UNIVERSIDAD DE GUANAJUATO
División de Ciencias Naturales y Exactas
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Synthesis of bis-heterocycles type spacer containing 1,5-disubstitutes-1H-tetrazoles

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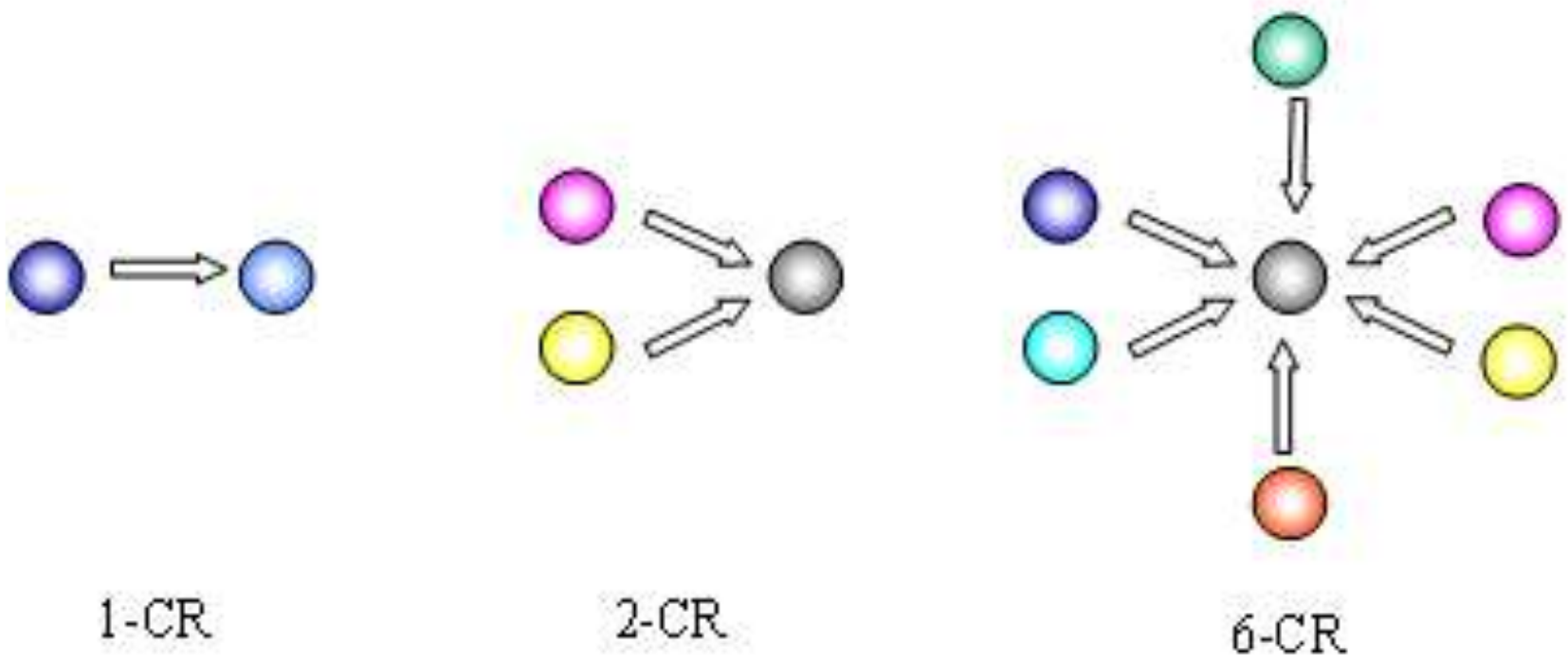
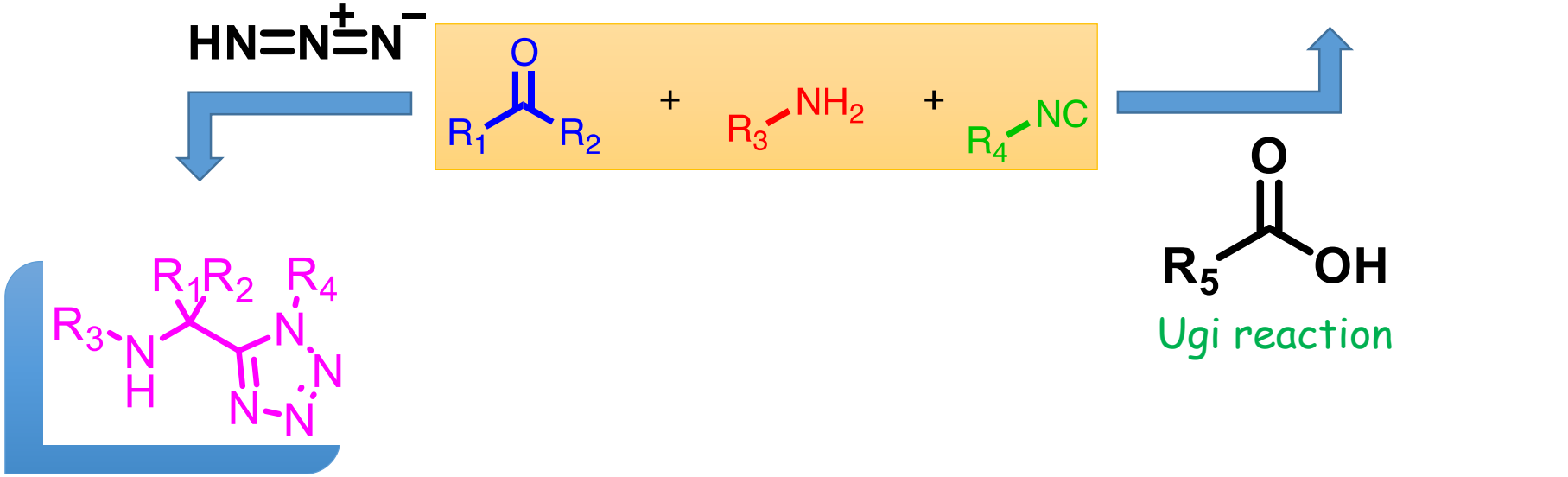
Multicomponent reaction



