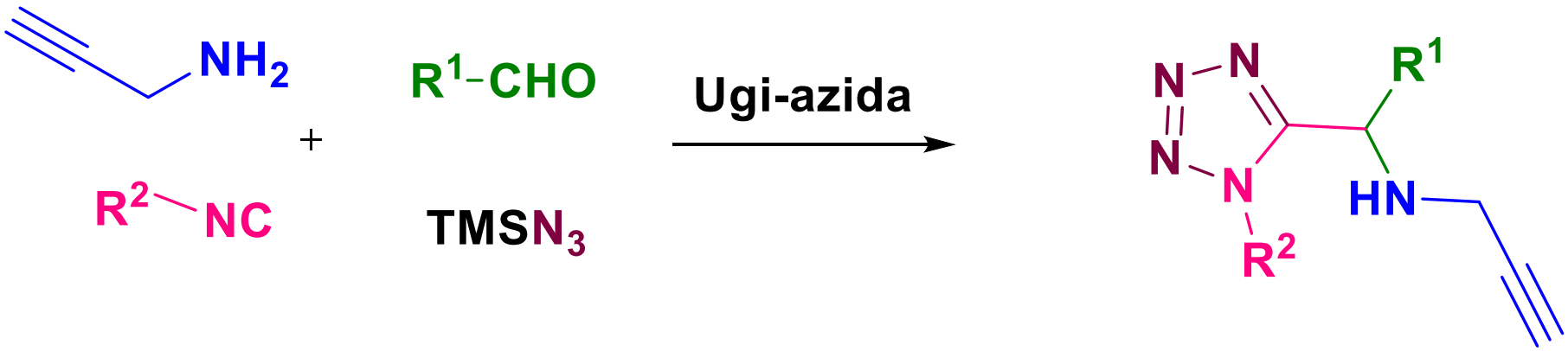
(a) Cárdenas-Galindo, L. E.; Islas-Jácome, A.; Alvarez-Rodríguez, N. V.; El Kaïm, L.; Gámez-Montaño, R. *Synthesis* **2014**, *46*, 49; **(b)** Gordillo-Cruz, R. E.; Rentería-Gómez, A.; Islas-Jácome, A.; Cortes-García, C. J.; Díaz-Cervantes, E.; Robles, J.; Gámez-Montaño, R. *Org. Biomol. Chem.* **2013**, *11*, 6470.

