

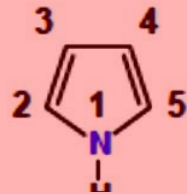
**COMPUESTOS  $\pi$  EXCESIVOS  
NO BÁSICOS  
FURANO, PIRROL Y TIOFENO  
INDOL Y BENZOFURANO**



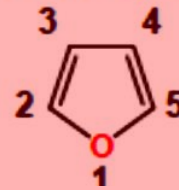
# Classification – Aromatic Five-Membered

Isoelectronic carbocycle

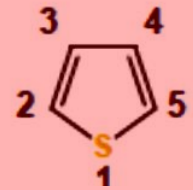
Heterocycles



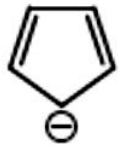
Pirrol



Furano



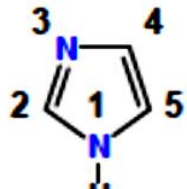
Tiofeno



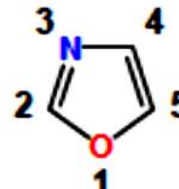
Anión ciclopentadienilo

6 electrones  $\pi$

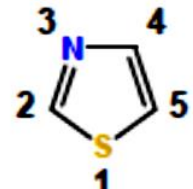
5 átomos



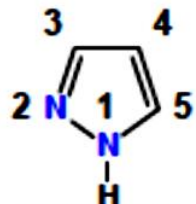
Imidazol



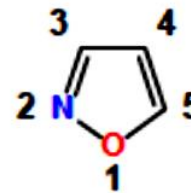
Oxazol



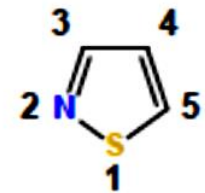
Tiazol



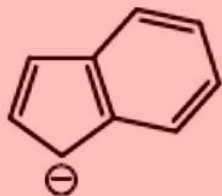
Pirazol



Isoxazol



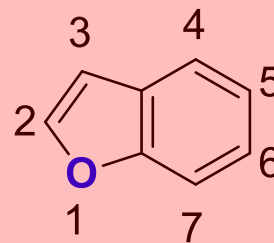
Isotiazol



Anión del indeno



Indol

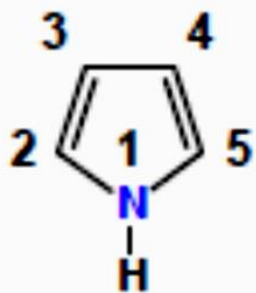


Benzofurano

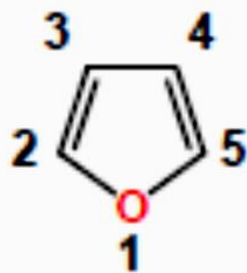
Anión del indeno  
Indol y benzofurano

10 electrones  $\pi$

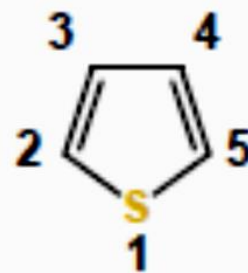
9 átomos



Pirrol

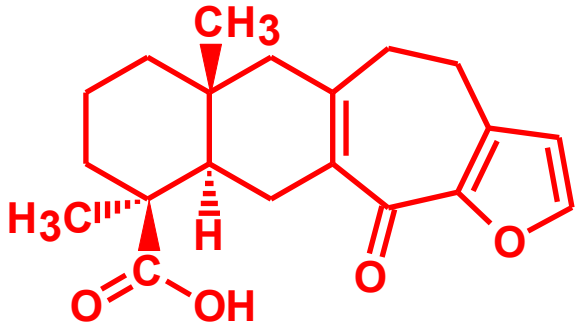


Furano



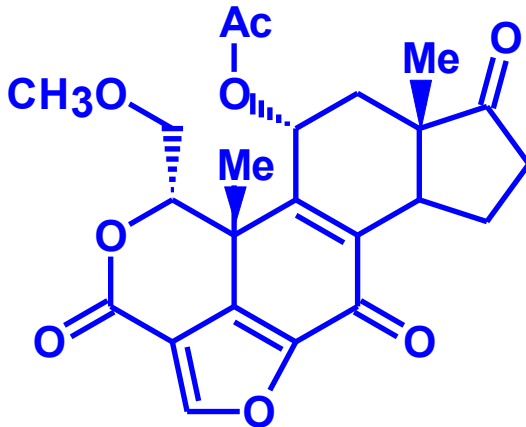
Tiofeno

## DERIVADOS DEL FURANO. PRODUCTOS NATURALES



### ÁCIDO HISPANOÍCO

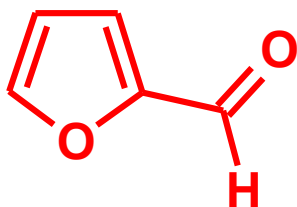
Aislado de la *ballota hispanica*, una planta que crece en españa



### WORTMANINA

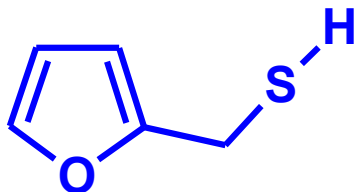
Antibiótico, antifungicida que se obtiene de la *penicillium wortmanni*

## DERIVADOS DEL FURANO. PRODUCTOS NATURALES



Aldehído del salvado (del latín *furfur*, salvado)

**FURFURAL**



Es uno de los compuestos responsables del aroma del café tostado

**FURILTOL**

Es uno de los terpenoides, un metabolito de las plantas

## DERIVADOS DEL FURANO. PRODUCTOS NATURALES



**ÁCIDO ASCÓRBICO**  
**(VITAMINA C)**

El enantiómero L (levógiro) de este ácido comúnmente se conoce como vitamina C. El nombre "ascórbico" proviene del prefijo *a-* ("sin") y del latín *scorbuticus* ("escorbuto"), procede de su propiedad de prevenir y curar el escorbuto.

## PIRROL:

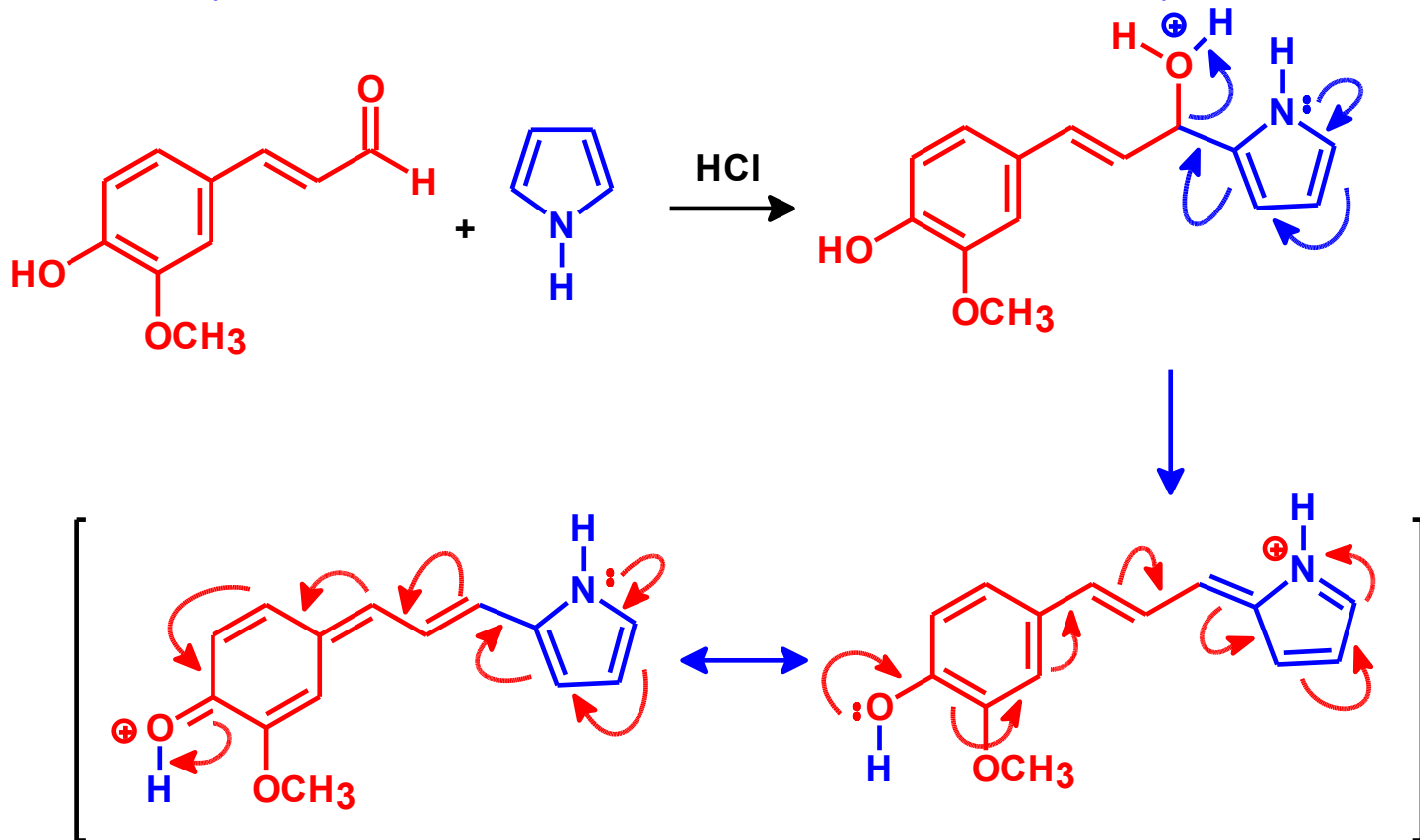
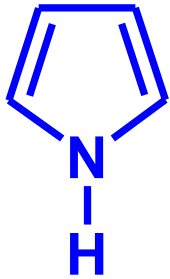
Se aisló por primera vez en 1857, de la pirólisis de huesos. La palabra deriva del griego *pûr*, πῦρ, 'fuego', 'fiebre' pyrr- πυρρός gr. (adj.), 'de color fuego'

Neologismos que usan el lexema

pirrol; pirrolina  
Lexemas que tienen la misma raíz pyr(o)- gr., 'fuego', 'fiebre'; pyret(o)- gr., 'fiebre'

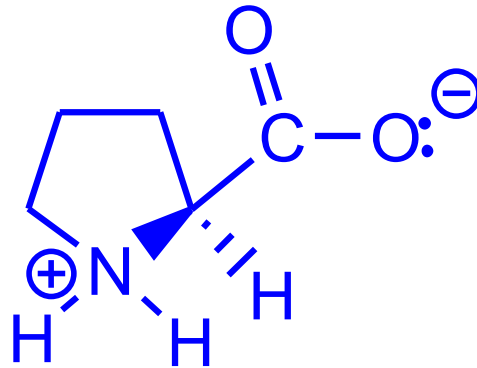
PYROS: ROJO

(ASTILLA DE PINO IMPREGNADA CON HCl)



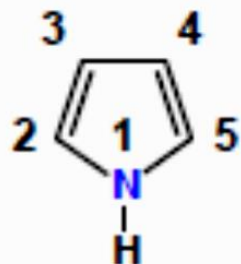
# DERIVADOS DEL PIRROL. PRODUCTOS NATURALES

La prolina, es un aminoácido con un grupo amino secundario dentro de un anillo de cinco miembros, con el nitrógeno y el carbono  $\alpha$  formando parte de la estructura cíclica

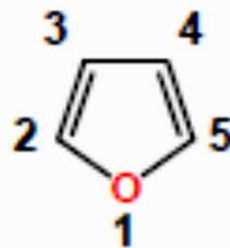


# MÉTODOS DE SÍNTESIS

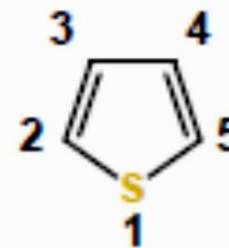
## ANILLOS HETEROCÍCLICOS DE 5 MIEMBROS CON UN HETEROÁTOMO



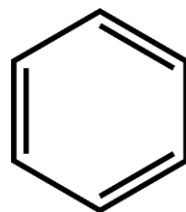
Pirrol



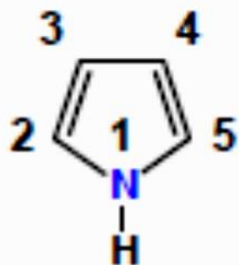
Furano



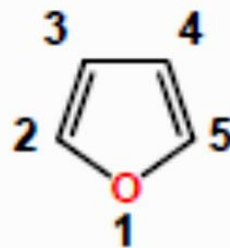
Tiofeno



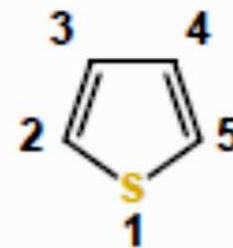
Benceno  
ER = 36 kcal/Mol



Pirrol  
ER = 21 kcal/Mol

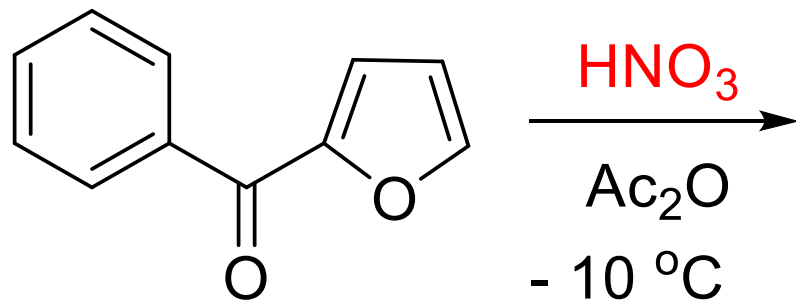


Furano  
ER = 16 kcal/Mol

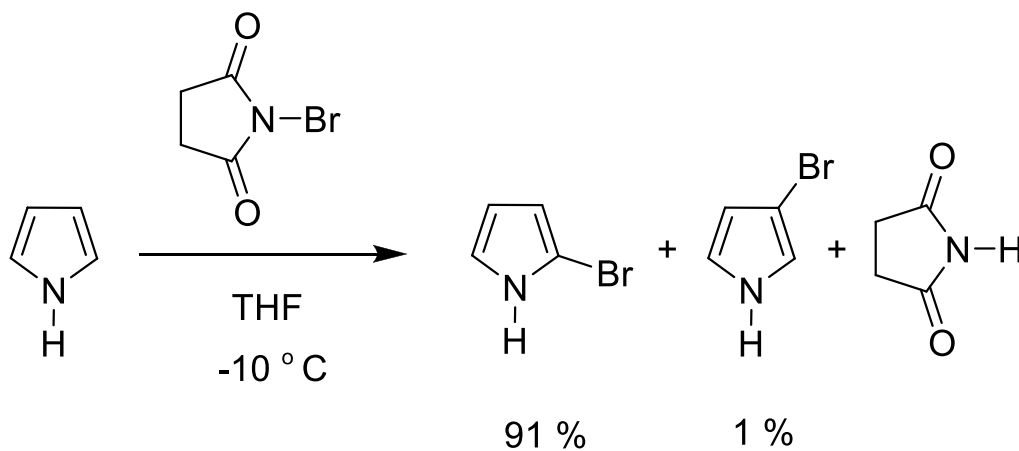
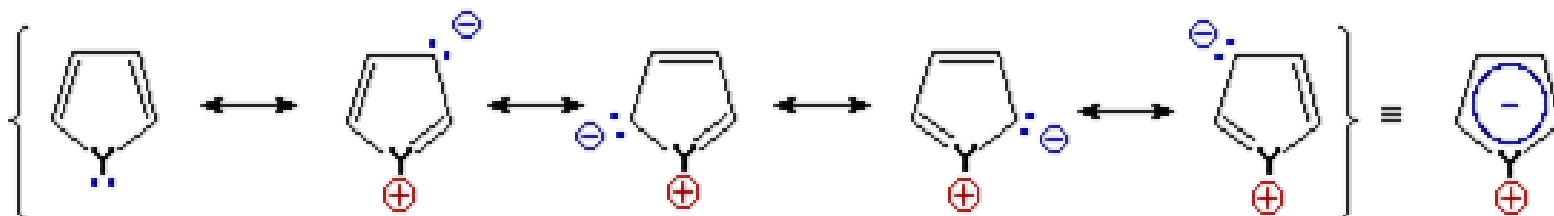