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

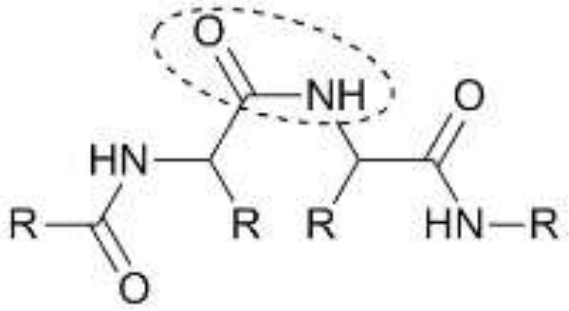
Ugi-Azide reaction



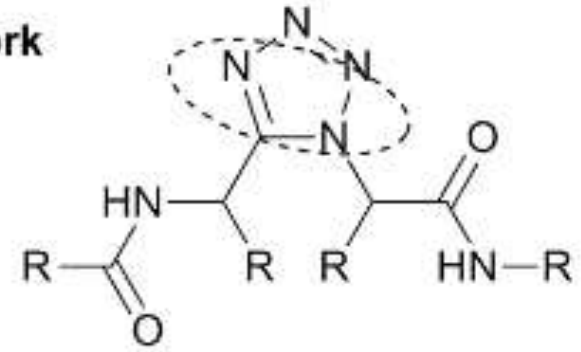
Ugi reaction

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

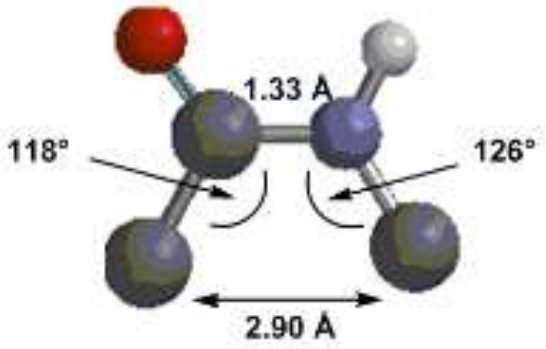
