Ugi - Smiles

Universidad Nacional Autónoma de México

Facultad de Química

Maestría en Ciencias Químicas

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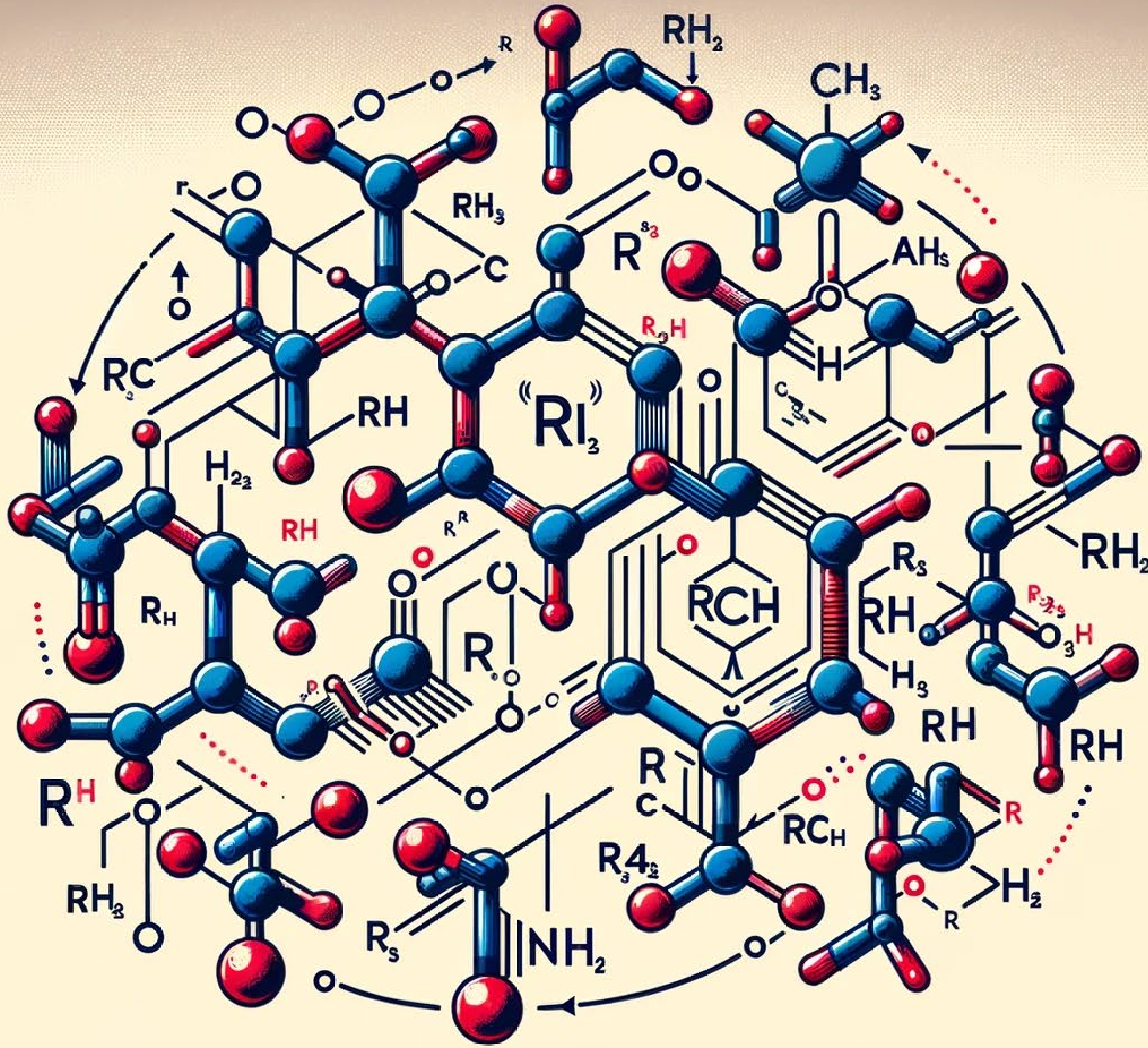