1,5-disubstituted-1*H*-tetrazoles containing propargyl moiety

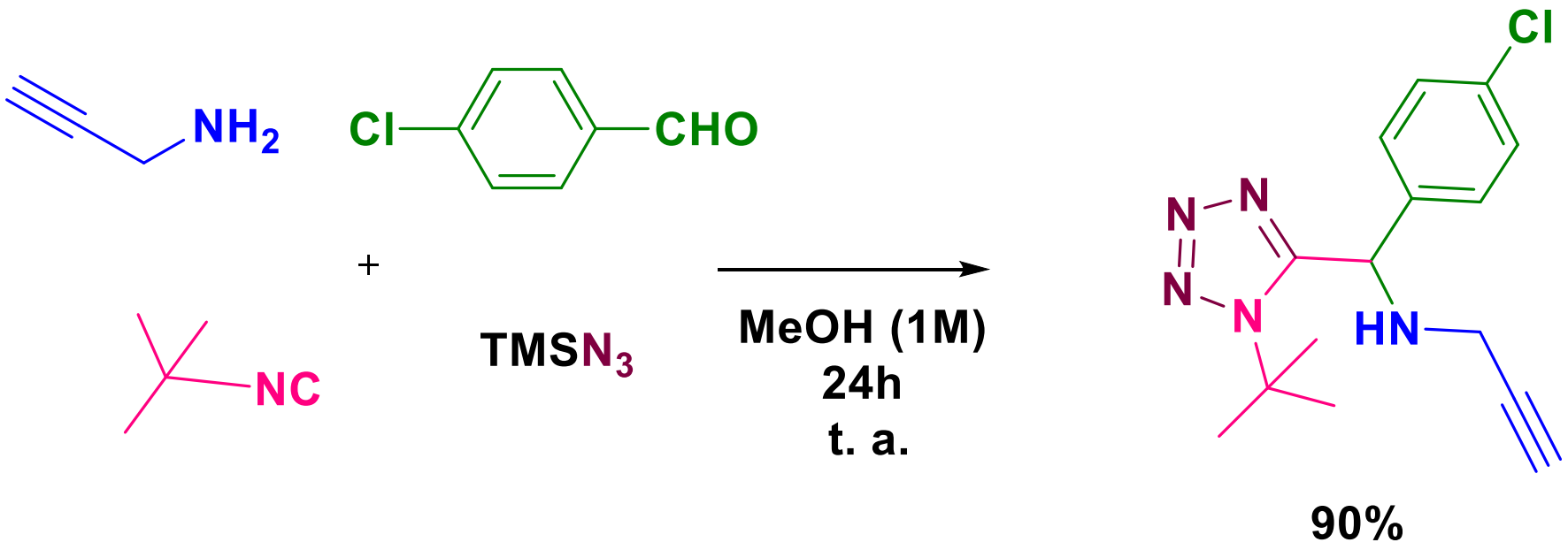


Kambe, T.; Correia, B. E.; Niphakis, M. J.; Cravatt, B. F. *J. Am. Chem. Soc.* **2014**, *136*, 10777.