Marshall's work

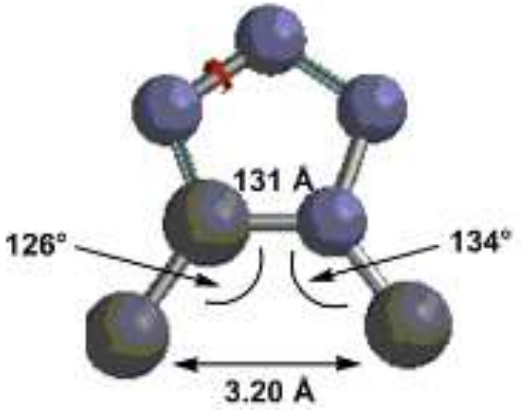


cis amide bond of peptides

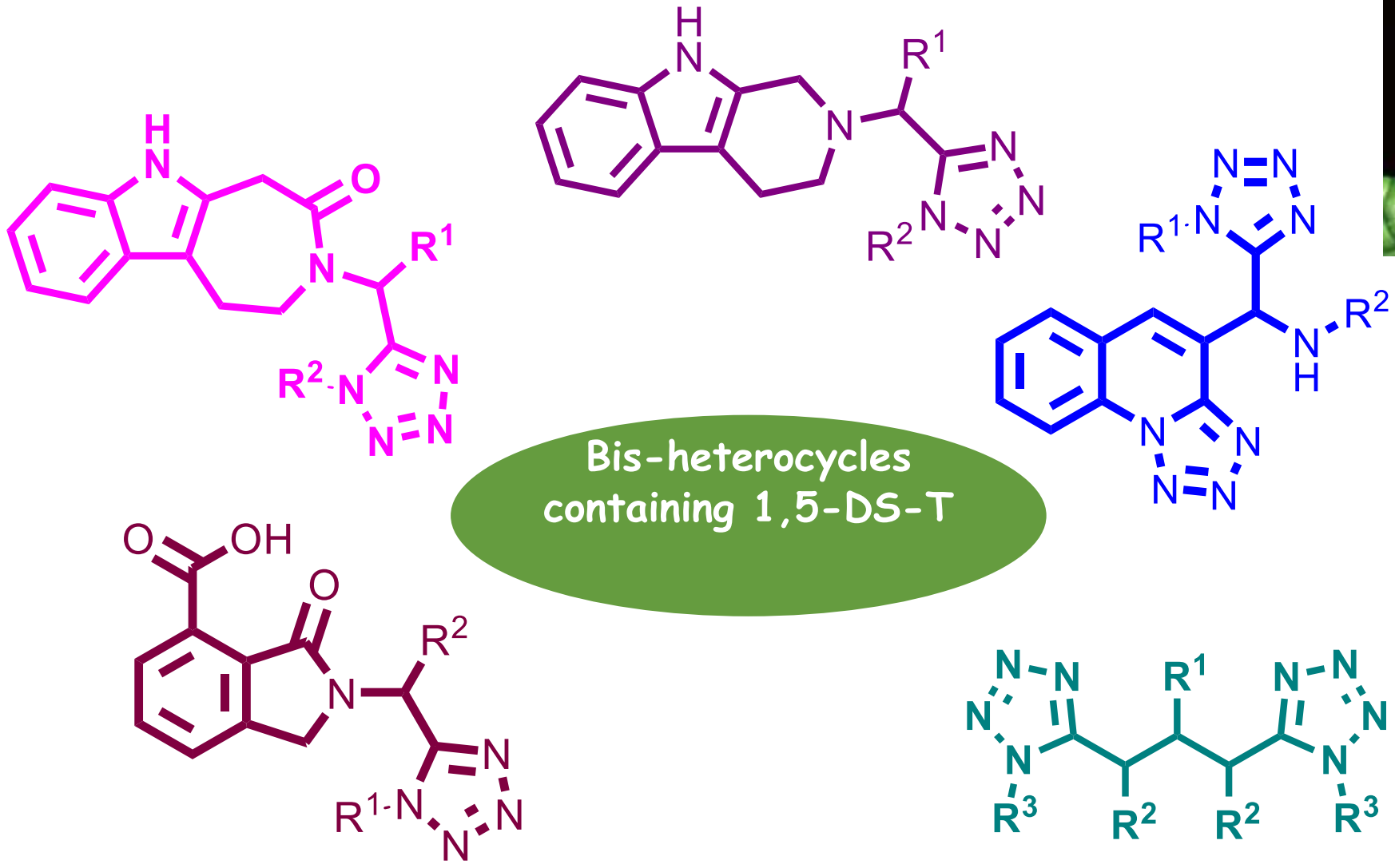


bioisosters of *cis* amides



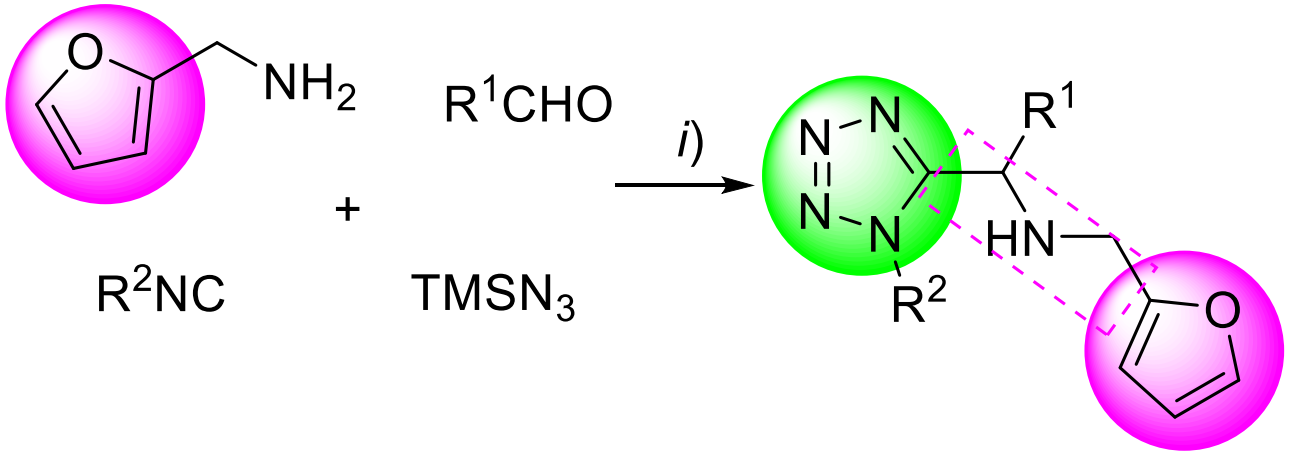


G. R. Marshall *et al. J. Am. Chem. Soc.*, **1988**, *110*, 5875.