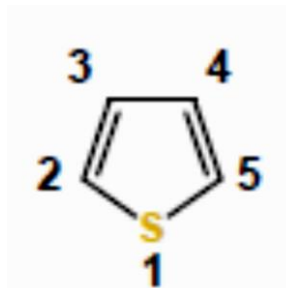
Tiofeno  
ER = 28 kcal/Mol



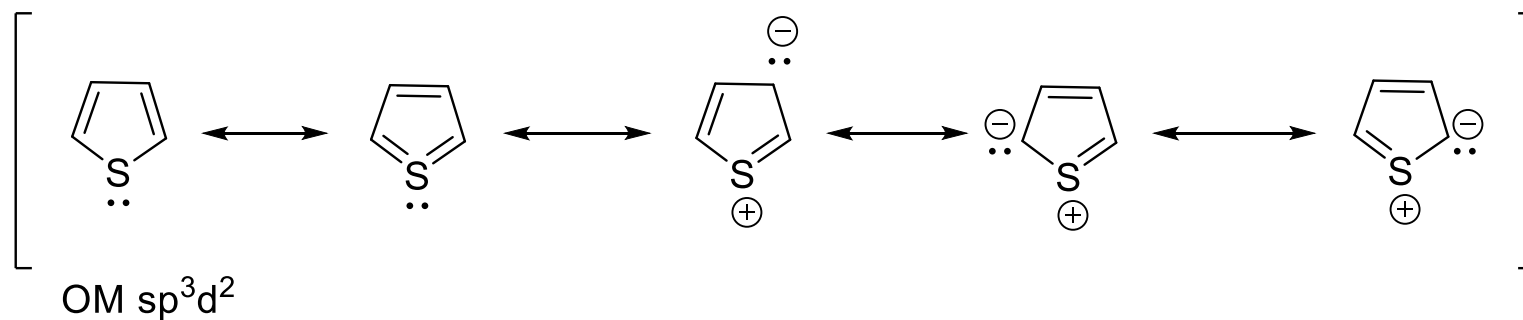
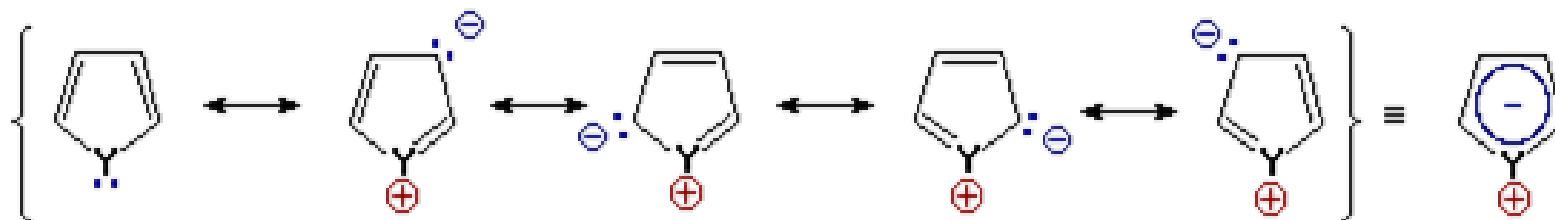


# COMPUESTOS $\pi$ -EXCESIVOS: FORMAS RESONANTES CON CARGA

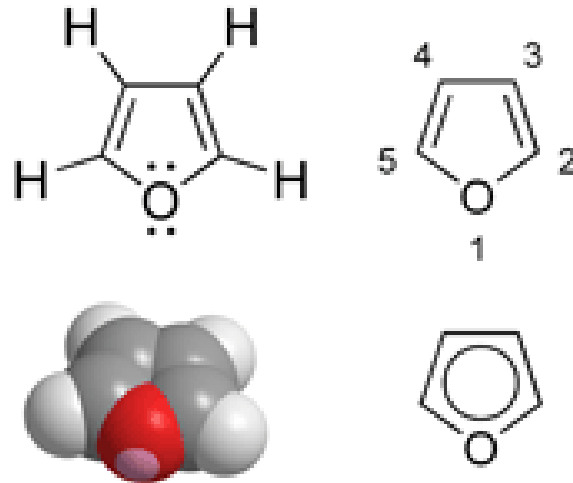


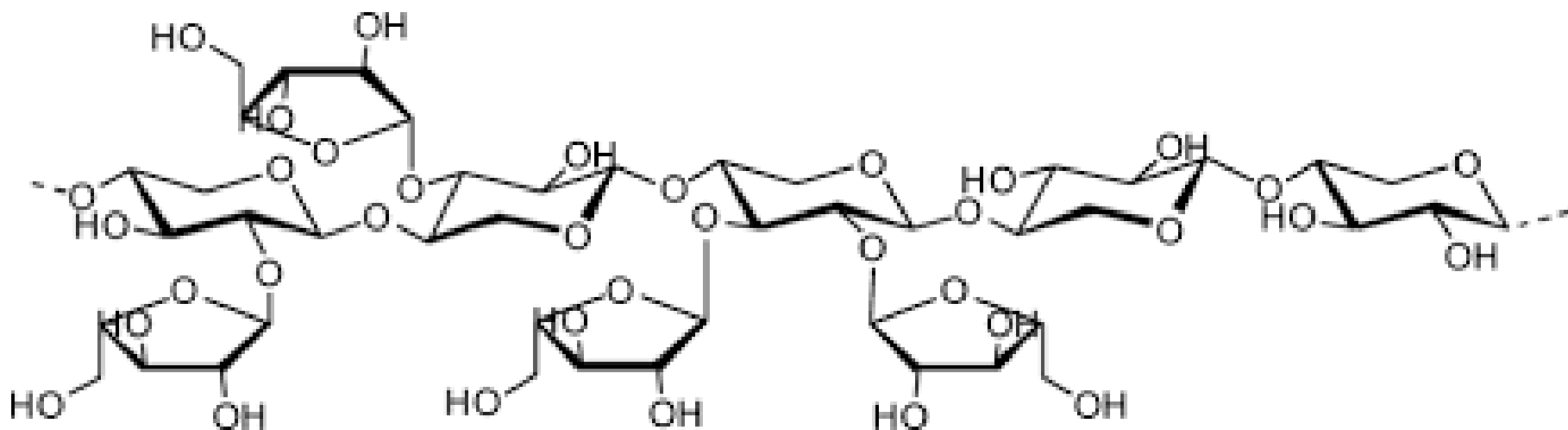


Tiofeno  
ER = 28 kcal/Mol



# FURANO

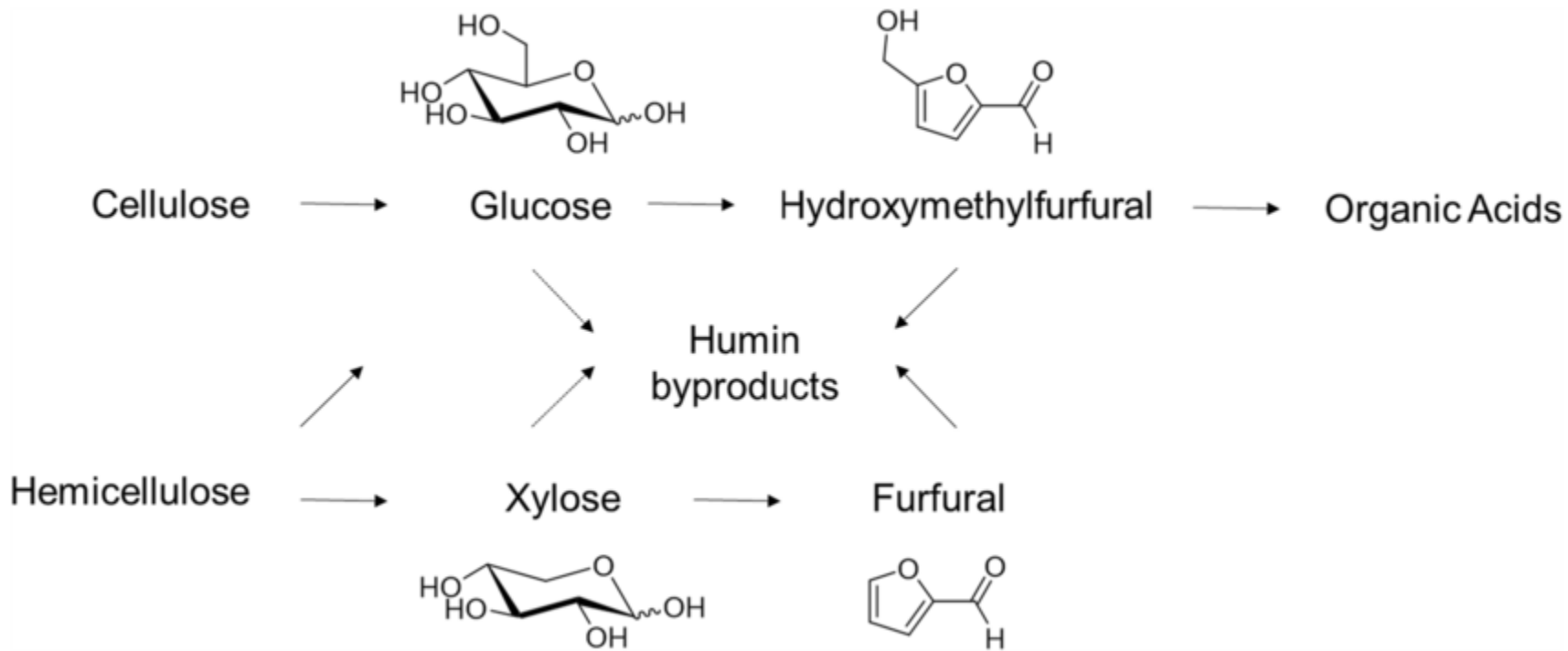




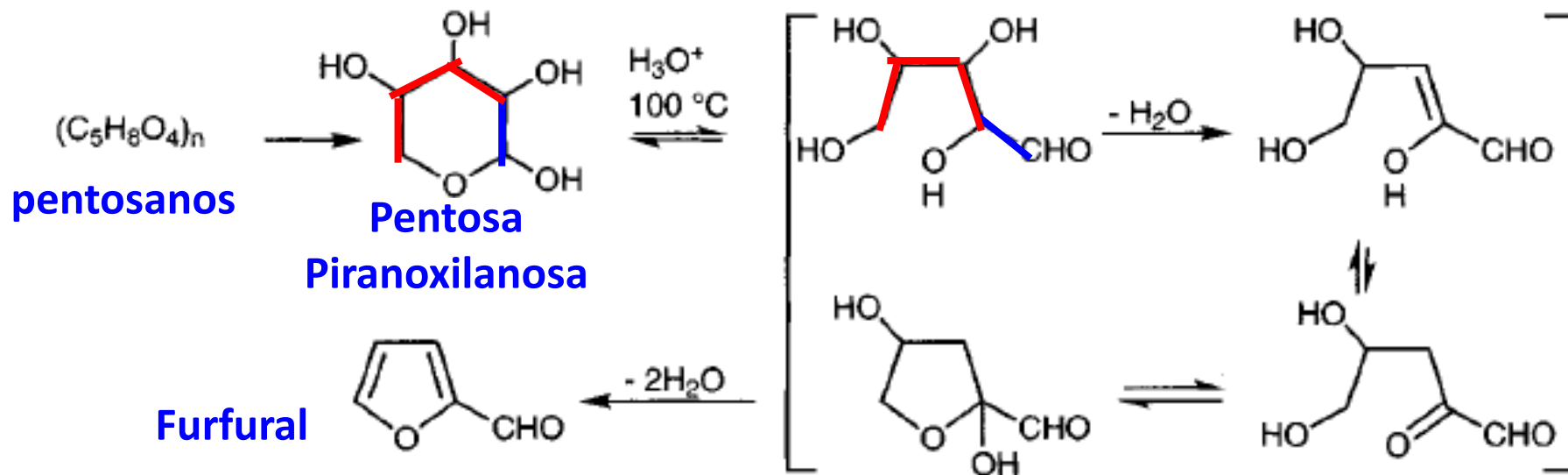
Estructura química parcial de un arabinoxilano pentosano: una estructura principal lineal de  $\beta$ -1,4-d-xilopiranosilo unida con cadenas laterales unidas aleatoriamente de  $\alpha$ -1-arabinofuranosilo en las posiciones 2 y/o 3 de la cadena de xilosa

Beckendorff, A., Lamp, A. & Kaltschmitt, M. Optimization of hydrolysis conditions for xylans and straw hydrolysates by HPLC analysis. *Biomass Conv. Bioref.* **2023**, *13*, 3361–3374.  
<https://doi.org/10.1007/s13399-021-01429-6>

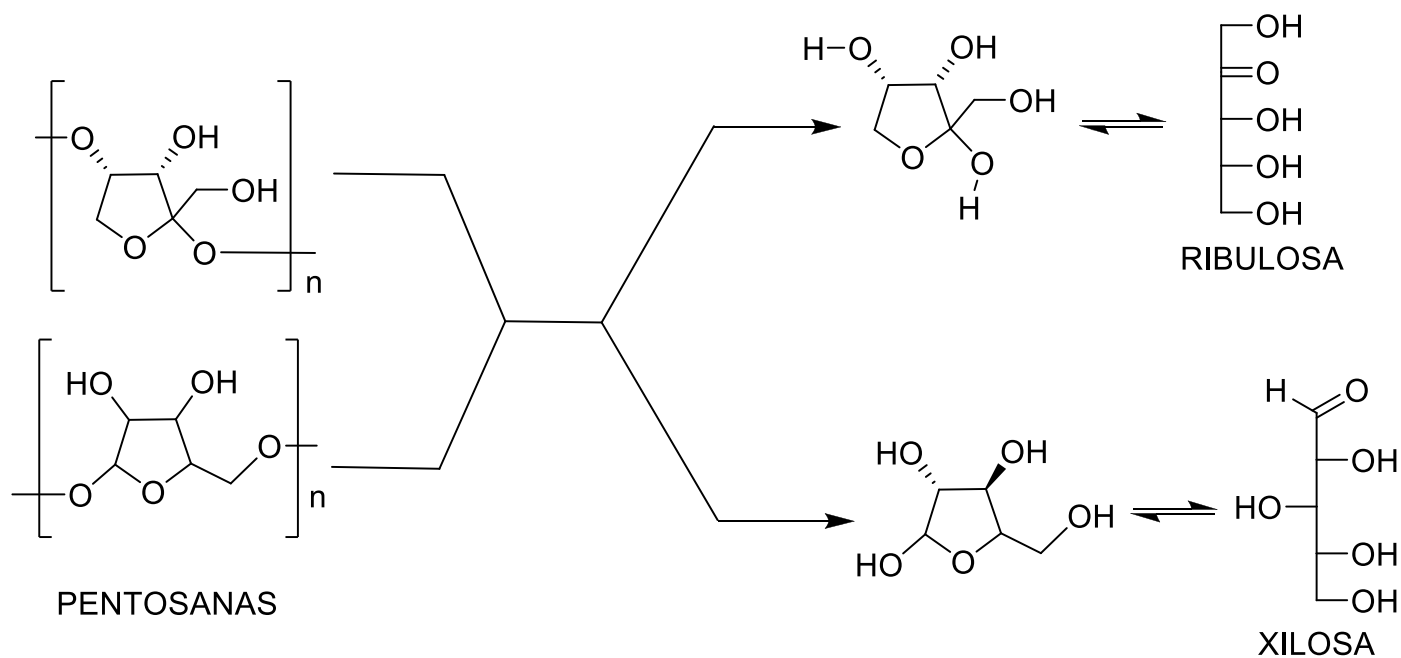
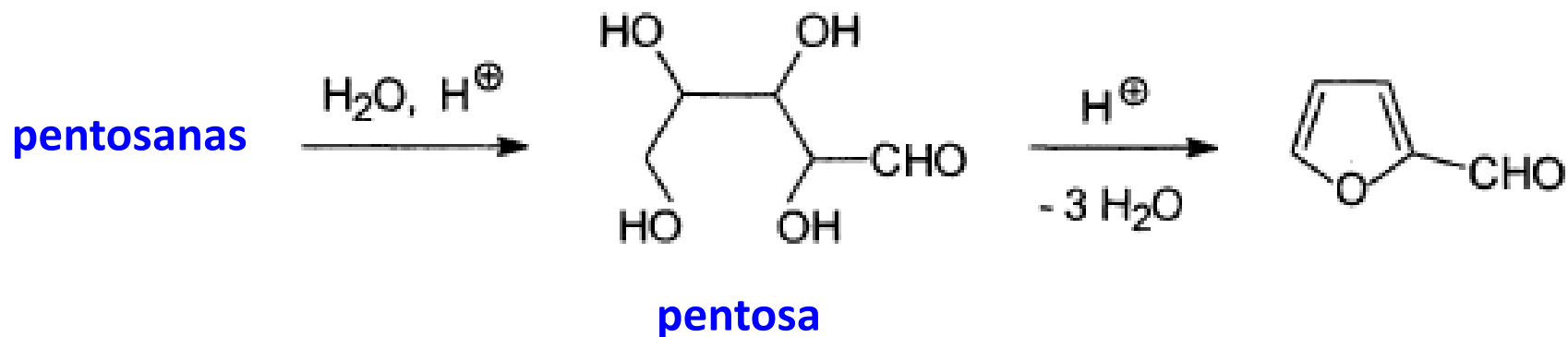