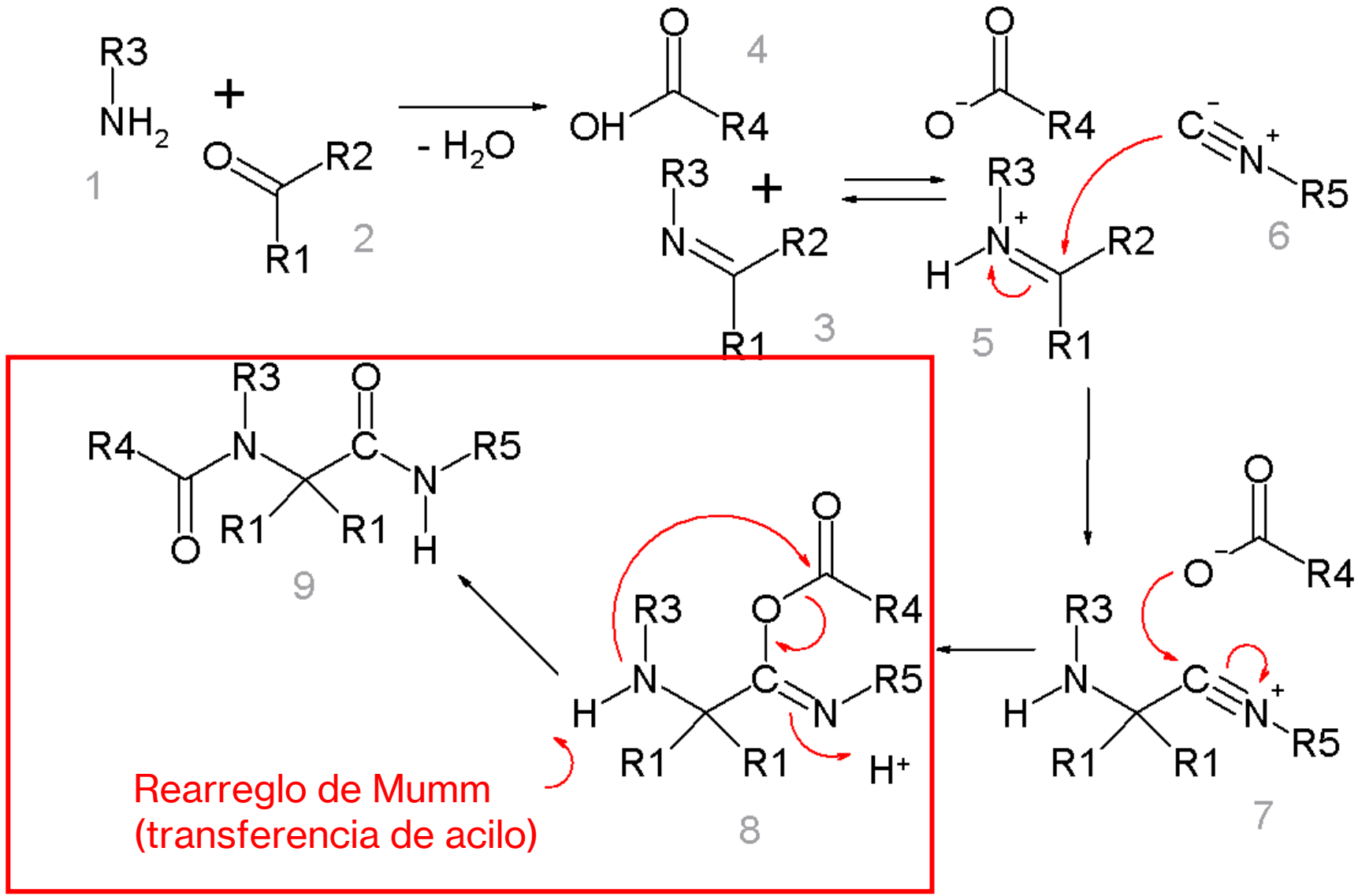
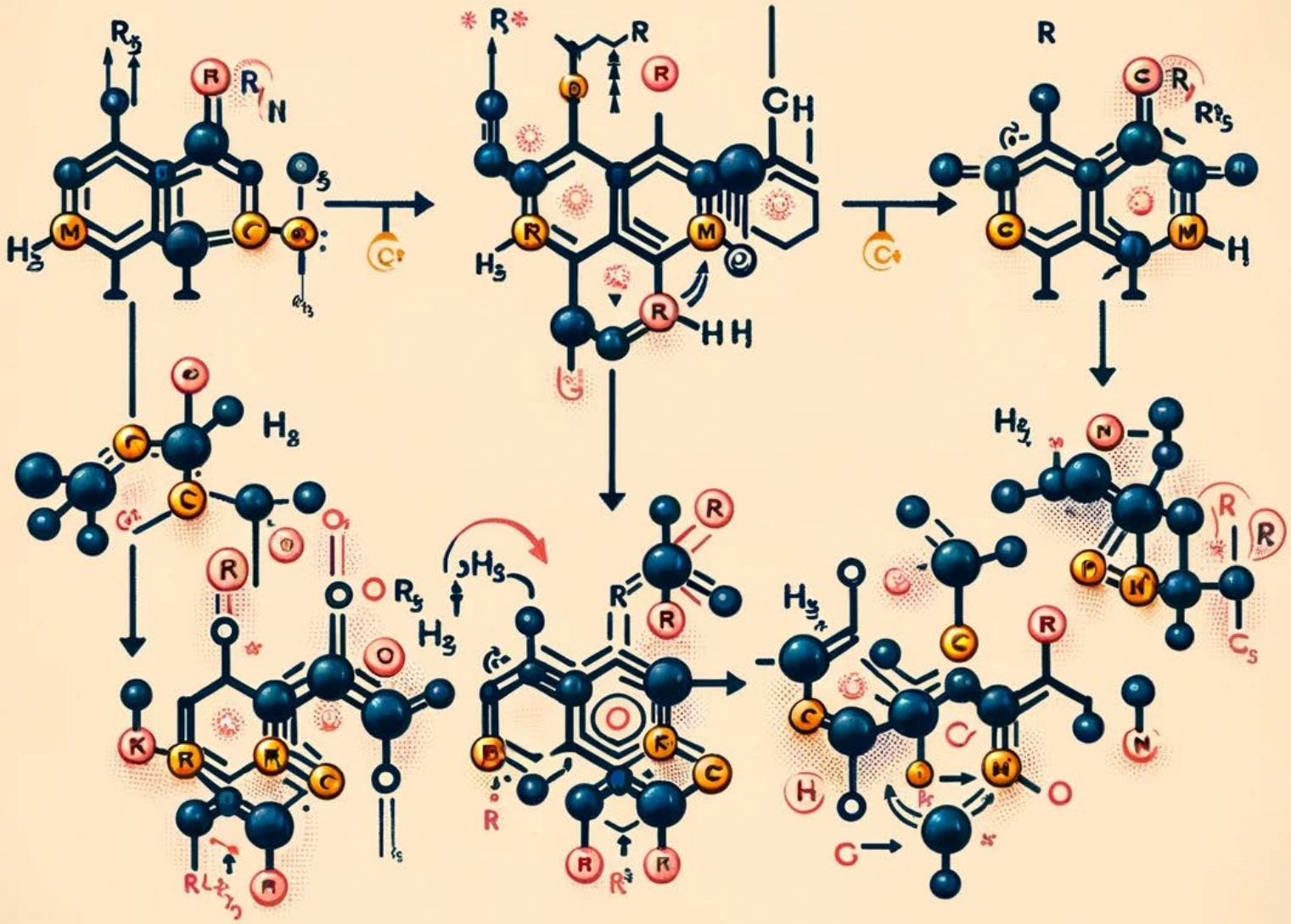