(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.* **2016**, *81*, 10576.

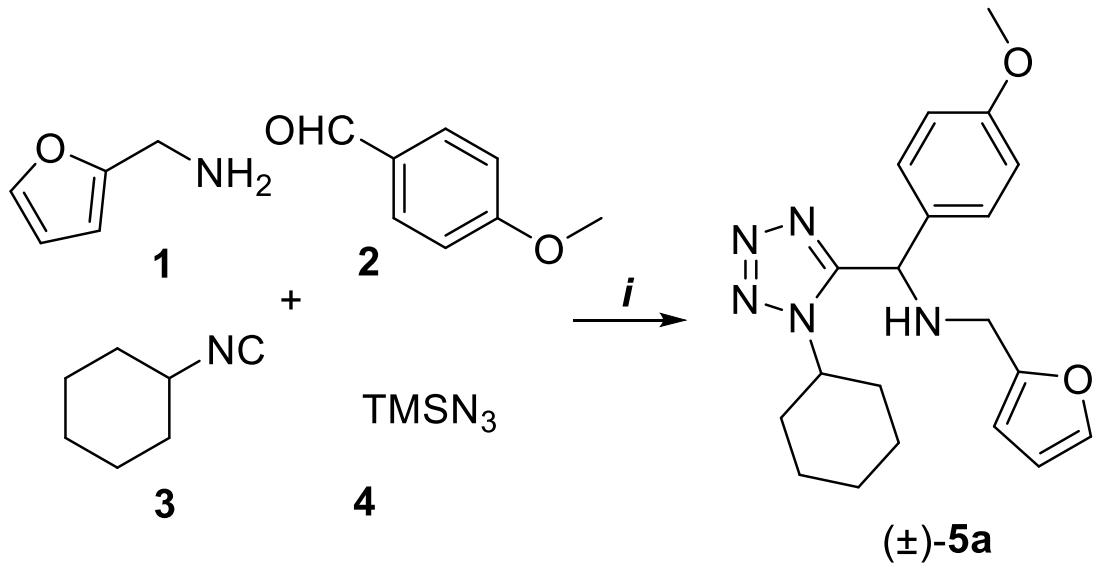
Synthetic Strategy



10 examples
79-99%

i) MeOH [1.0 M]; rt; 24 h
R^1= 4-OMePh, 3,4-diOMePh, 4-ClPh, Ph
R^2= *c*-Hex, *t*-Bu, 2,6-diMePh