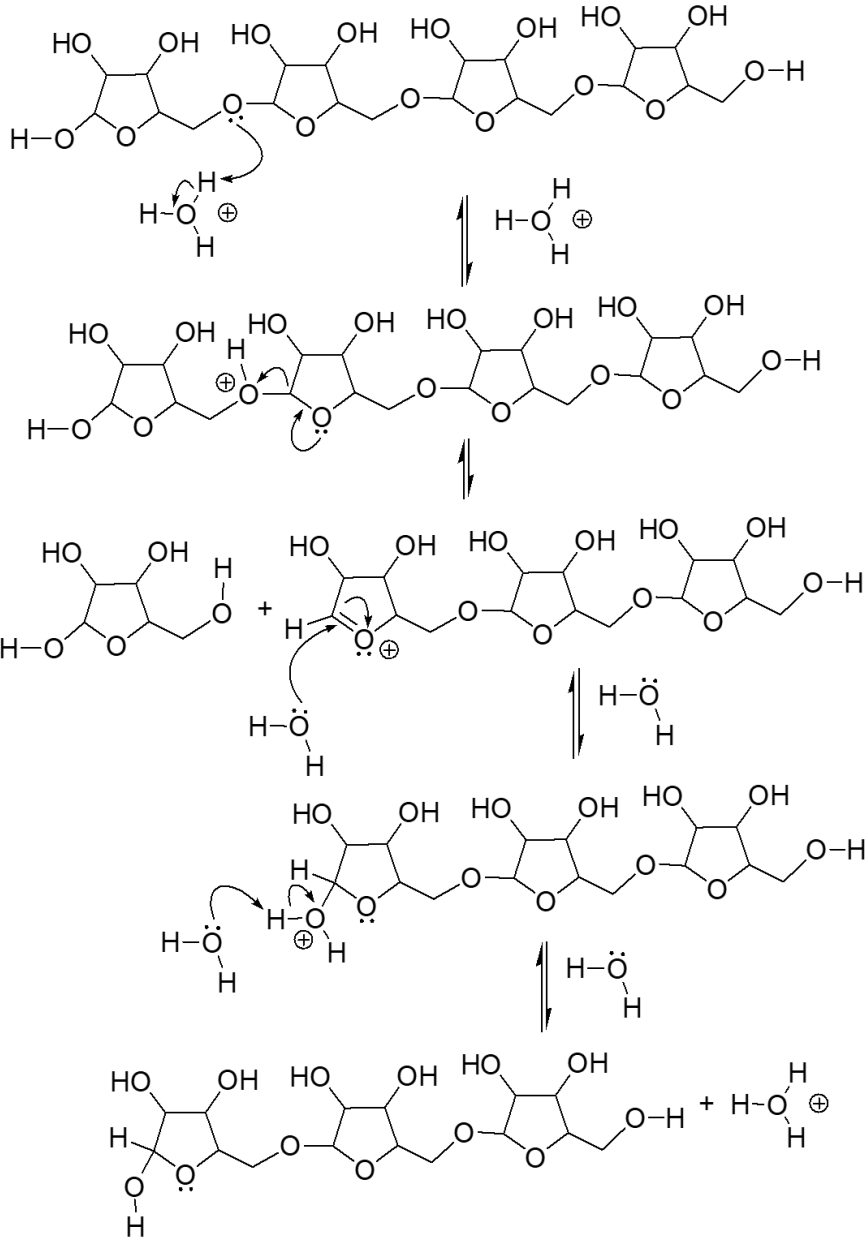
# MÉTODOS DE OBTENCIÓN DE FURANO

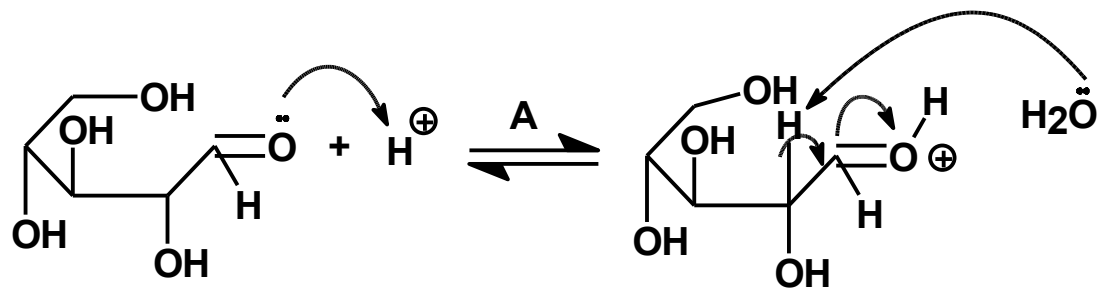


# DESHIDRATACIÓN DE AZÚCARES



HIDRÓLISIS DE UNA  
CADENA DE  
PENTOSANA DE  
n = 4

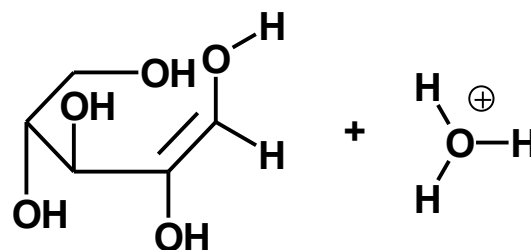
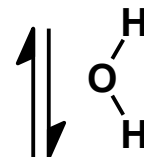




TAUTOMERO CETO

TAUTOMERO CETO  
PROTONADO

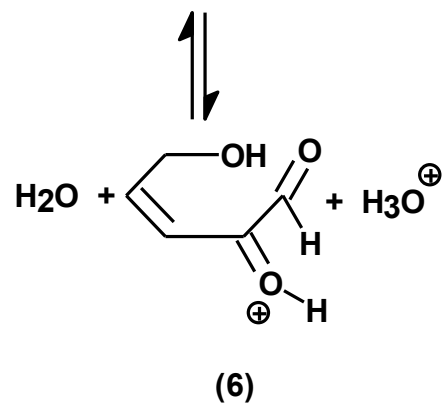
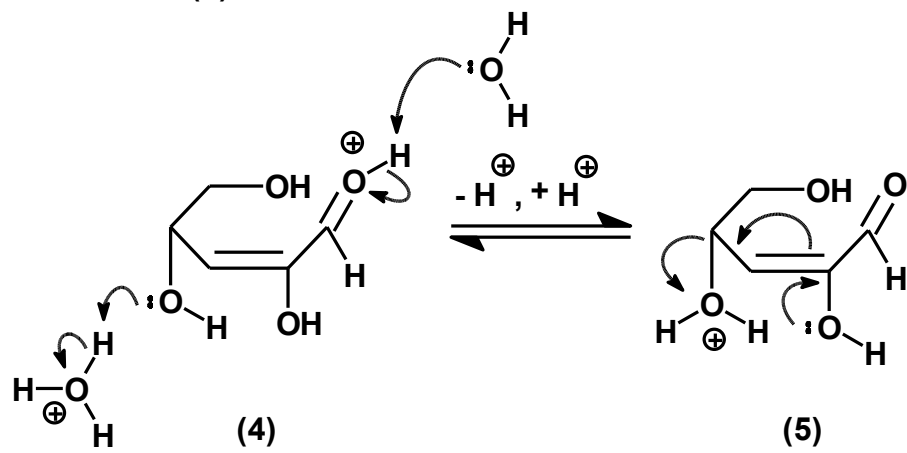
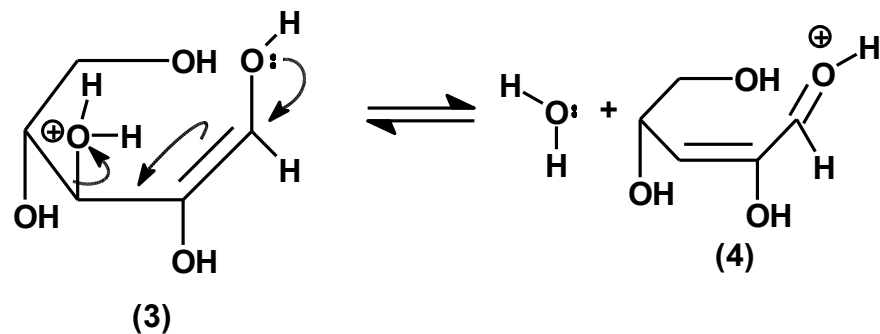
(1)

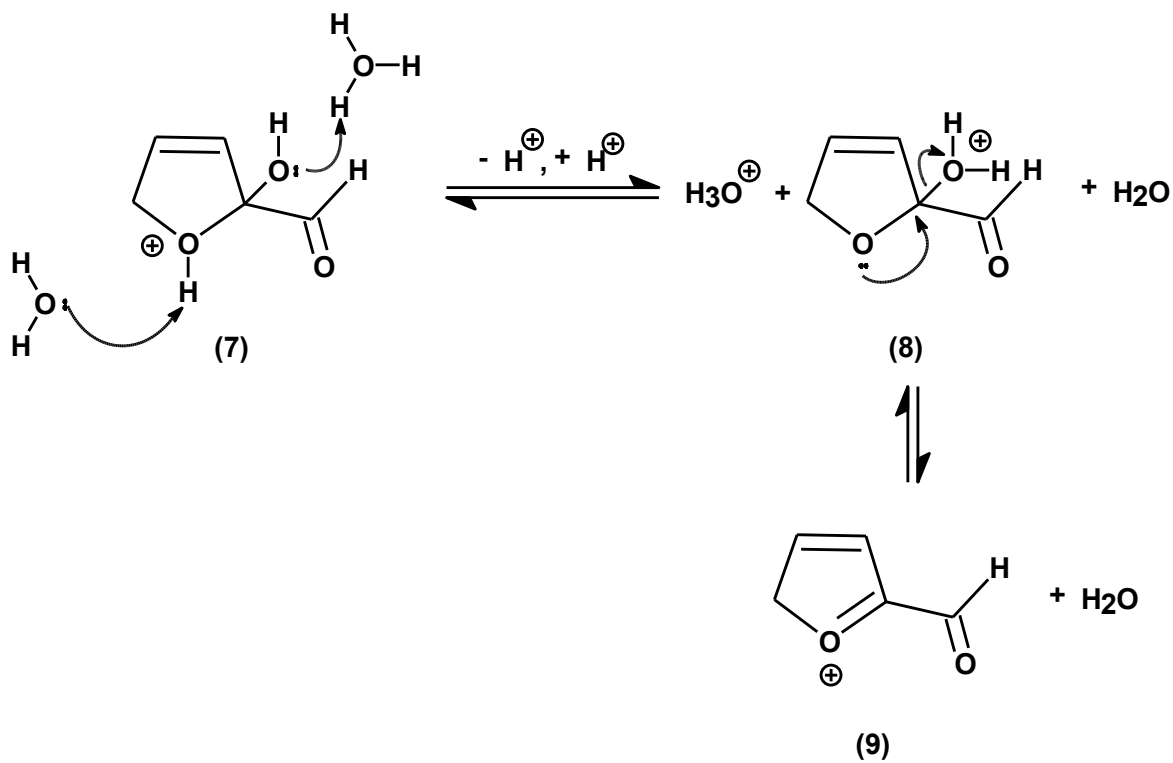
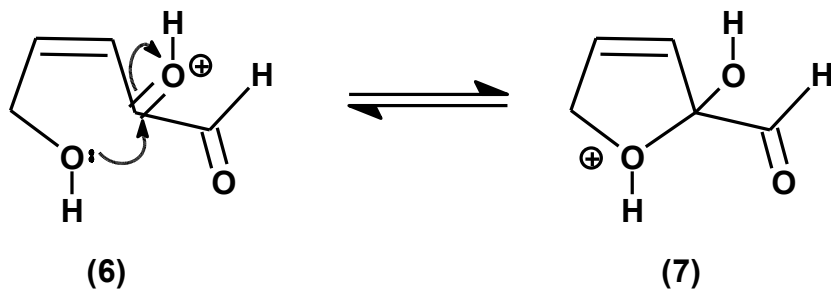


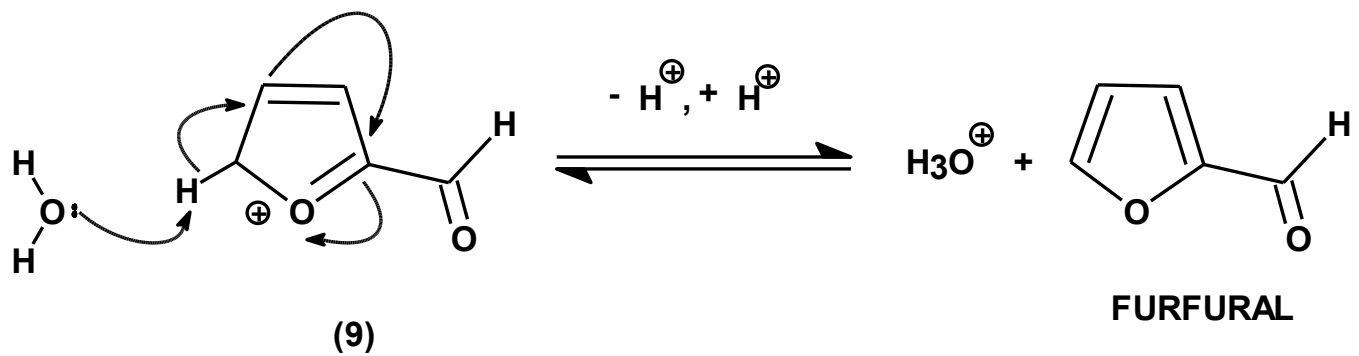
TAUTOMERO ENOL

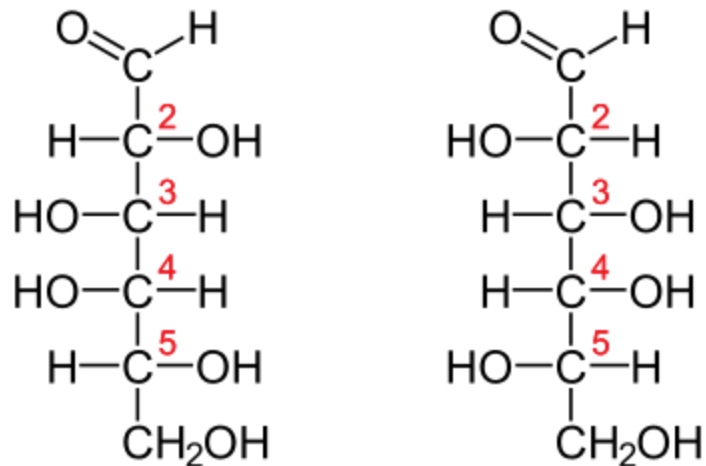
(2)