CH3
RH2
RH
RCH
RH2
RH
RH
NH2
RCH

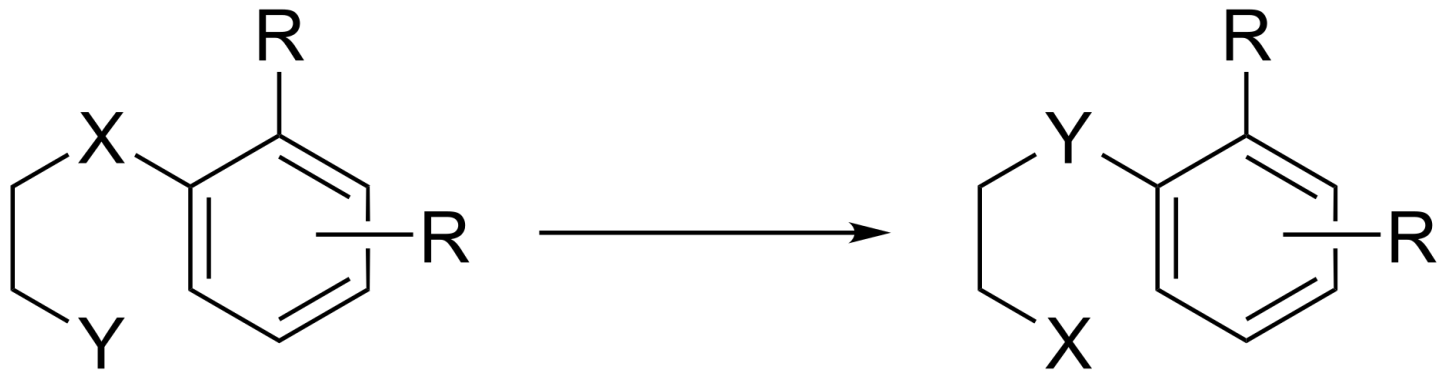
Reacción de Ugi




SMILES REARRANGENMENT

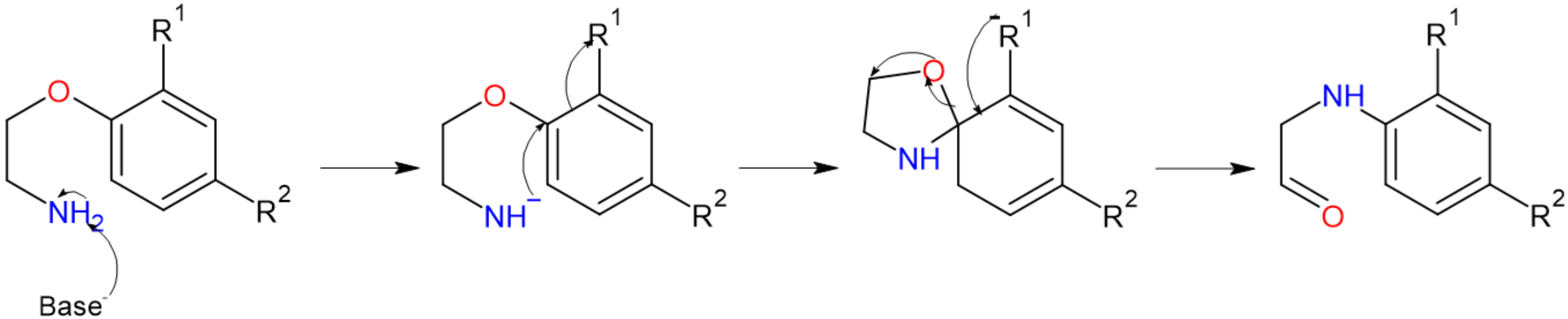
Reordenamiento de Smiles

El reordenamiento de Smiles es una sustitución nucleofílica aromática intramolecular en la cual el nucleófilo (Y) desplaza a un buen grupo saliente (X).