Synthetic Strategy

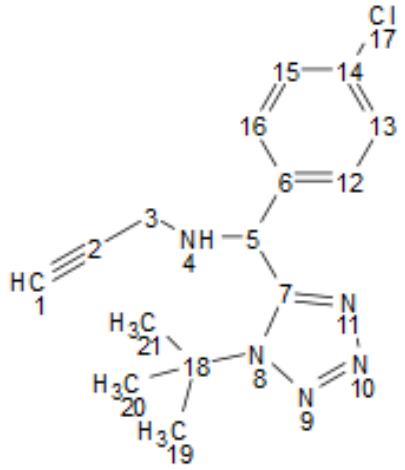


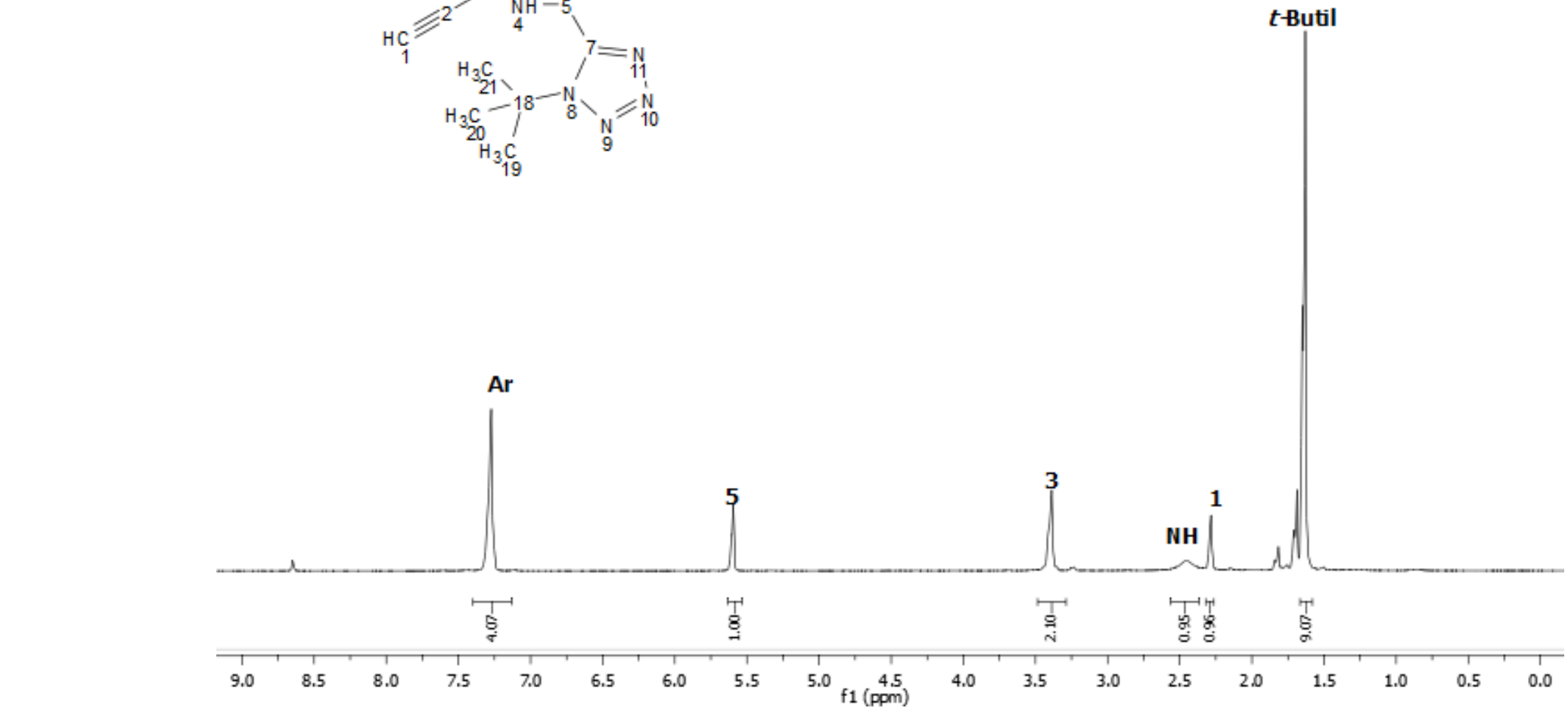
Ugi-azida reaction



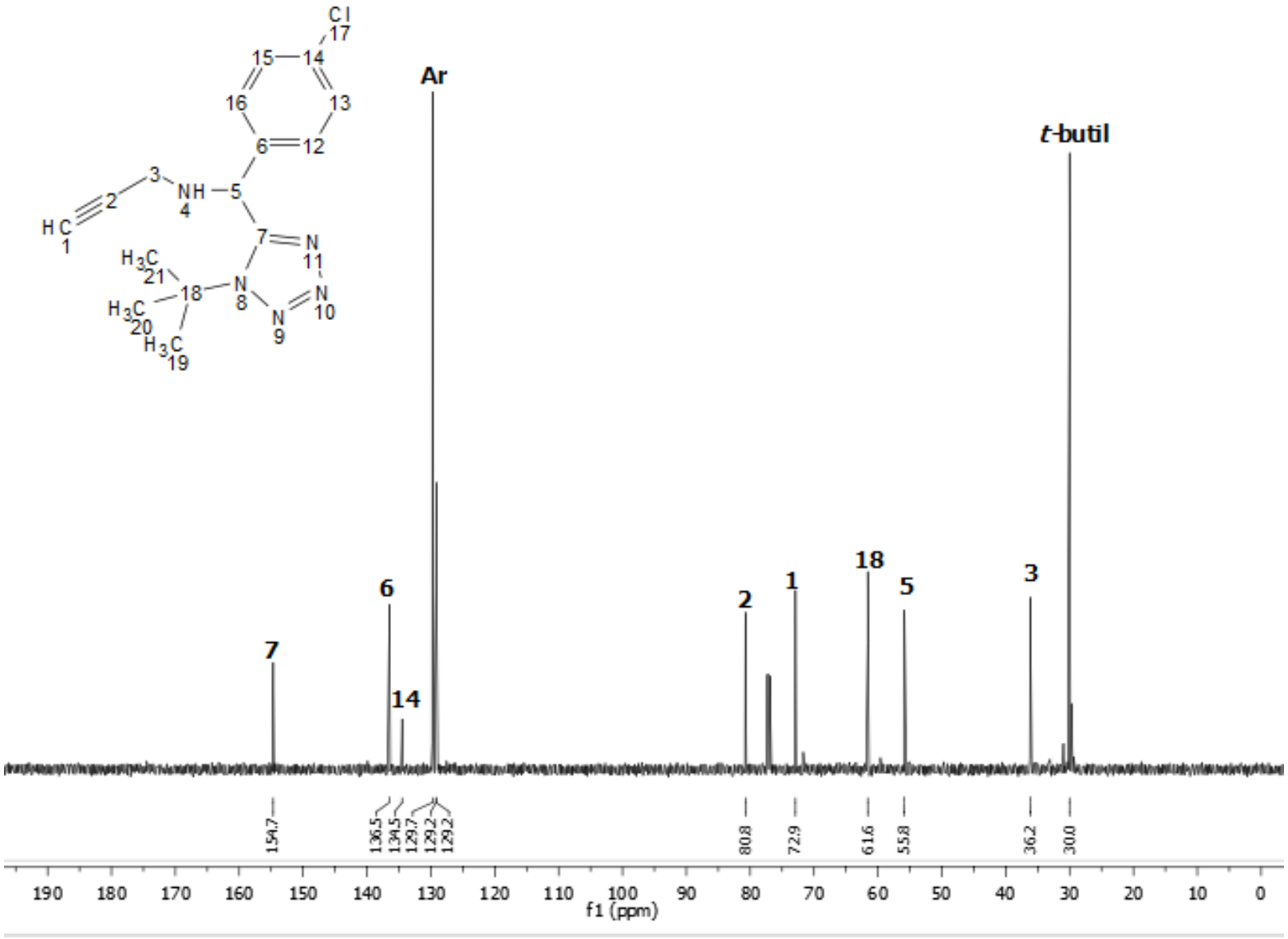
90%

Spectrum NMR-^{1}H

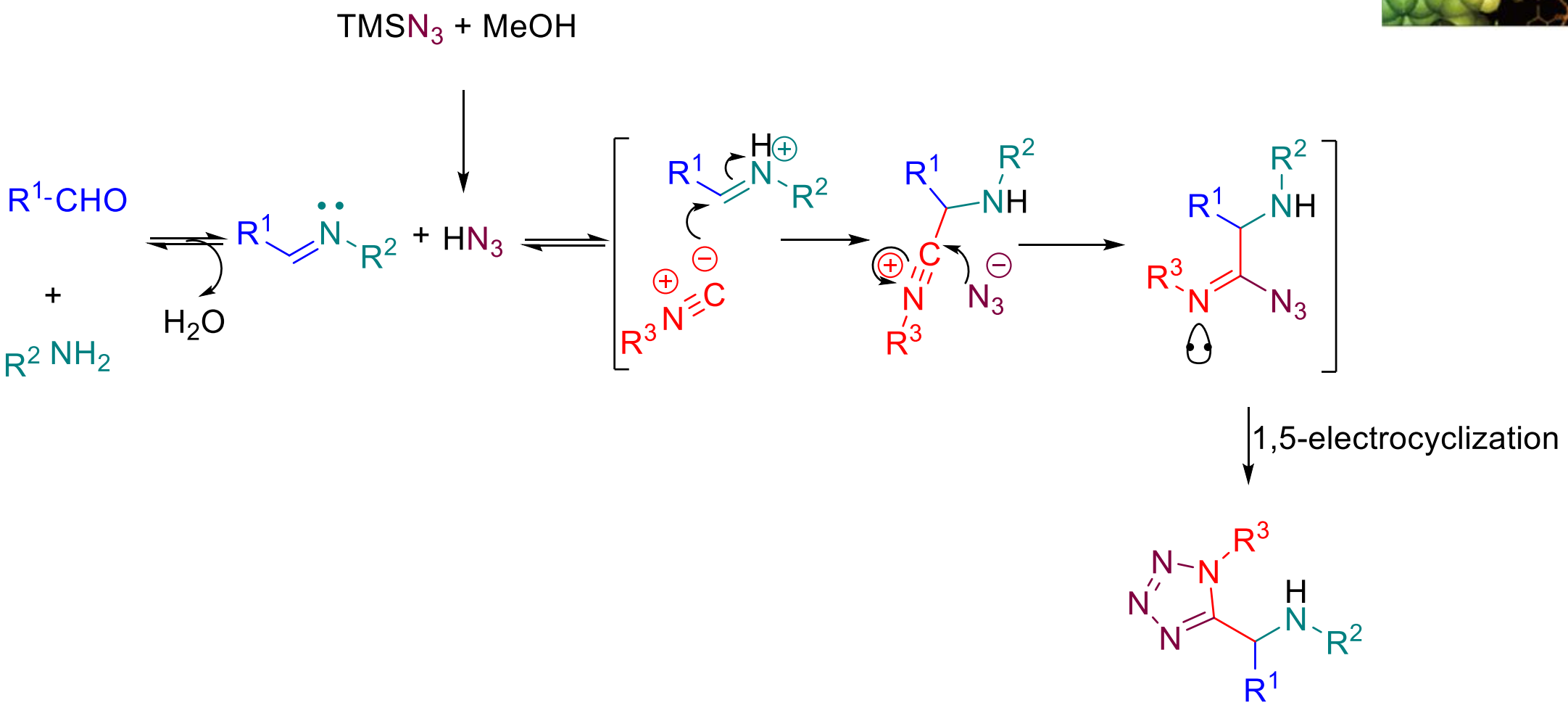