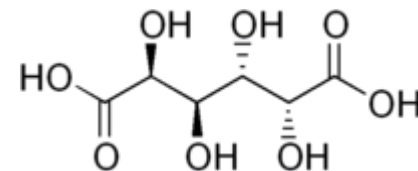




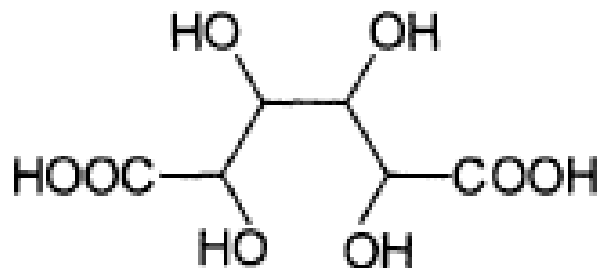


**D-GALACTOSA**

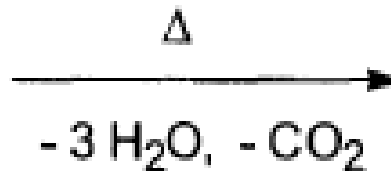
**L-GALACTOSA**



**Ácido mucico**  
**Ácido galactárico**



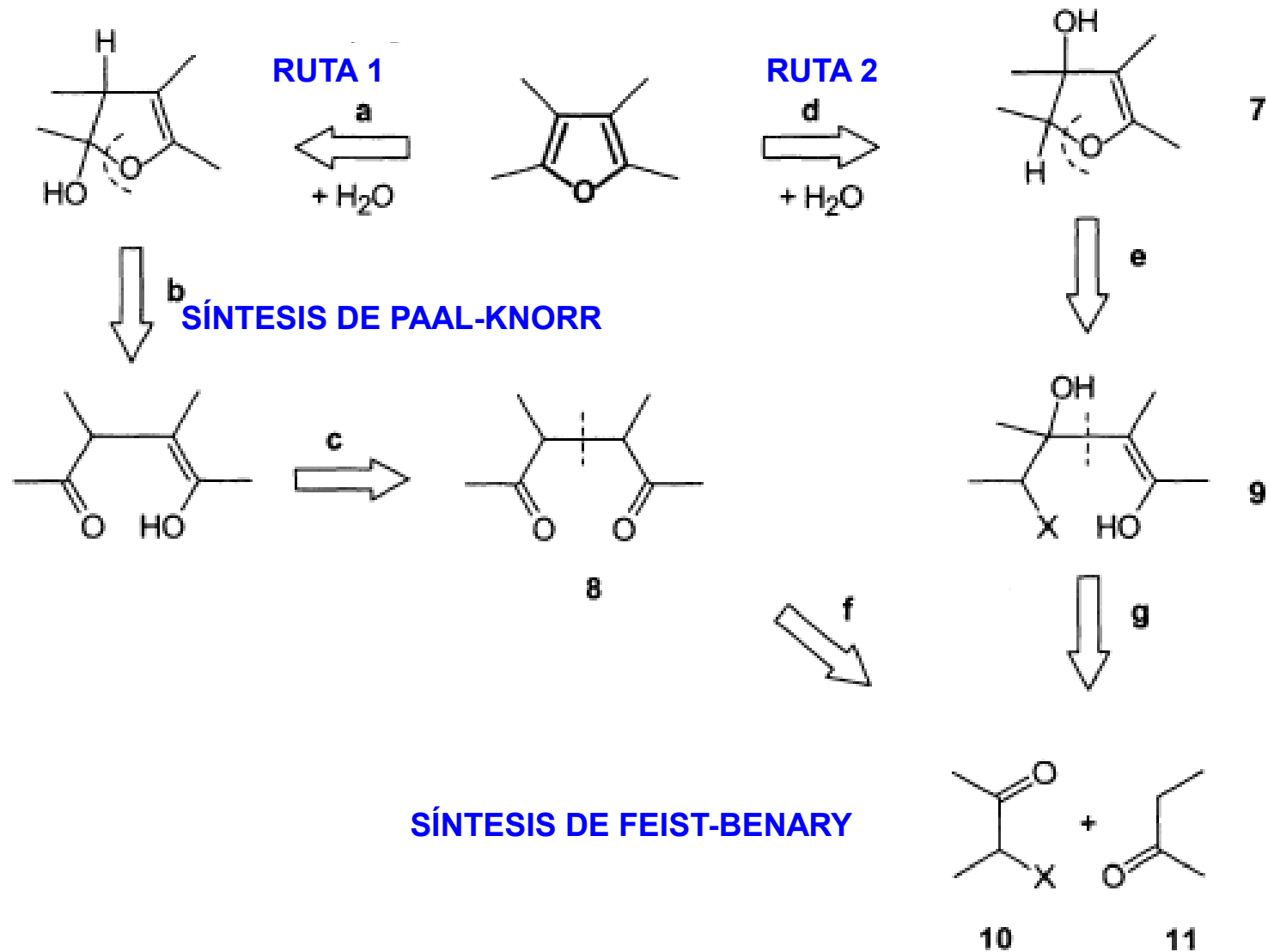
**Ácido mucico**



**Ácido piromúxico**  
**Ácido furoico**

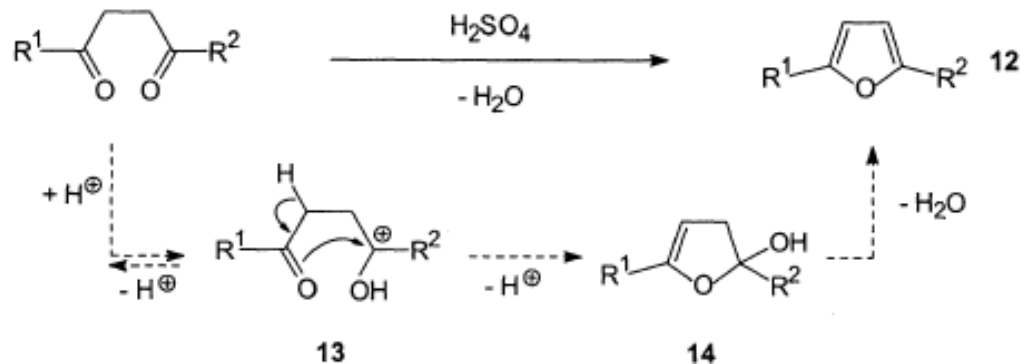


# MÉTODOS DE OBTENCIÓN DE FURANO

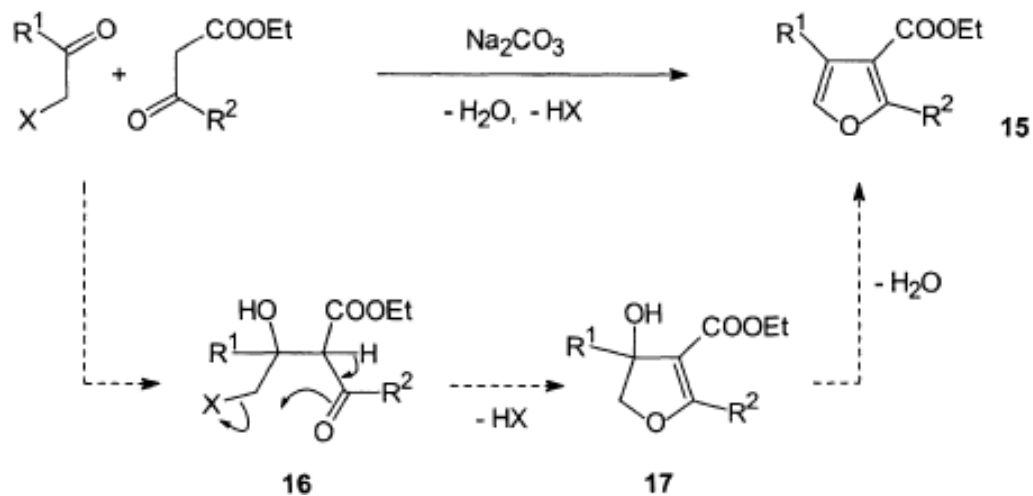


# MÉTODOS DE OBTENCIÓN DE FURANO

## SÍNTESIS DE PAAL-KNORR

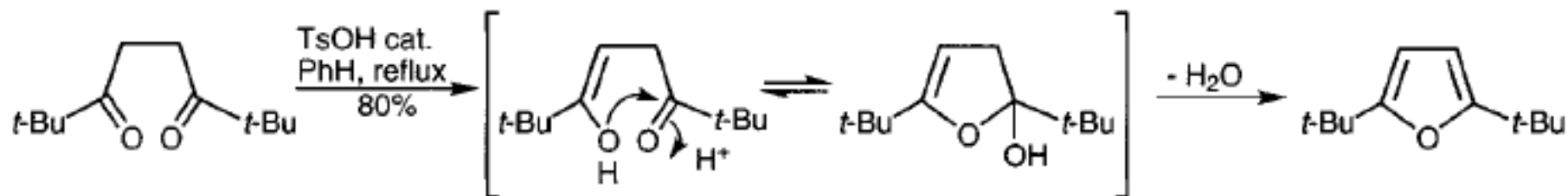


## SÍNTESIS DE FEIST-BENARY

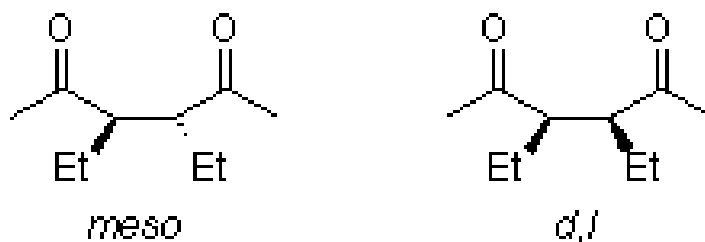


# MÉTODOS DE OBTENCIÓN DE FURANO

## SÍNTESIS DE PAAL-KNORR



### Mecanismo de la reacción

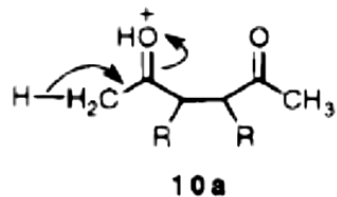


Intermediates in the Paal-Knorr Synthesis of Furans  
Venkataraman Amarnath, and Kalyani Amarnath  
*J. Org. Chem.*, **1995**, *60* (2),301–307

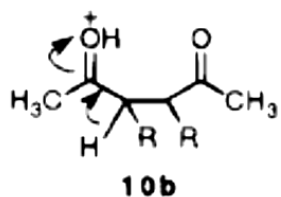




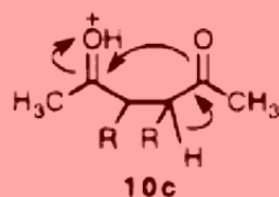
*pathway a*



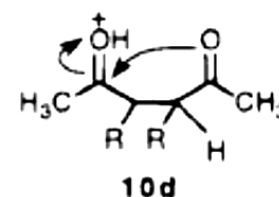
*pathway b*



*pathway c*



*pathway d*

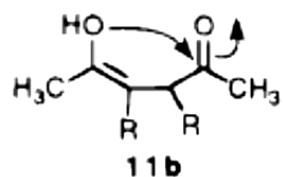
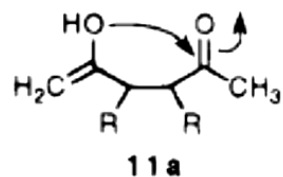


**10a**

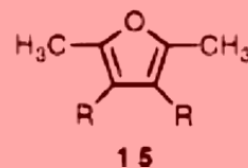
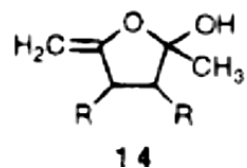
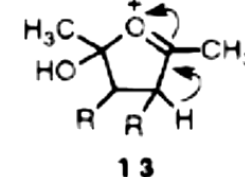
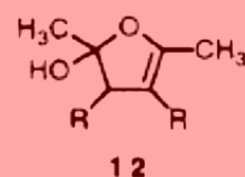
**10b**

**10c**

**10d**



slow

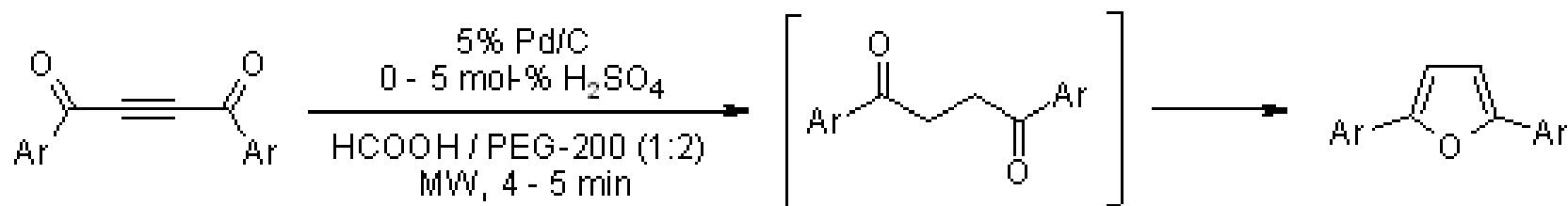
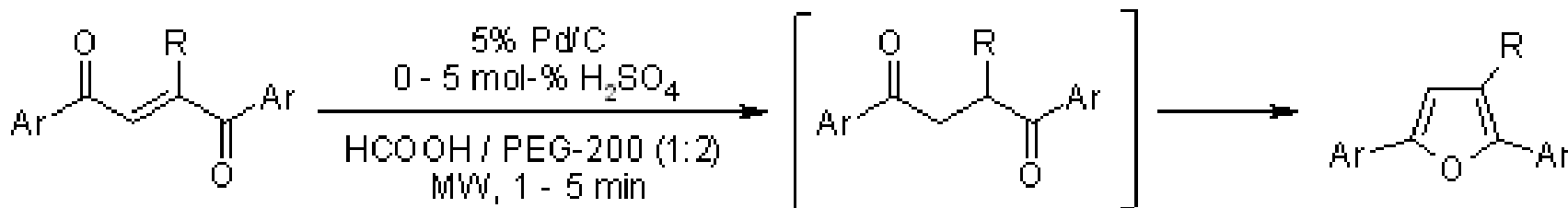


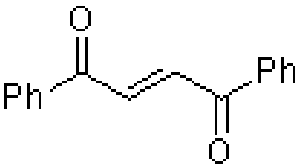
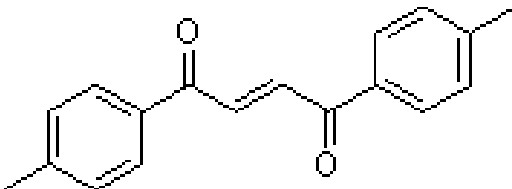
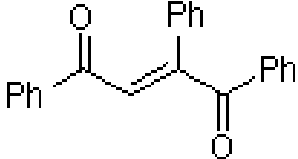
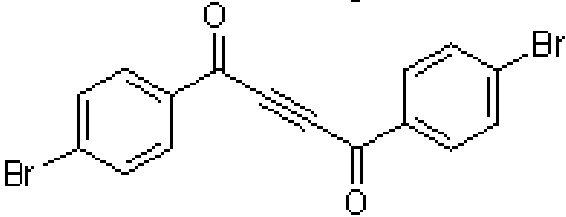
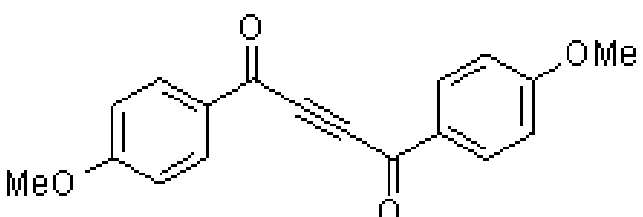
- a. R = CH<sub>3</sub>
- b. R = C<sub>2</sub>H<sub>5</sub>
- c. R = CH(CH<sub>3</sub>)<sub>2</sub>



## Facile Microwave-Mediated Transformations of 2-Butene-1,4-diones and 2-Butyne-1,4-diones to Furan Derivatives

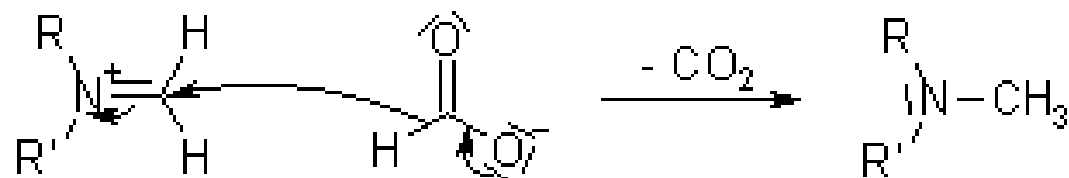
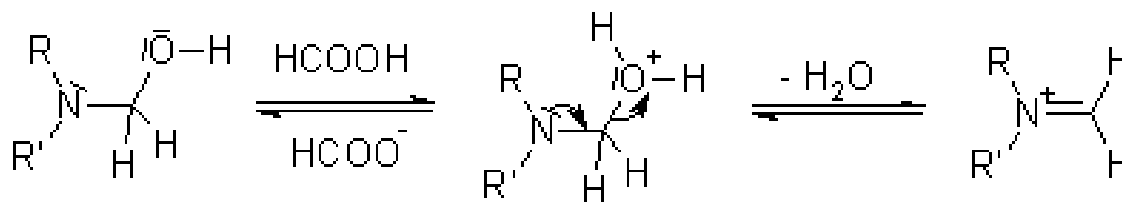
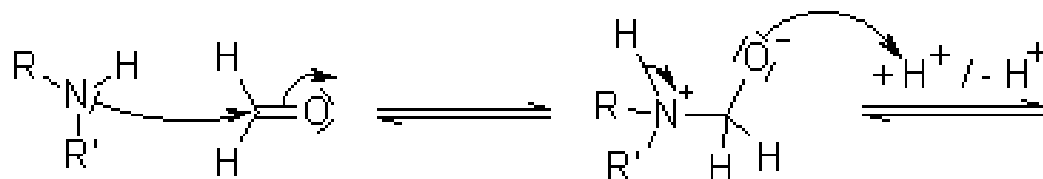
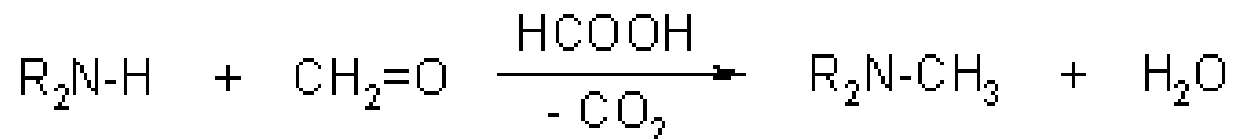
H. S. P. Rao, S. Jothilingam, *J. Org. Chem.*, **2003**, *68*, 5392-5394.