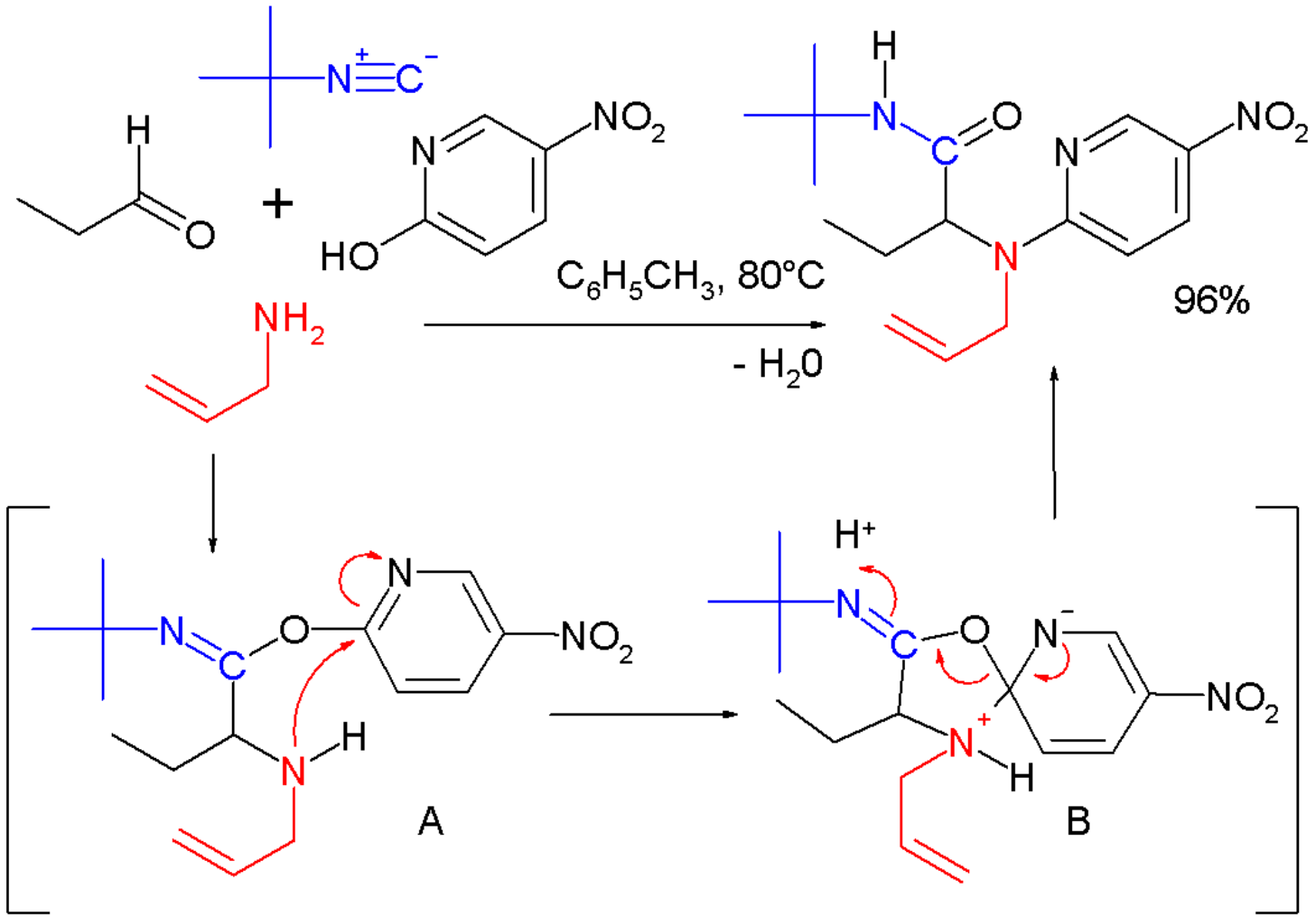


X= S, SO, SO_2, O, CO_2
Y= OH, NHR, SH

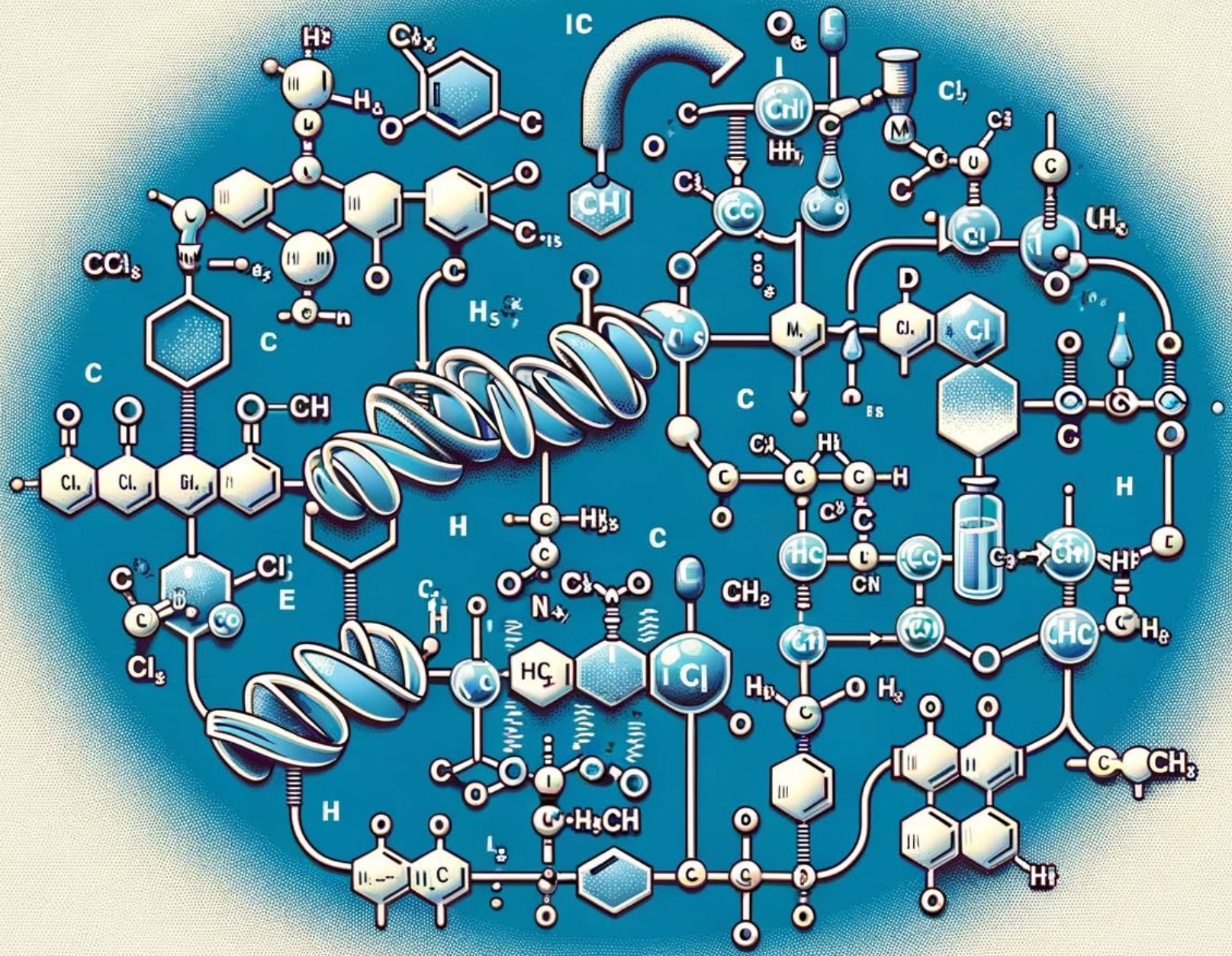
Mecanismo



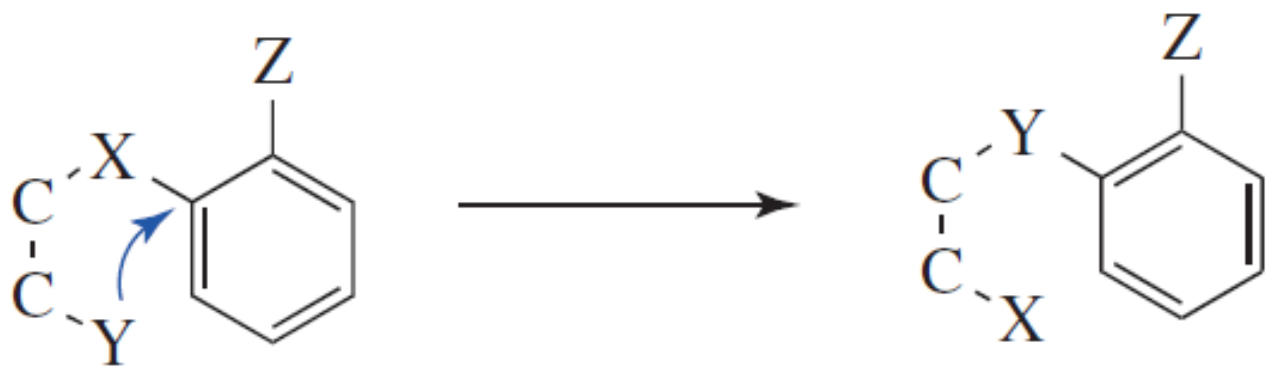
Acoplamiento Ugi - Smiles



Direct Access to Heterocyclic Scaffolds by New Multicomponent Ugi–Smiles Couplings
Laurent El Kaim, Marie Gizolme, Laurence Grimaud, and Julie Oble
Organic Letters **2006** *8* (18), 4019-4021
DOI: 10.1021/ol061605o