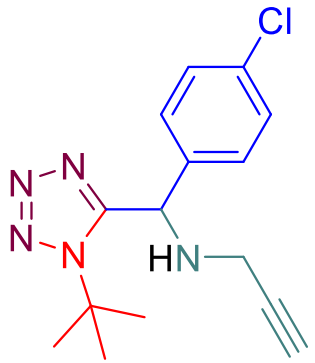
Spectrum NMR-^{13}C



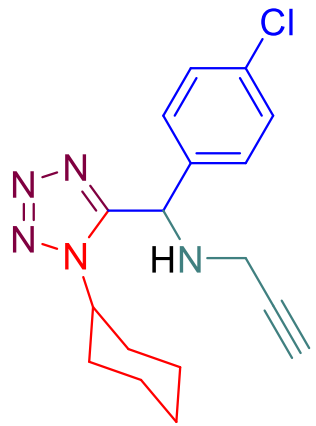
Plausible Mechanism reaction



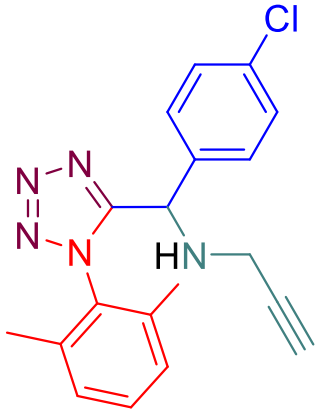
Substrate Scope.