Ugi-azida reaction

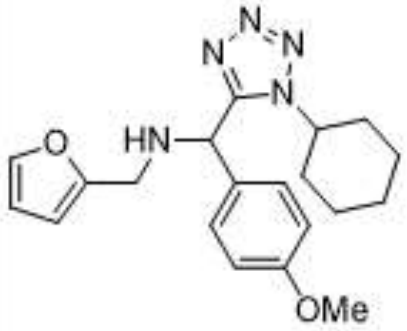


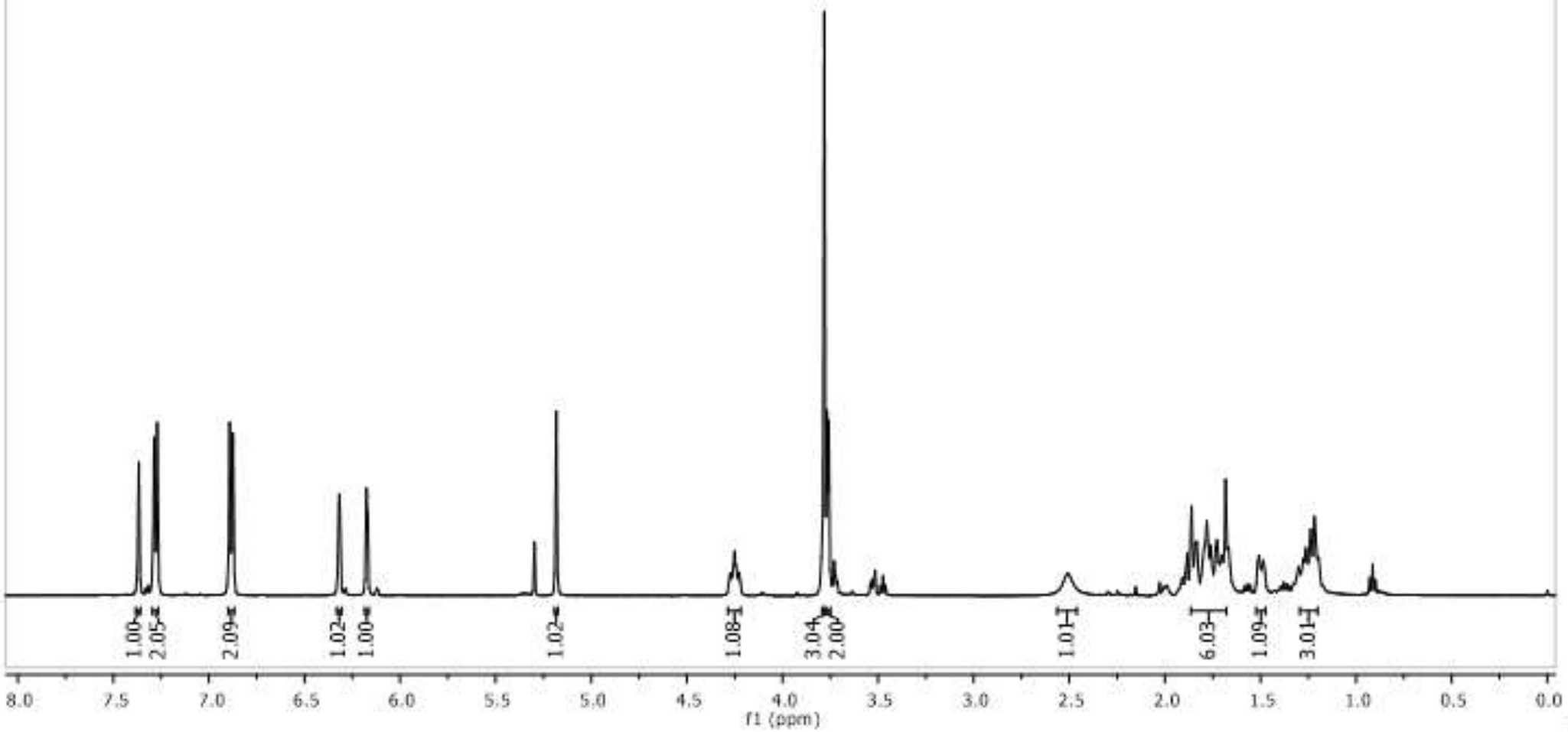
(±)-**5a**

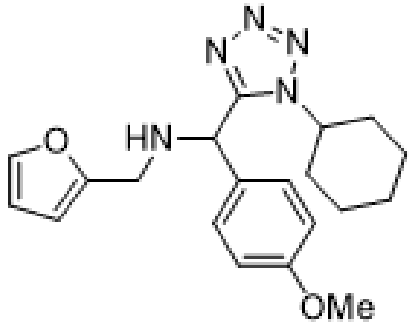
Entry	Conditions	T (°C)	t(h)	Yield[b] (%)
1	MeOH [1.0 M]	rt	24	99[c]
2	neat	rt	24	22
3	MeOH [1.0 M]	65	1	84
4	MeOH [1.0M]	65[a]	0.2	88