Mumm vs Smiles

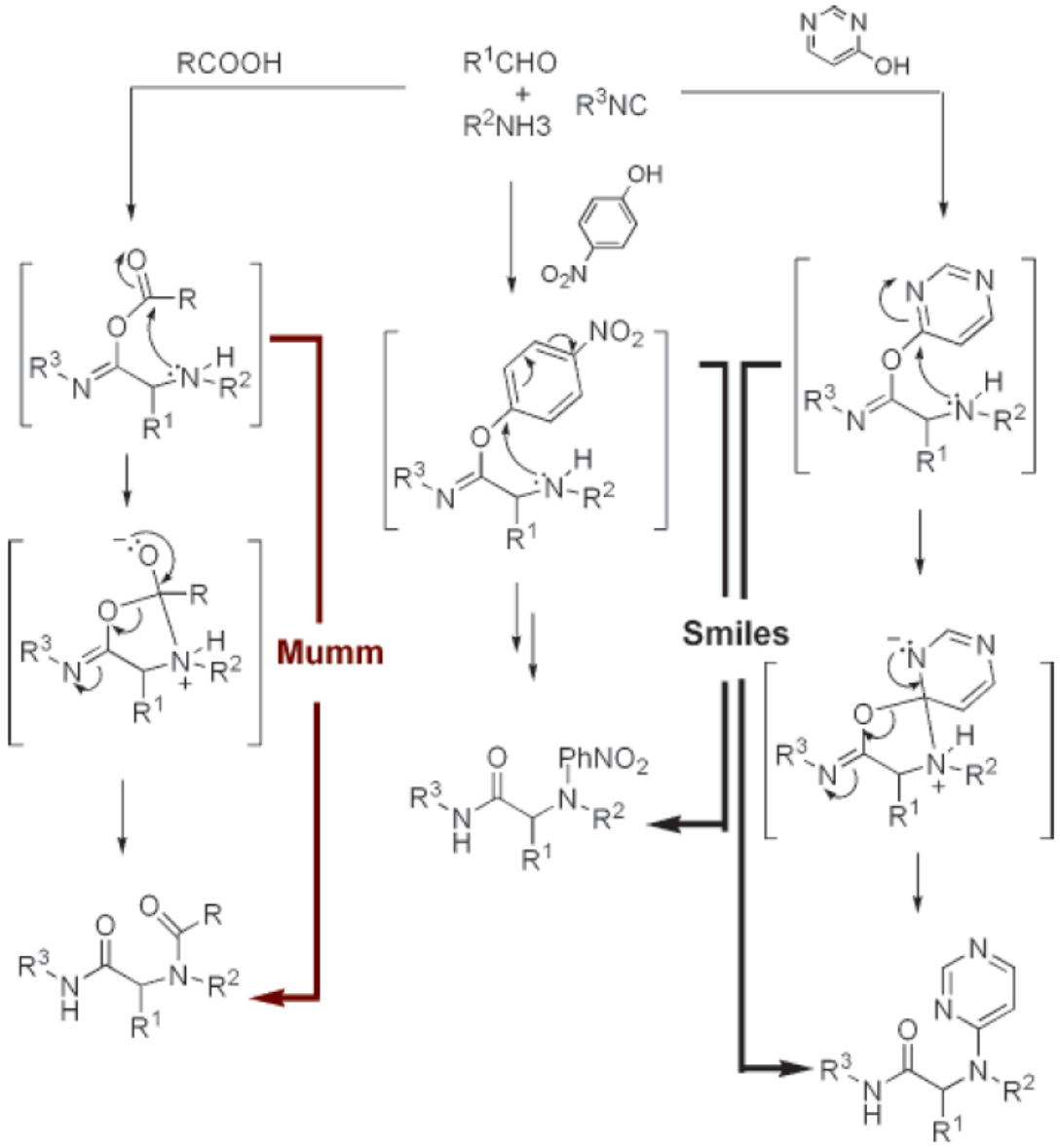


Mumm

vs

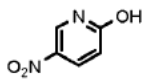
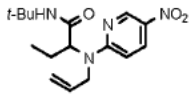
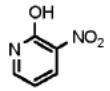
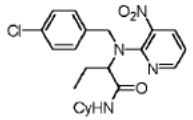
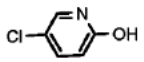
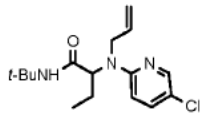
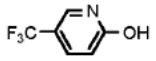
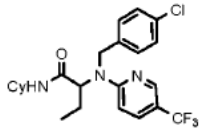
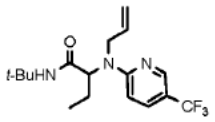
Smiles

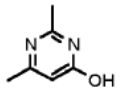
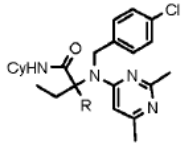
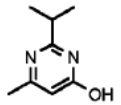
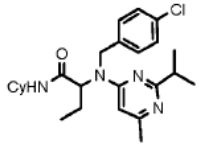
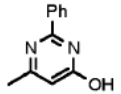
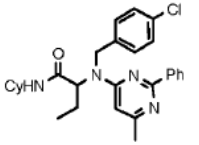
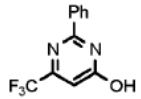
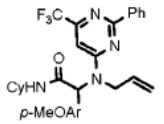
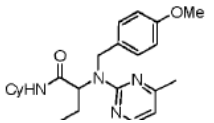
Scheme 2. Smiles vs Mumm Rearrangements in Ugi Processes



Pruebas con sustituyentes

Table 1. Heteroaromatic Phenol Ugi−Smiles Coupling

entry	phenol	product	yield (%)[a]	pKa
1			96	7.37
2			62	7.40
3			54[b]	9.69
4			44[b]	9.58
5			58[b]	

				pKa
6			A: (R=H) 78 B: (R=Me) 54	9.04
7			63	8.98
8			89	8.82
9			51[c]	8.91
10			38[d]	

Importancia

- Generar mayor diversidad de moléculas para aumentar el tamaño de la biblioteca

- El uso de heterociclos, sustancias de interés por su importancia en el diseño de compuestos con actividad biológica:
  - Agentes terapéuticos para el tratamiento de enfermedades inflamatorias (asma, artritis reumatoide, etc), cáncer y epilepsia entre otros.

- Su posible uso para la formación de tioamidas que serían difíciles de obtener por otros métodos.