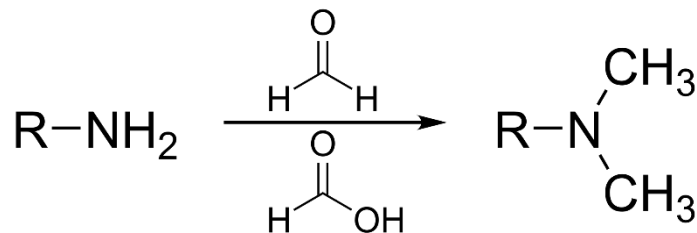


substrate	H <sub>2</sub> SO <sub>4</sub> (mol-%)	Power (W)	t (min)	yield (%; isol.)
	0	400	1.0	95
	5	200	5.0	96
	5	200	5.0	84
	0	155	4.0	93
	5	200	5.0	88



## Reacción Eschweiler-Clarke

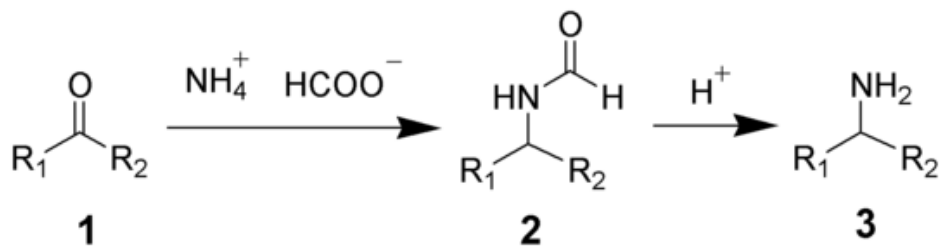




[https://en.wikipedia.org/wiki/Formic\\_acid#/media/File:Eschweiler-Clarke\\_Reaction.svg](https://en.wikipedia.org/wiki/Formic_acid#/media/File:Eschweiler-Clarke_Reaction.svg)

## Reacción de Leuckart

Es la reacción química que convierte aldehídos o cetonas en aminas por aminación reductiva en presencia de calor. La reacción, que lleva el nombre de Rudolf Leuckart, utiliza formiato de amonio o formamida como donador de nitrógeno y agente reductor. Requiere altas temperaturas, generalmente entre 120 y 130 ° C; para la variante de formamida, la temperatura puede ser superior a 165 ° C

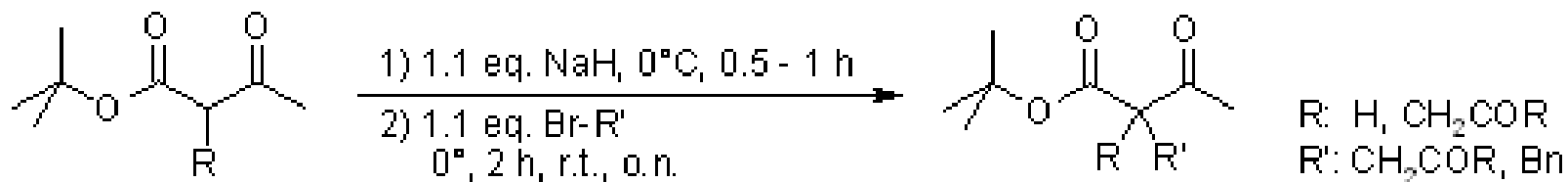


[https://en.wikipedia.org/wiki/Leuckart\\_reaction#/media/File:Leuckart\\_Reaction\\_Scheme.png](https://en.wikipedia.org/wiki/Leuckart_reaction#/media/File:Leuckart_Reaction_Scheme.png)



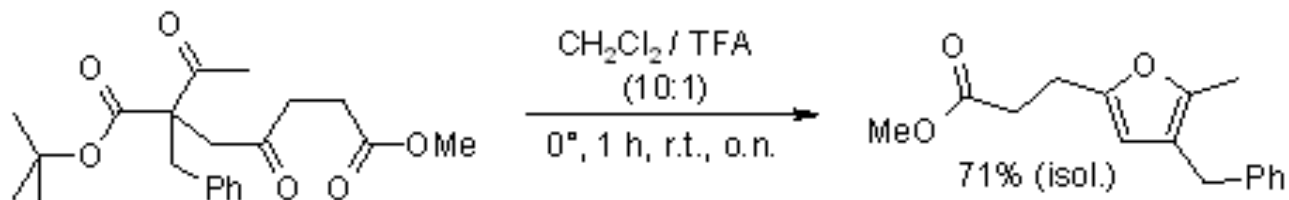
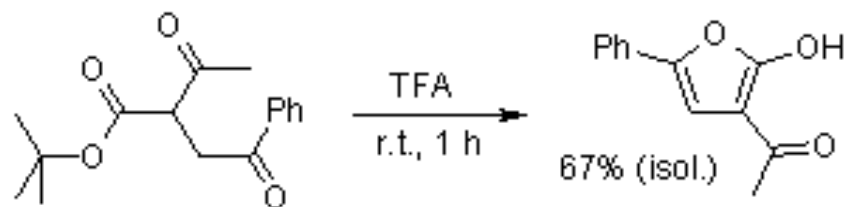
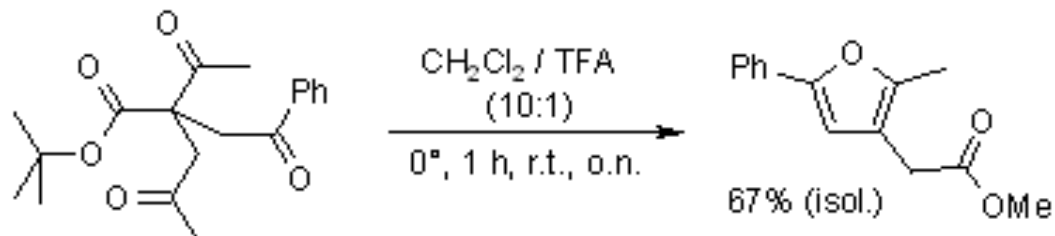
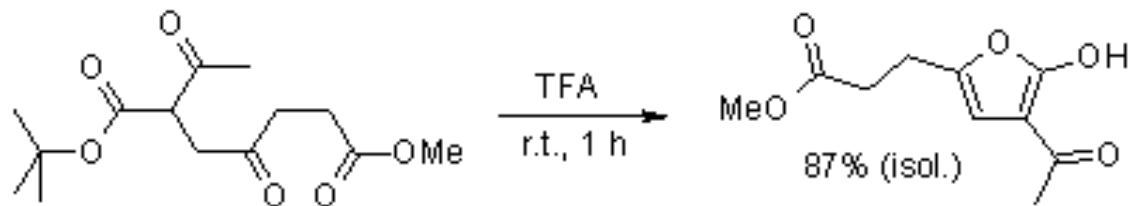
# Synthesis of Tri- and Tetrasubstituted Furans Catalyzed by Trifluoroacetic Acid

F. Stauffer, R. Neier, *Org. Lett.*, **2000**, *2*, 3535-3537.



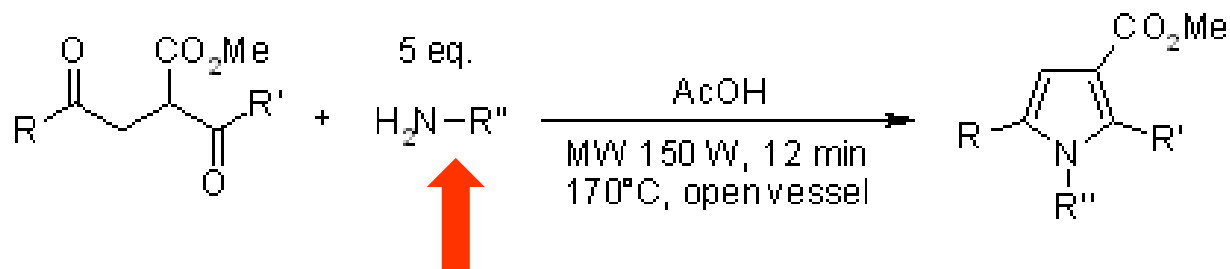
substrate	product	yield (% <sub>2</sub> , isol.)	substrate	product	yield (% <sub>2</sub> , isol.)
		92			56
		95			89





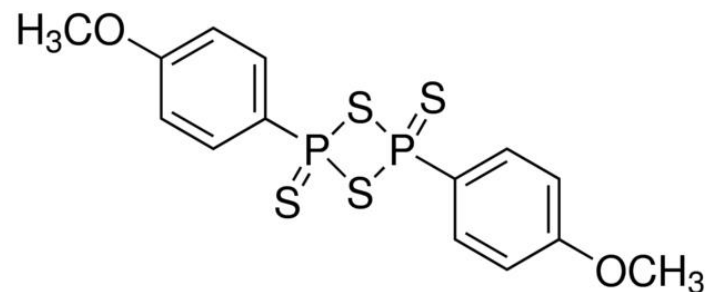
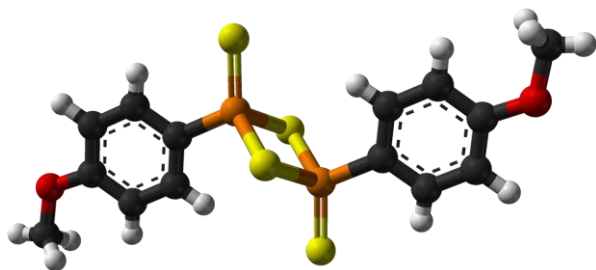
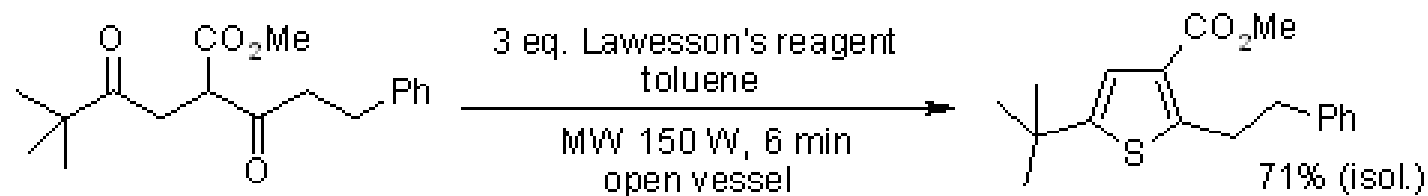
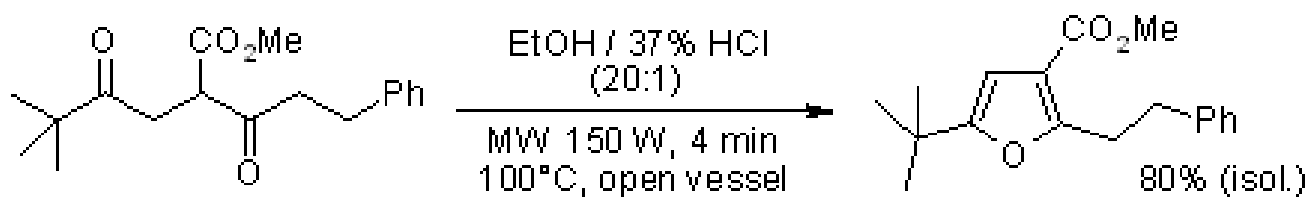
# Microwave-Assisted Paal-Knorr Reaction - Three-Step Regiocontrolled Synthesis of Polysubstituted Furans, Pyrroles and Thiophenes

G. Minetto, L. F. Raveglia, A. Segá, M. Taddei, *Eur. J. Org. Chem.*, **2005**, 5277-5288.



Product	Yield (% isol.)	Product	Yield (% isol.)	Product	Yield (% isol.)
	88		77		79
	82		88		79



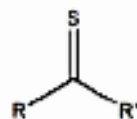
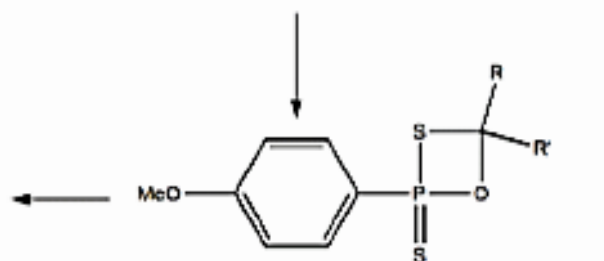
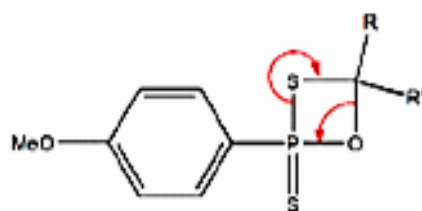
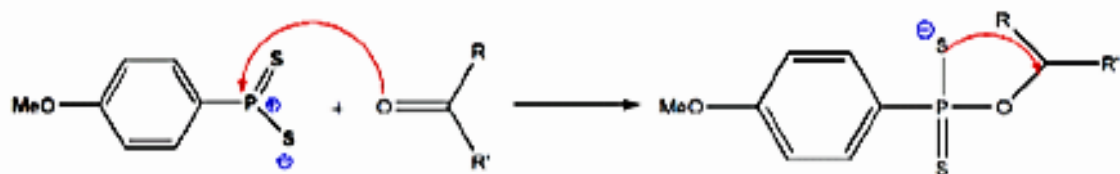
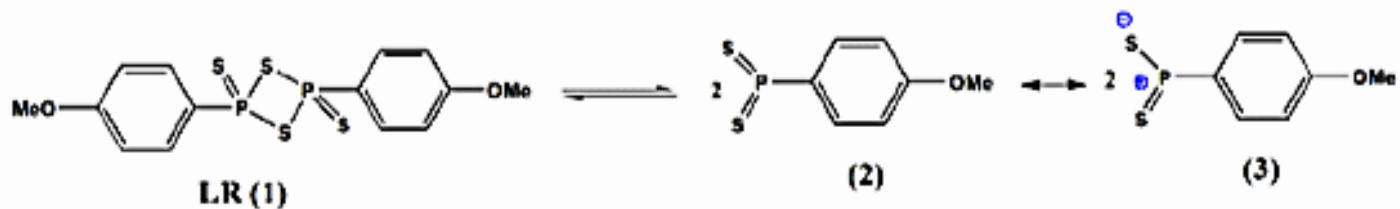


A Focused Review of Synthetic Applications of Lawesson's Reagent in Organic Synthesis

Hena Khatoon, Emilia Abdulmalek

Molecules **2021**, *26*(22), 6937; <https://doi.org/10.3390/molecules26226937>

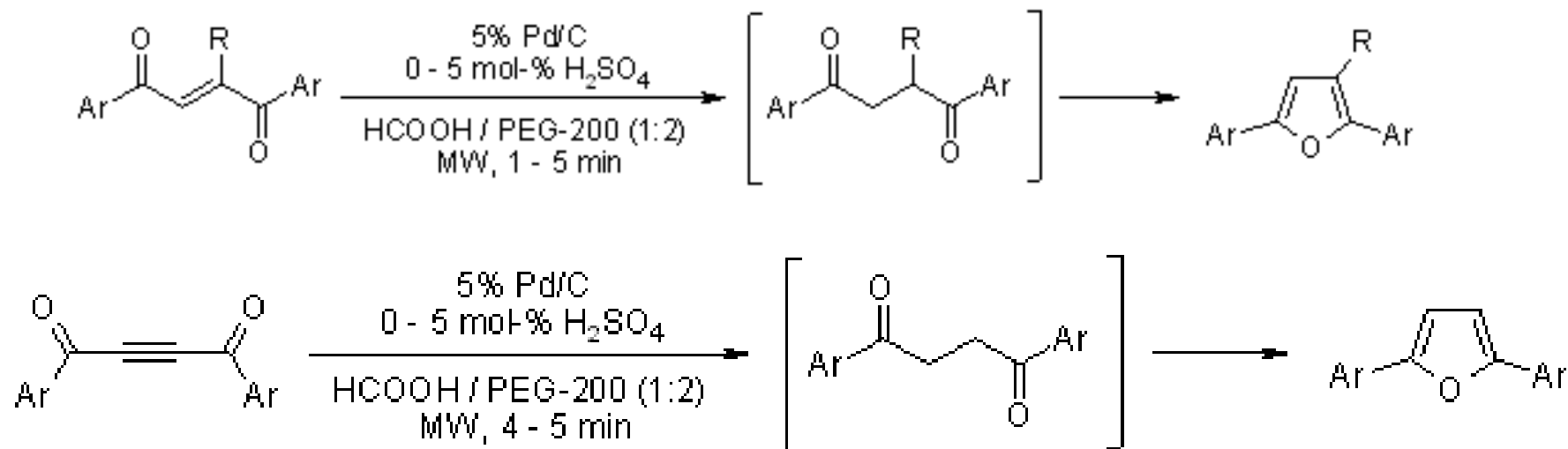


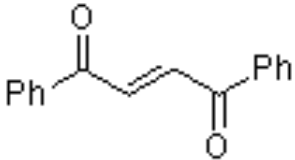
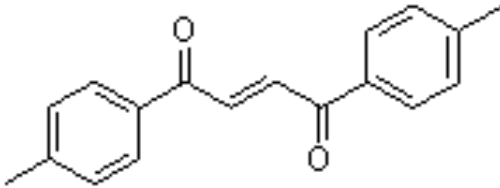
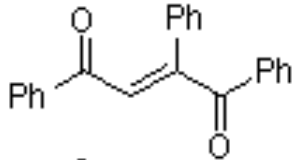
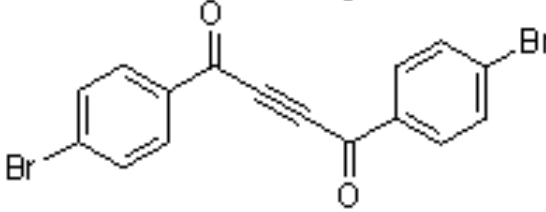
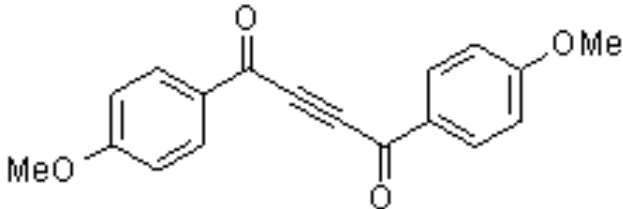