[a]MW (100 W). [b]Determined after purification. [c]Optimal conditions.

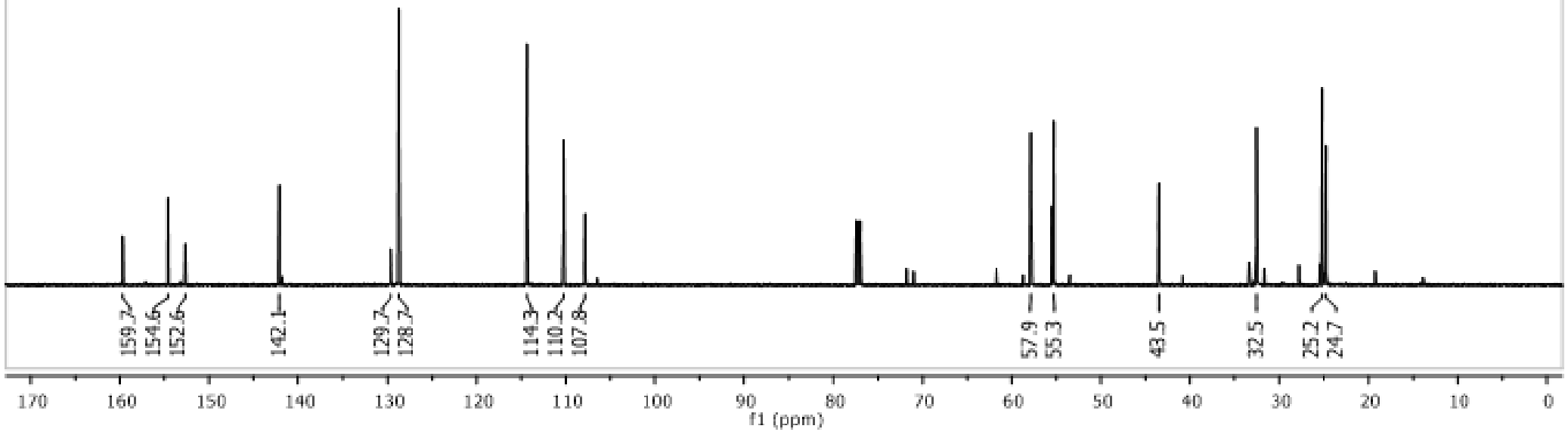
Spectrum NMR-^{1}H



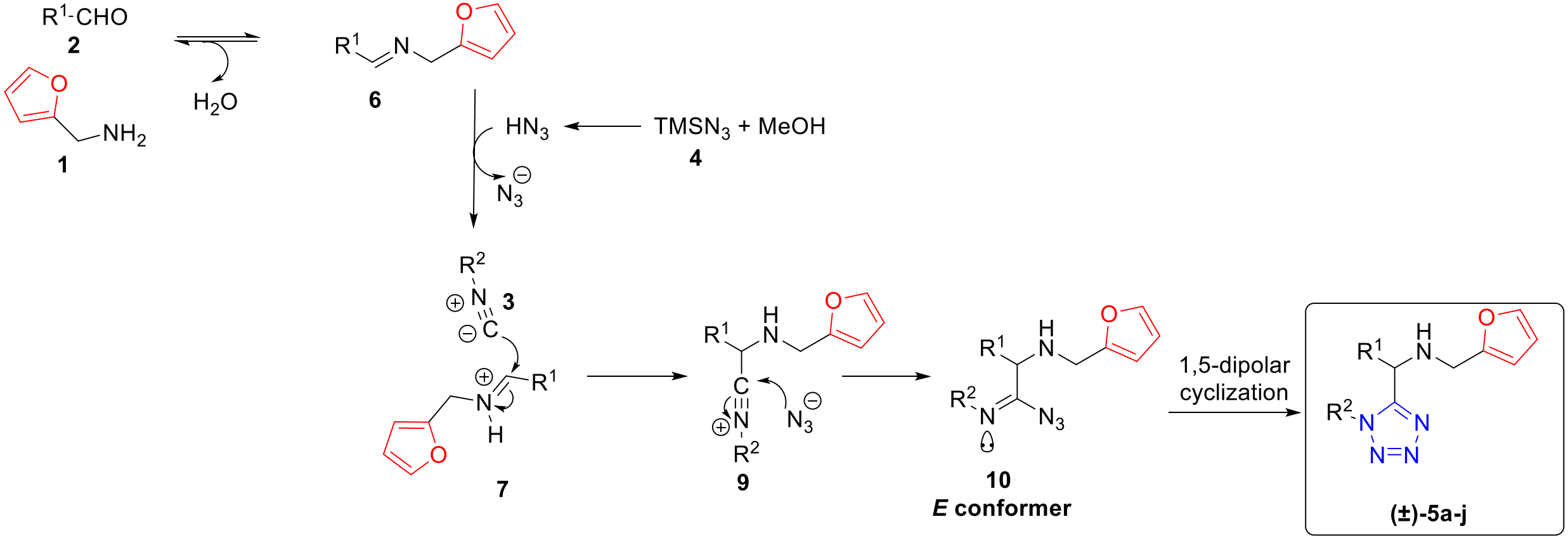