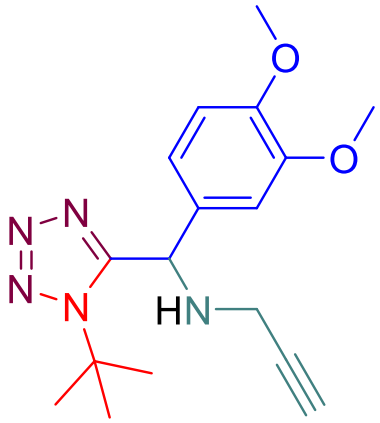
r. t.(90%)
))) (77%)
15d



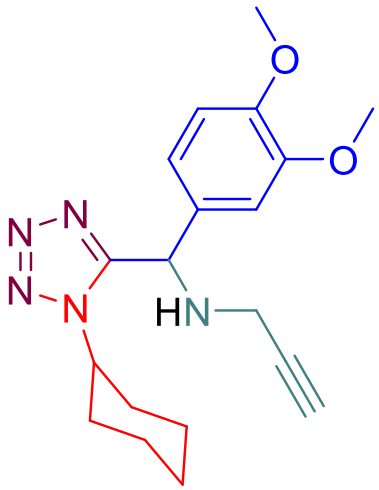
r. t. (92%)
))) (75%)
15e



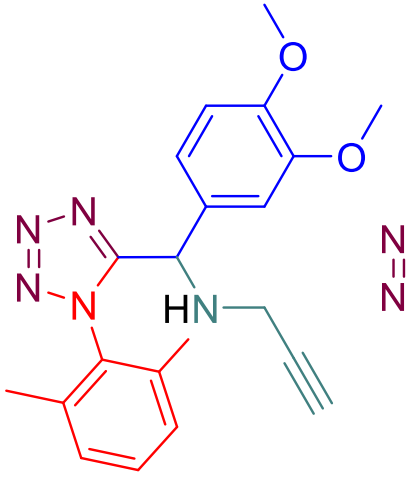
r. t. (82%)
))) (5%)
15f



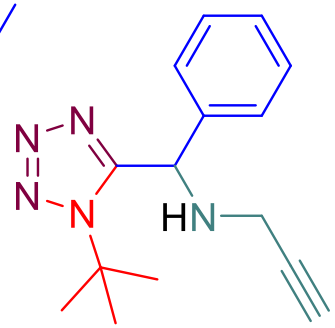
r. t.(94%)
))) (83%)
15g



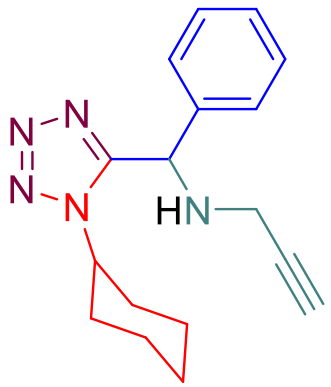
r. t. (95%)
))) (80%)
15h



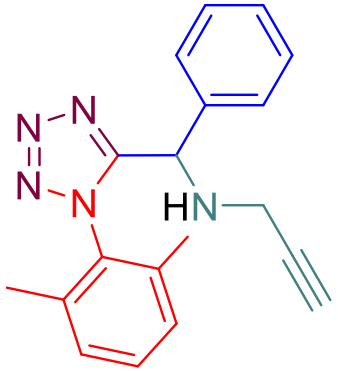
r. t. (85%)
))) (20%)
15i



r. t. (87%)
))) (75%)
15a



r. t.(88%)
))) (69%)
15b



r. t. (80%)
))) (12%)
15c

Conclusions

A series of nine novels 1,5-disubstituted-1*H* tetrazoles containing propargyl moiety was synthetize with good to excellent overall yields in one simple operational reaction step using mild conditions at room temperature.

Acknowledgements

R.G.-M. is grateful for financial support from CIO-UG (009/2015), DAIP (859/2016) and CONACYT (CB-2011-166747-Q) projects. A.R.-G. (554166/290817) acknowledge CONACYT-México for his graduate scholarship. All authors kindly acknowledge to National Laboratory for the instrumentation time provided (UG-UAA-CONACYT: 123732).

Team Rocío Gámez Montaño