**Scheme 1.** Mechanism of the thionation reaction using Lawesson's reagent (1).

## Facile Microwave-Mediated Transformations of 2-Butene-1,4-diones and 2-Butyne-1,4-diones to Furan Derivatives

H. S. P. Rao, S. Jothilingam, *J. Org. Chem.*, **2003**, *68*, 5392-5394.

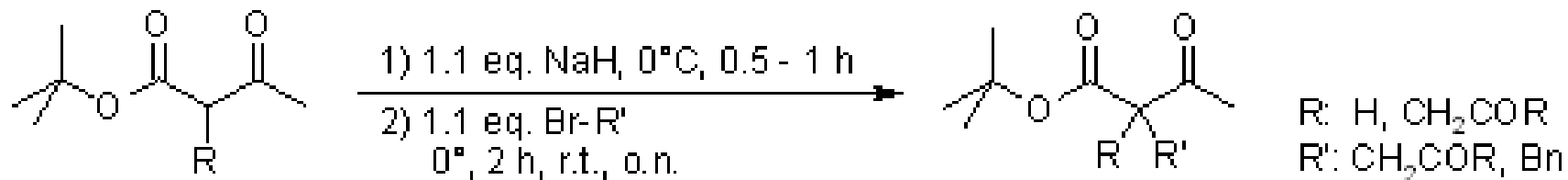


substrate	H <sub>2</sub> SO <sub>4</sub> (mol-%)	Power (W)	t (min)	yield (% , isol.)
	0	400	1.0	95
	5	200	5.0	96
	5	200	5.0	84
	0	155	4.0	93
	5	200	5.0	88



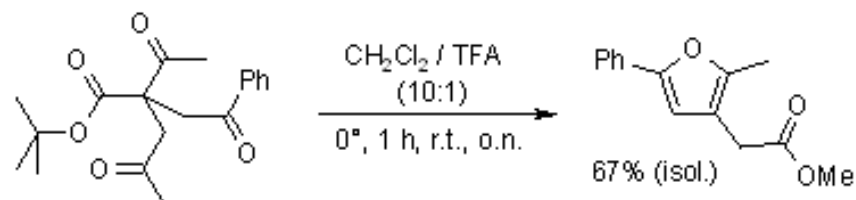
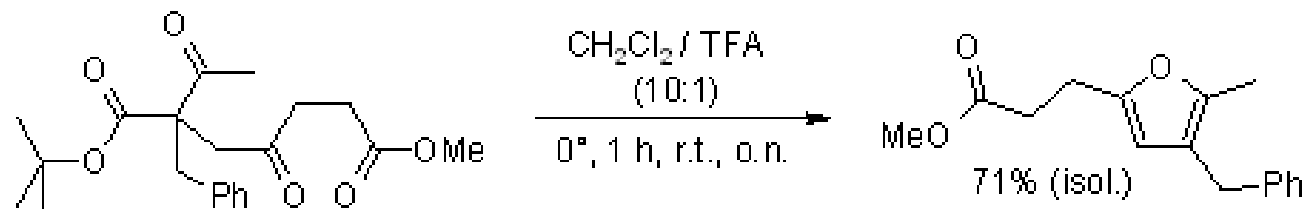
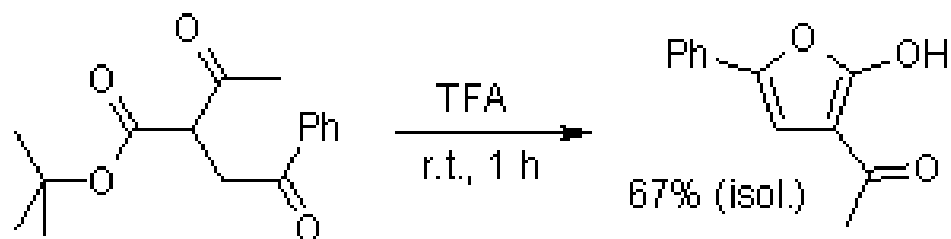
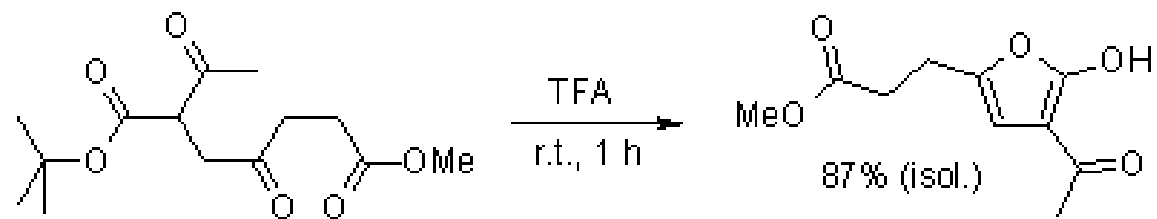
# Synthesis of Tri- and Tetrasubstituted Furans Catalyzed by Trifluoroacetic Acid

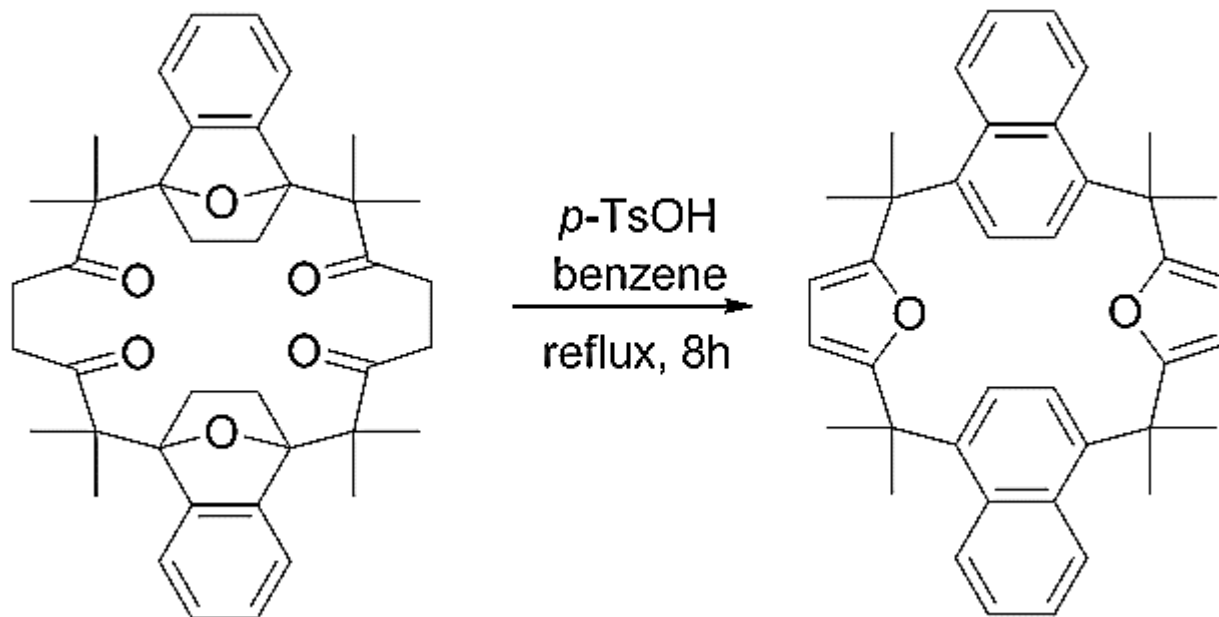
F. Stauffer, R. Neier, *Org. Lett.*, **2000**, *2*, 3535-3537.



substrate	product	yield (% isol.)
		92
		95
		56
		89





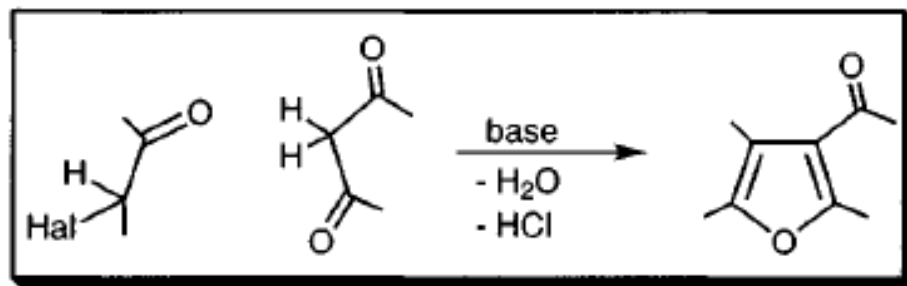


Hart, H.; Takehira, Y, *The Journal of Organic Chemistry*, **1982**,47, 4370,

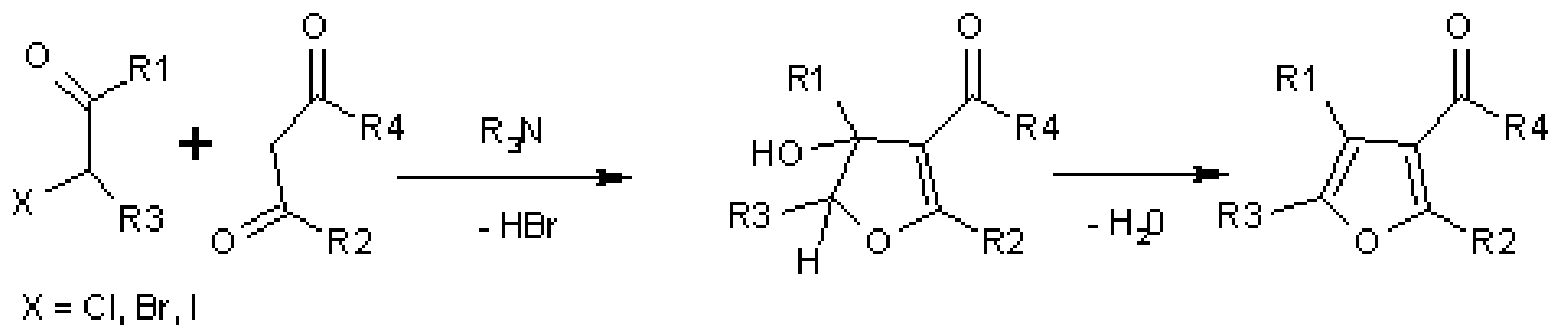


# MÉTODOS DE OBTENCIÓN DE FURANO

## SÍNTESIS DE FEIST-BENARY



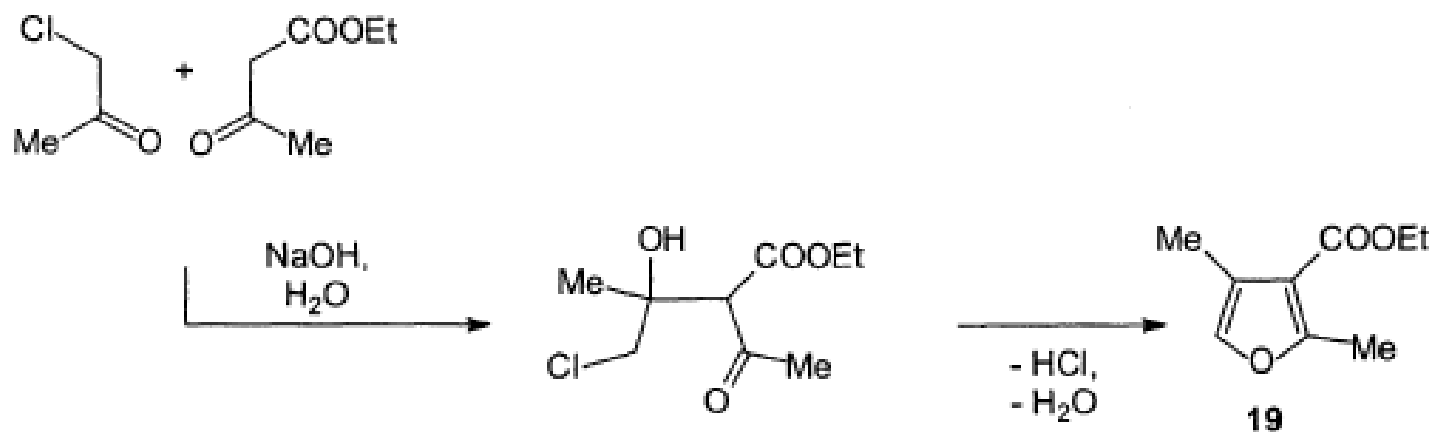
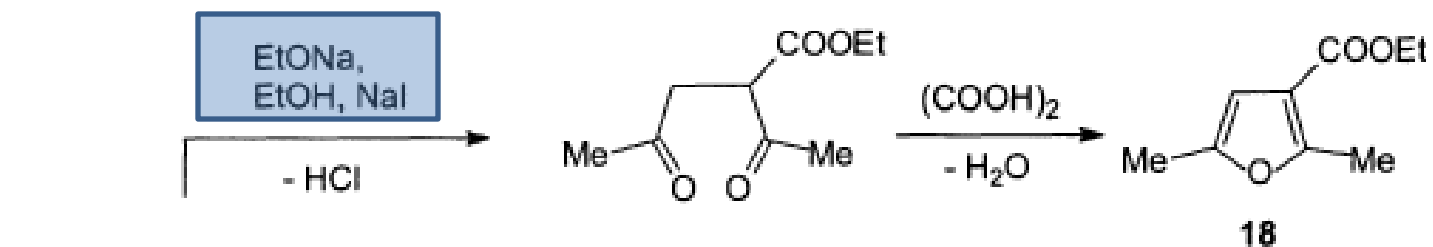
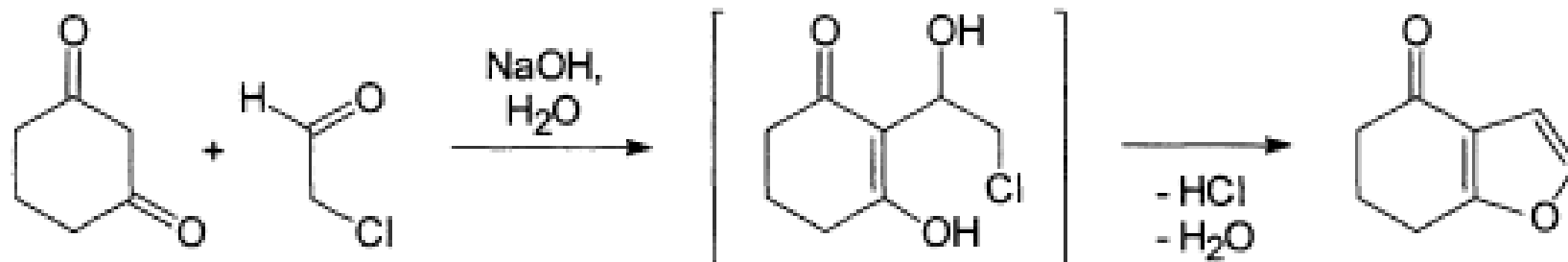
Franz Feist (1902), Erich Benary (1911)



Feist F., *Ber.*, **1902**, 35, 1539, 1547.  
Benary E., *Ber.*, **1911**, 44, 489, 493.



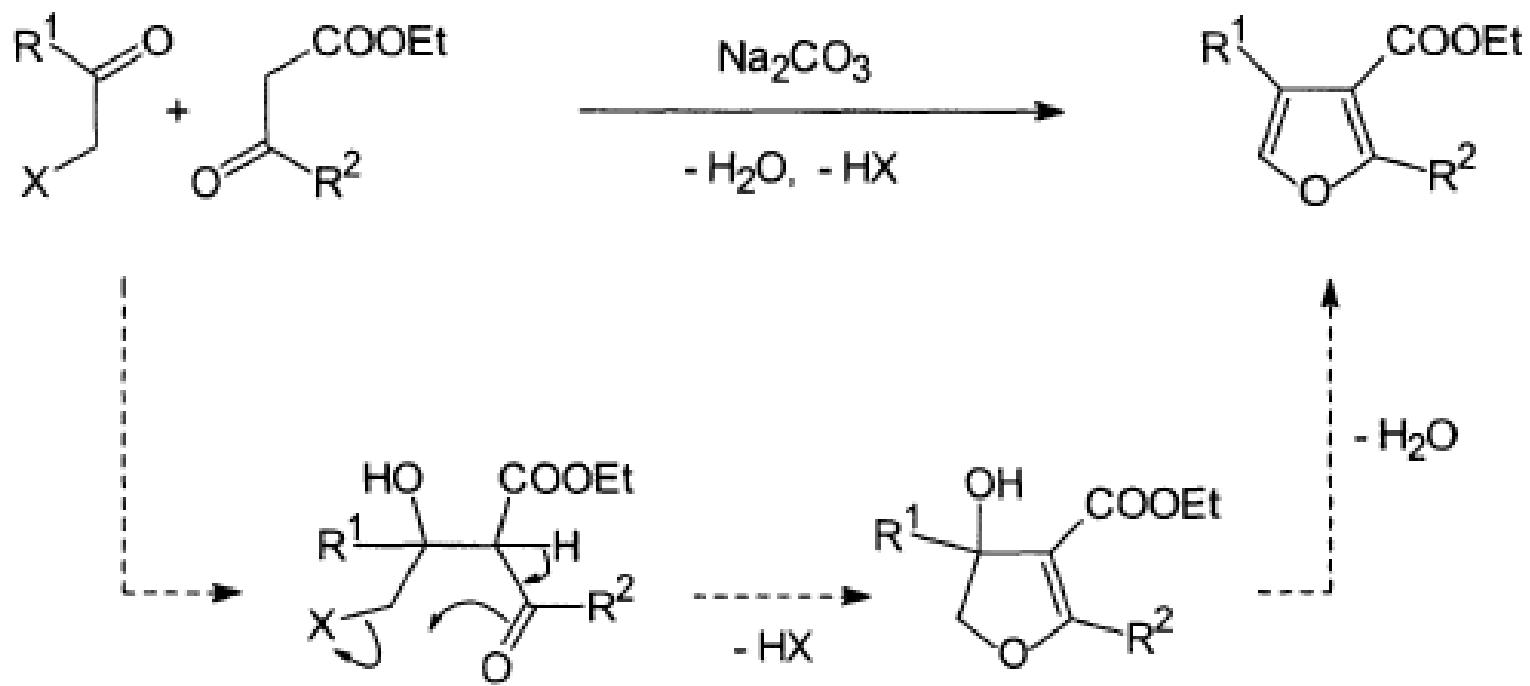
# MÉTODOS DE OBTENCIÓN DE FURANO



Feist F., *Ber.*, **1902**, 35, 1539, 1547  
 Benary E., *Ber.*, **1911**, 44, 489, 493