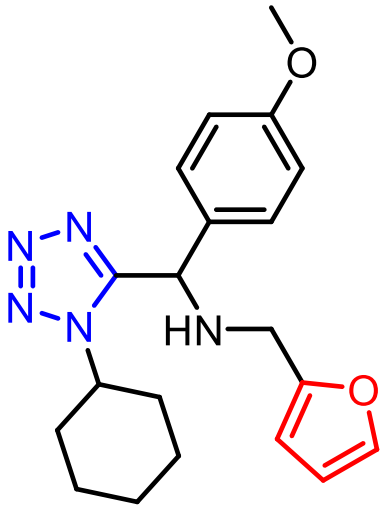
Spectrum NMR-^{13}C



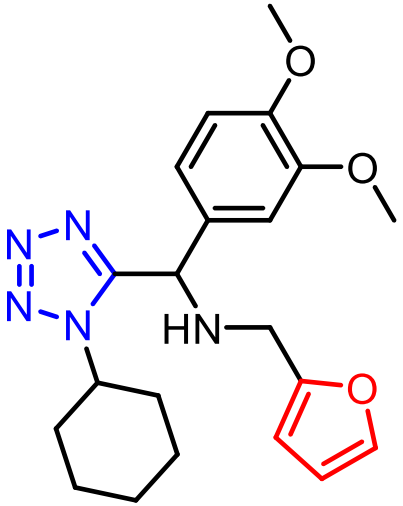
Plausible Mechanism reaction



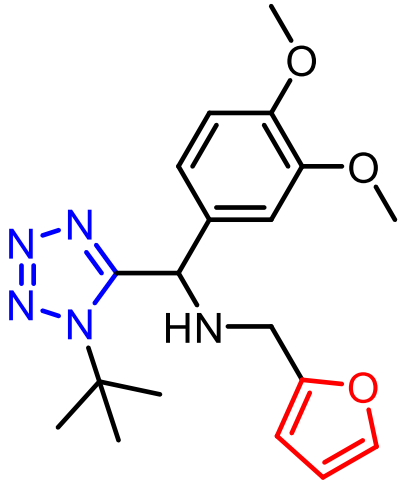
Substrate Scope.