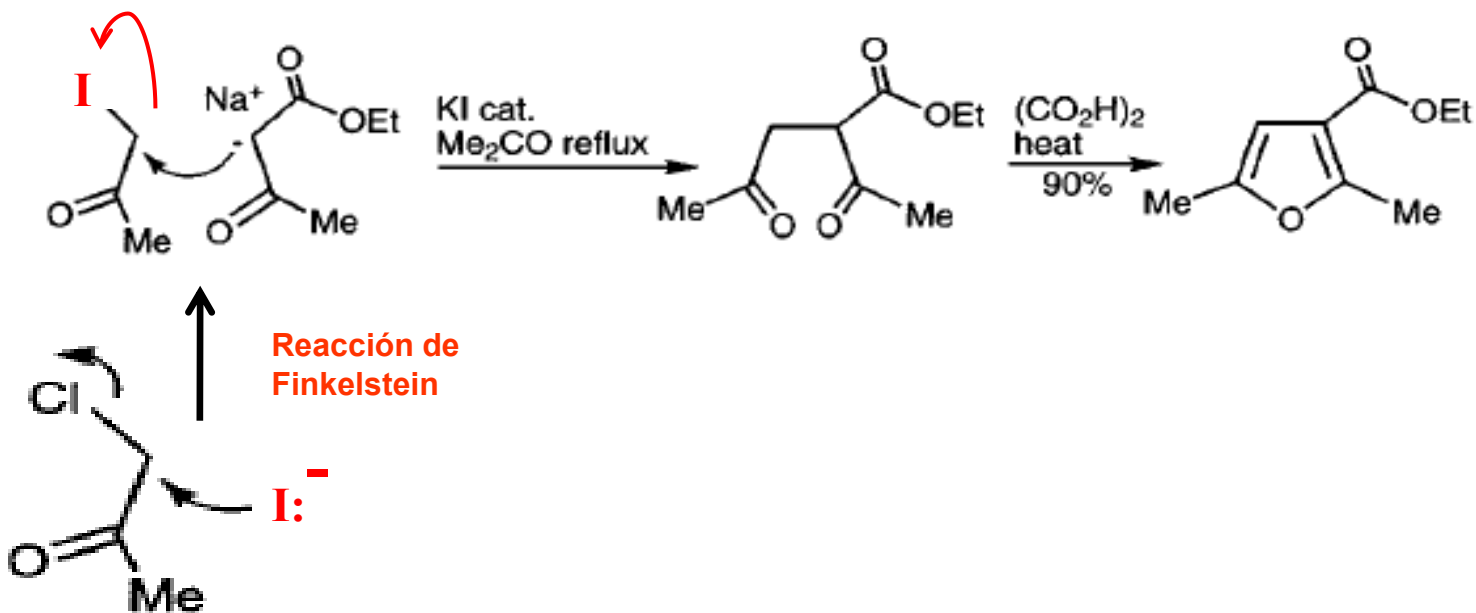
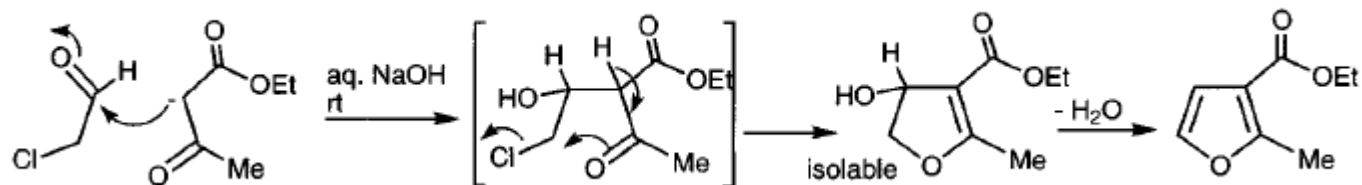


## SÍNTESIS DE FEIST-BENARY

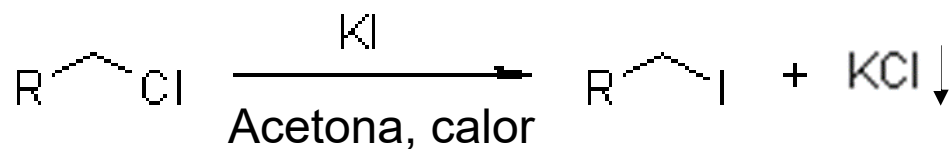
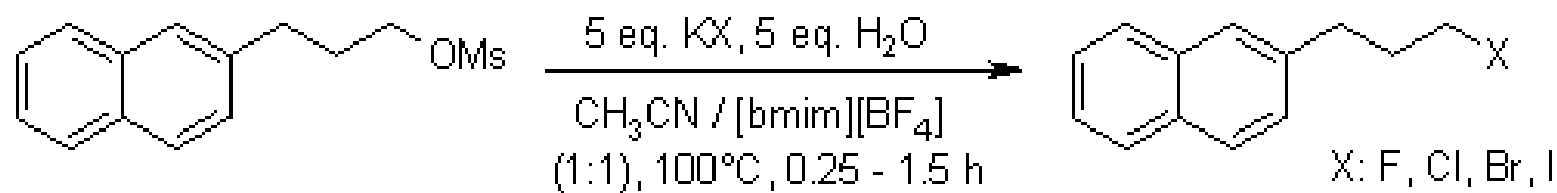
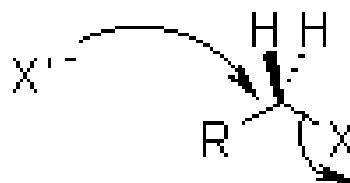
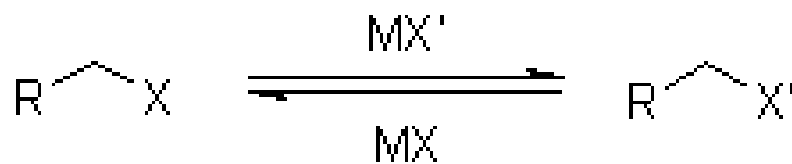


# MÉTODOS DE OBTENCIÓN DE FURANO

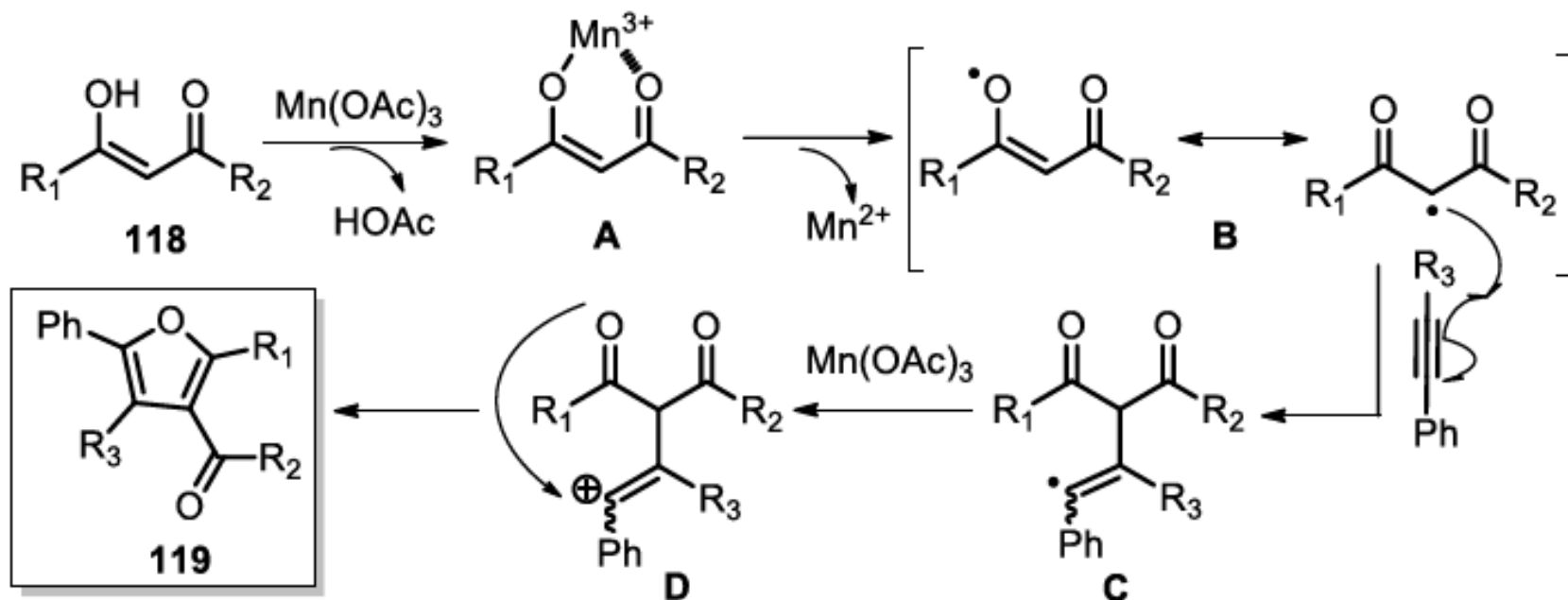
## SÍNTESIS DE FEIST-BENARY



## Reacción de Finkelstein



A) Mondal, 2013 **Mecanismo**



El  $Mn(OAc)_3$  reacciona con la forma enólica del sistema 1,3-dicarbonílico **118** formando un complejo Mn(III)-enolato **A**. En esta estructura el Mn(III) es reducido a Mn(II) para formar el radical centrado en oxígeno **B**, el cual se encuentra en resonancia para generar el radical  $\alpha$ -carbonilo más estable. Dicho radical se puede adicionar de forma intra o intermolecular a diversos aceptores. Por ejemplo, puede adicionarse a un alquino interno para formar el intermediario **C**, el cual puede ser oxidado al carbocatión **D** con otra molécula de  $Mn(OAc)_3$  y finalmente formar el núcleo de furano **E** luego de una ciclación intramolecular **A**.

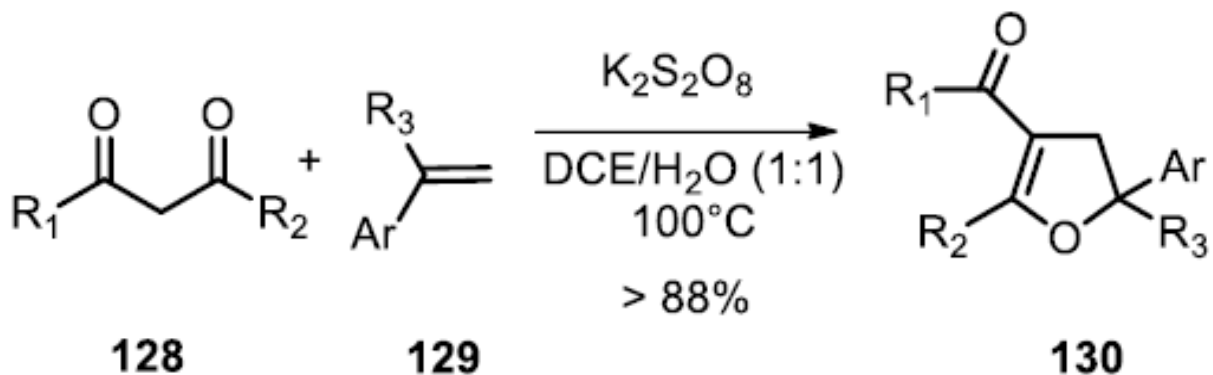
Snider, B., B. *Tetrahedron*. **2009**, 65, 10738-10744.

Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1972**, 94, 2888–2889.

Alagoz, O.; Yilmaz, M.; Pekel, A. T. *Synth. Commun.* **2006**, 36, 1005-1013



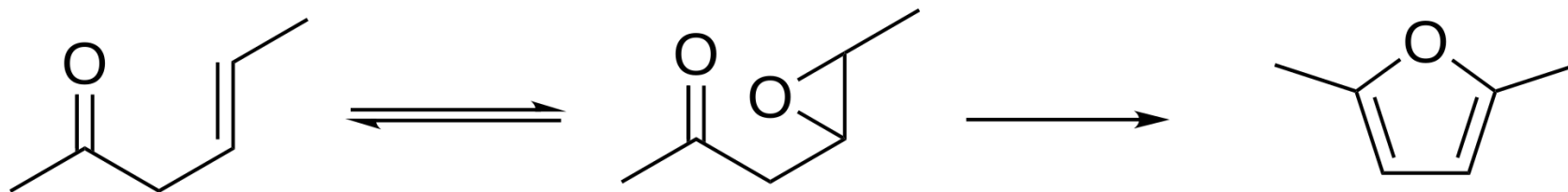
A) Guo, 2015



De otra parte, Guo y colaboradores reportaron en 2015 una metodología libre de metales para la síntesis de dihidrofuranos **130** mediante una adición/ciclación tándem entre un sistema 1,3-dicarbonílico **128** y estireno **129** promovido por  $K_2S_2O_8$  (A).

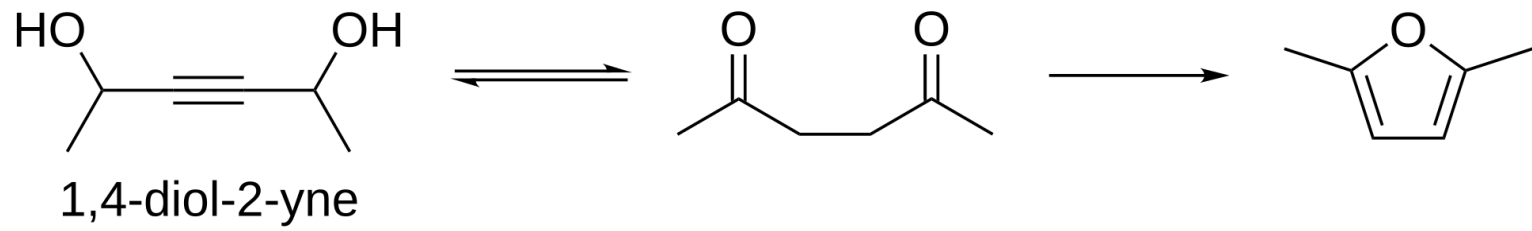
Wang, S.; He, L.; Guo, L. *Synthesis* **2015**, *47*, 3191-3197.