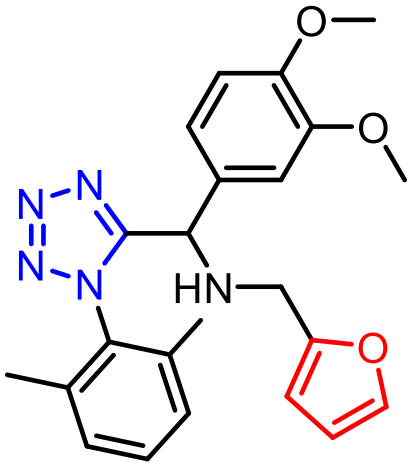
(±)-**5a**
99%



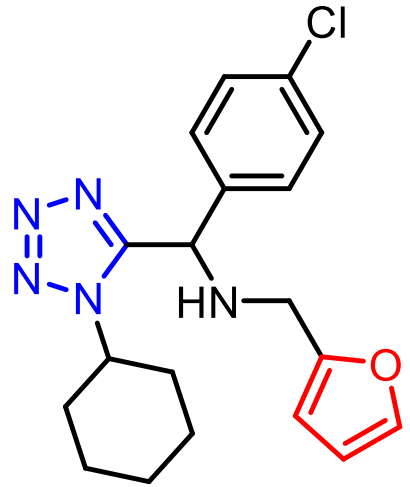
(±)-**5b**
86%



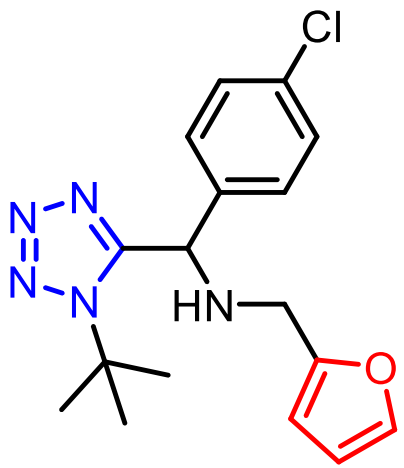
(±)-**5c**
82%



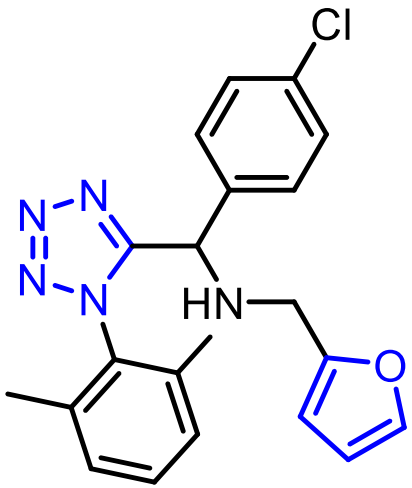
(±)-**5d**
79%



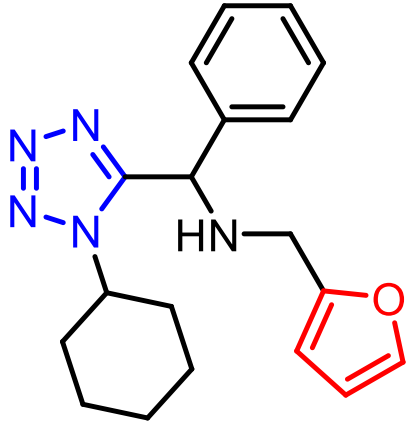
(±)-**5e**
95%



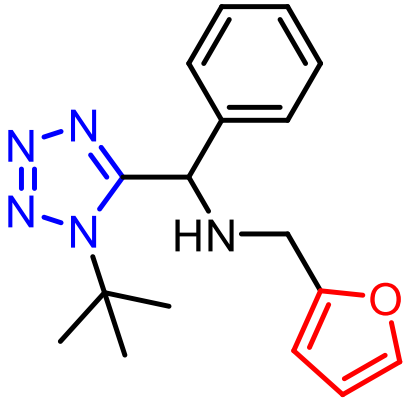
(±)-**5f**
90%



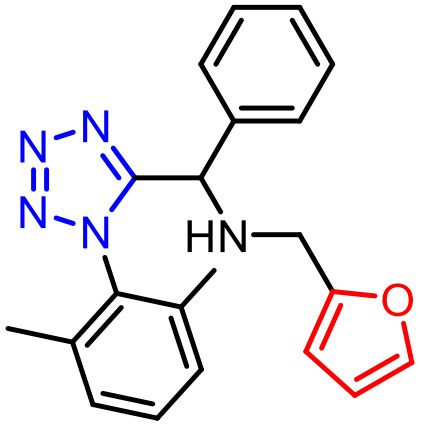
(±)-**5g**
85%



(±)-**5h**
92%



(±)-**5i**
86%



(±)-**5j**
80%

Conclusions

In this work, we report the first methodology for the synthesis of the bis-heterocycles type spacer (±)-**5a-j** containing 1,5-DS-T and highly functionalized furan scaffolds via Ugi azide I-MCR. This high functionalization of furan has ultimately increased the complexity of the synthesized compounds.

Acknowledgements

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