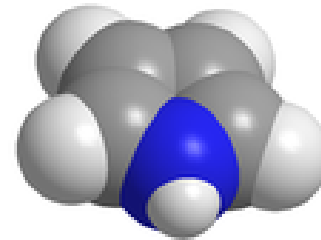
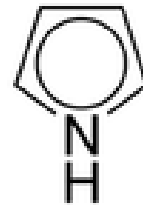
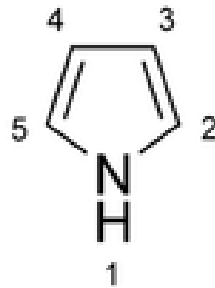
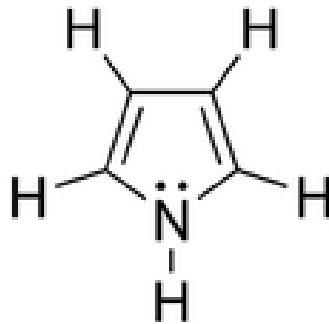


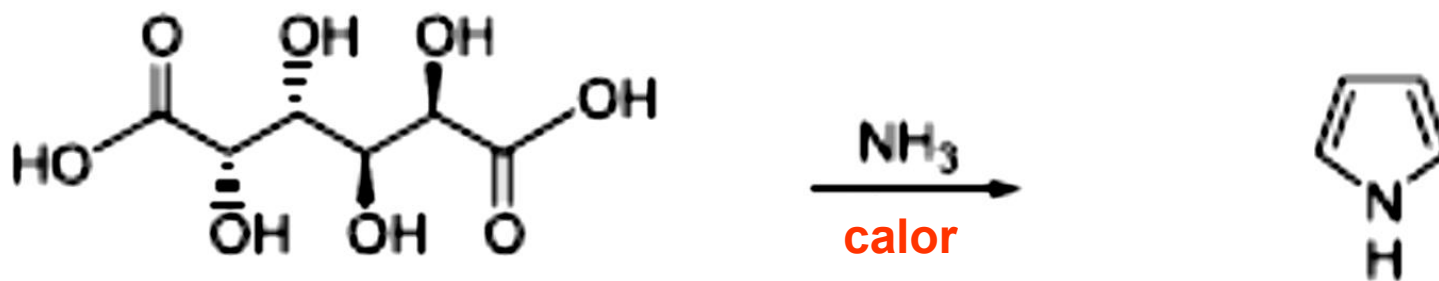
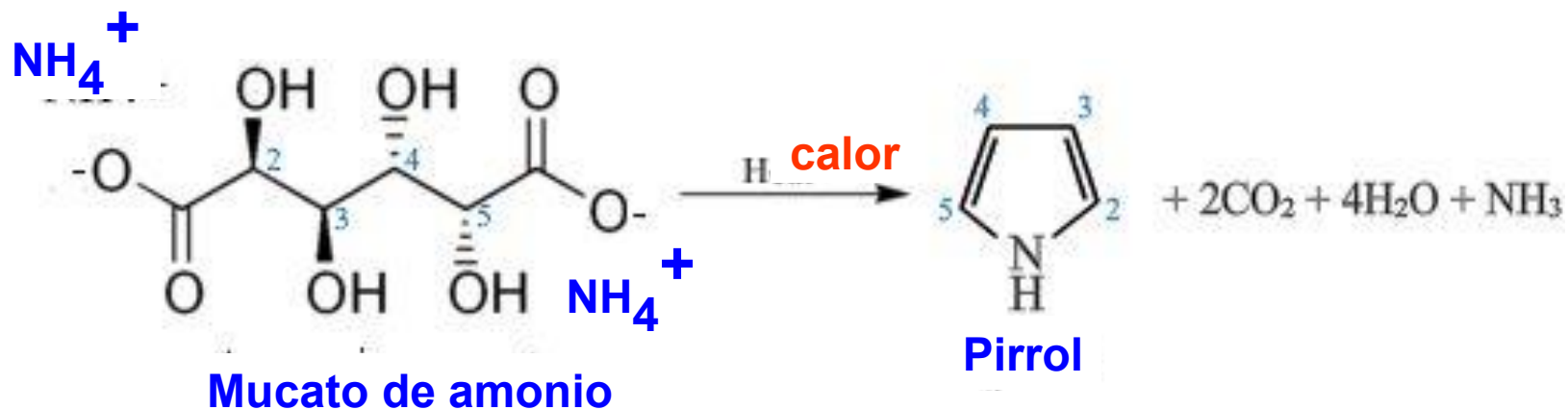
epoxy carbonyl



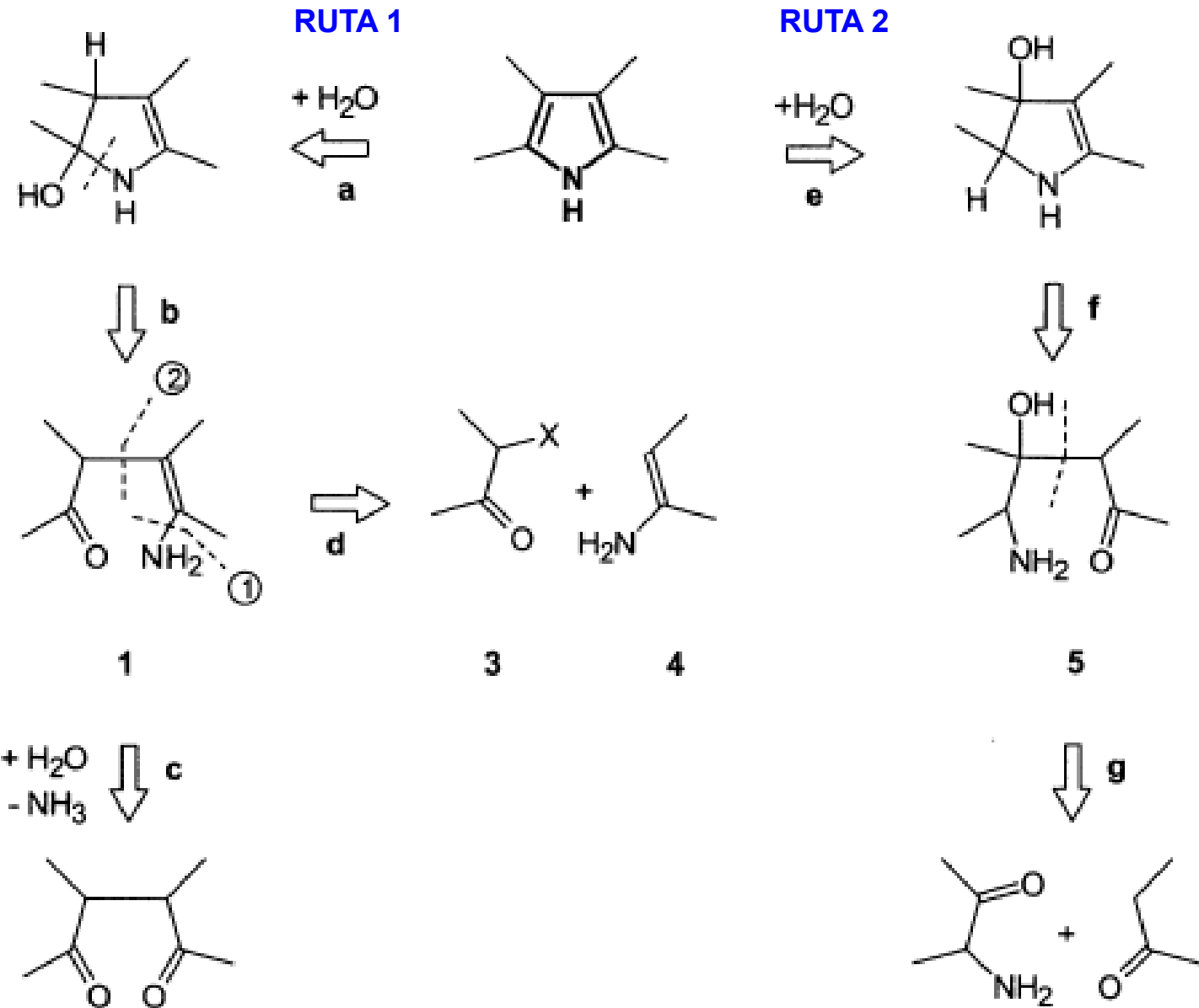


# PIRROL

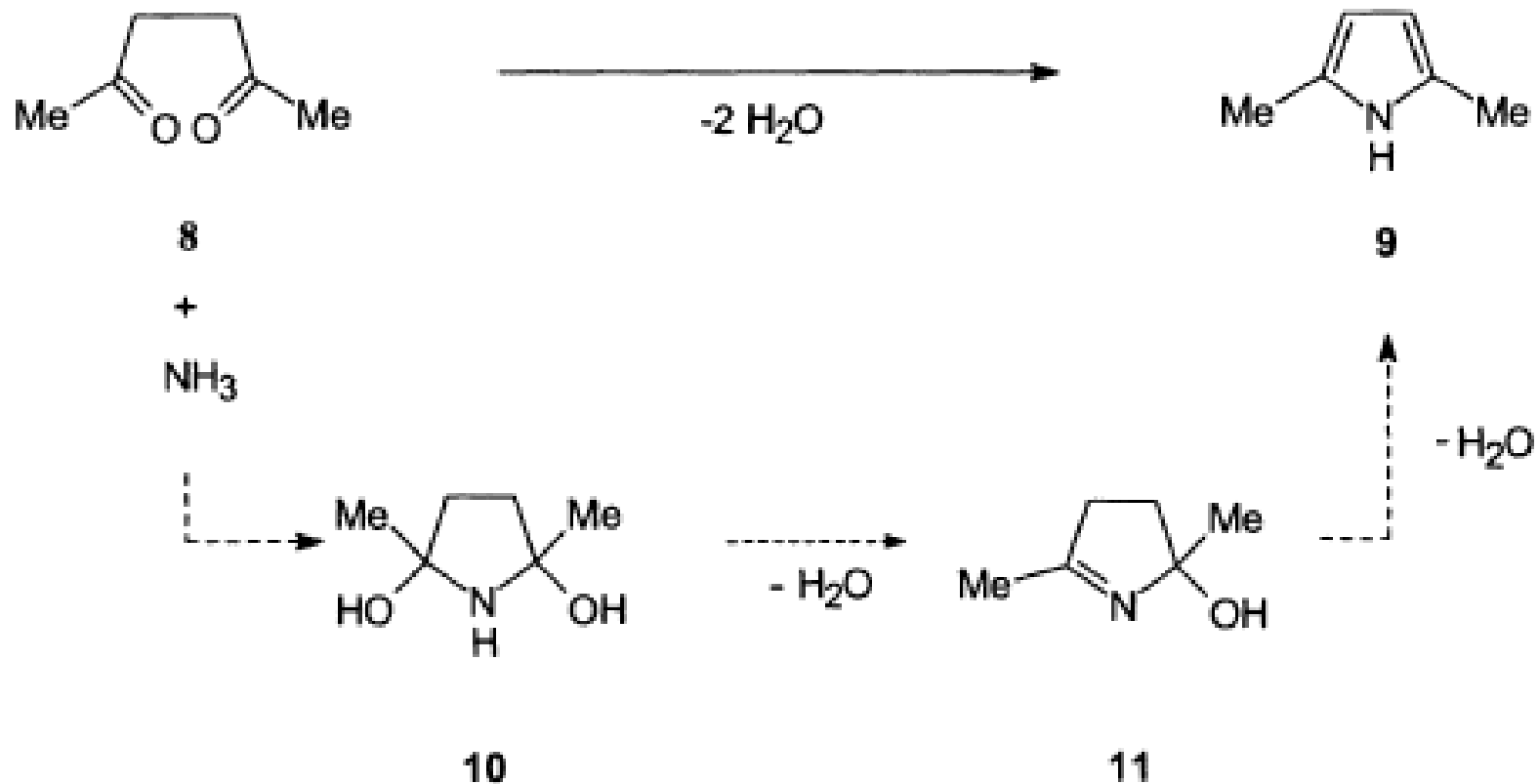




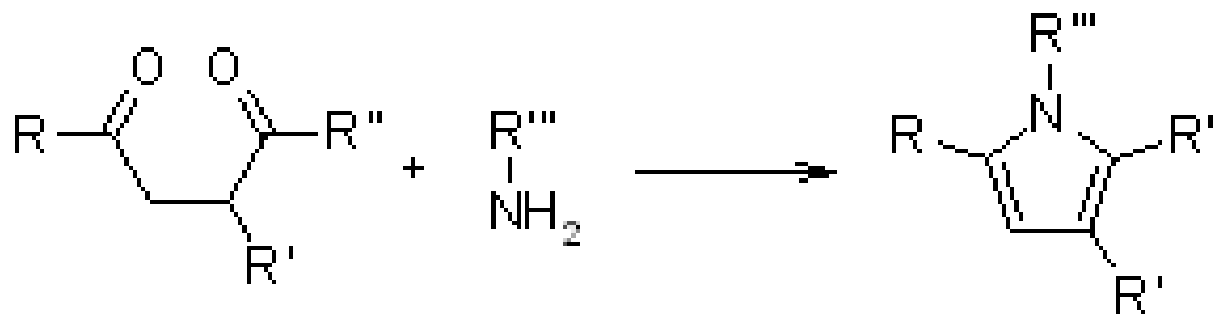
# MÉTODOS DE OBTENCIÓN DE PIRROL



# SÍNTESIS DE PAAL-KNORR



## Síntesis de pirroles de Paal-Knorr



**Ludwig Knorr**  
(1859 — 1921)  
Químico Alemán

<https://www.wikidata.org/wiki/Q63983>

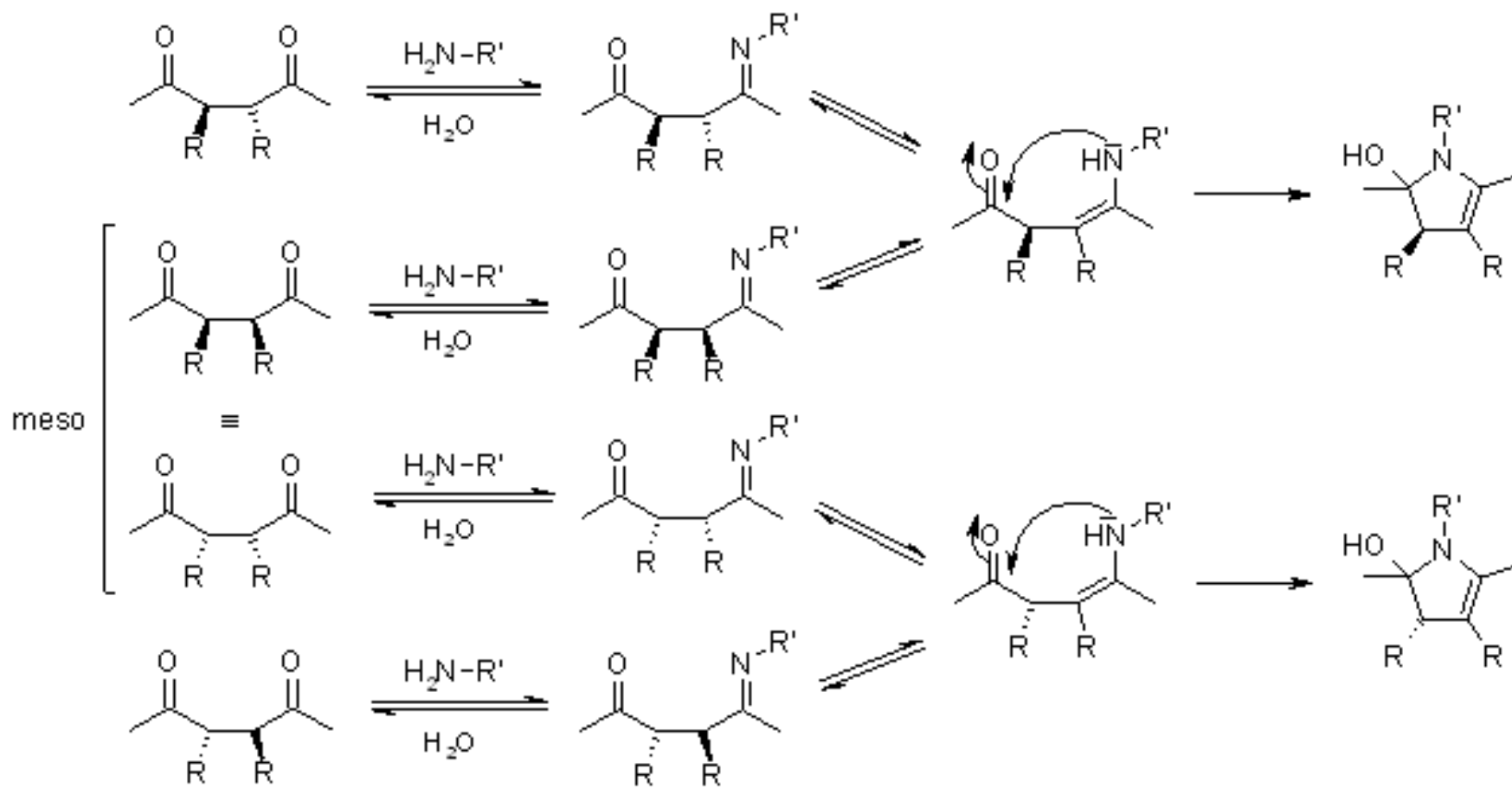
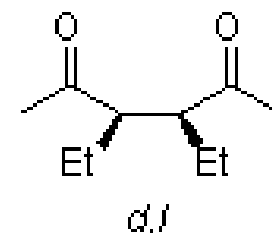
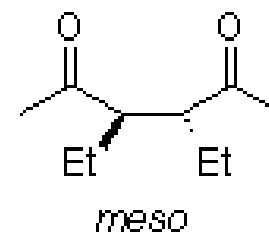


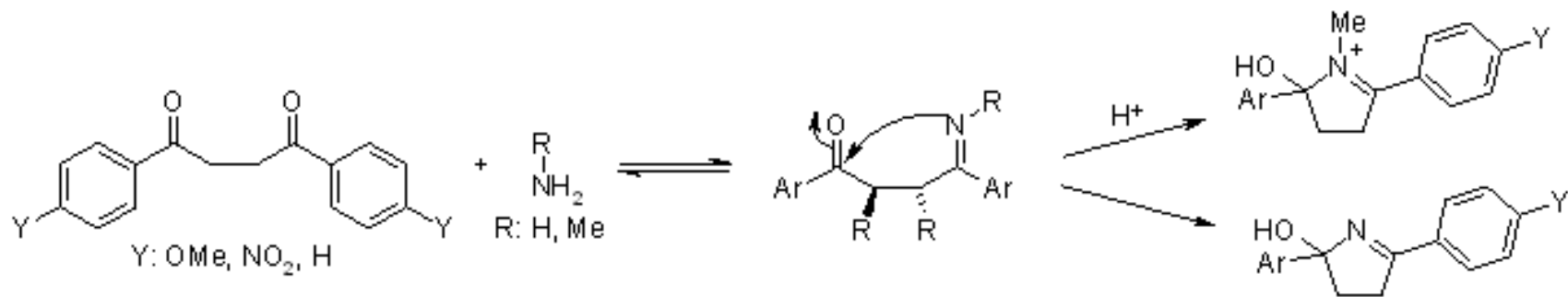
Prof. Dr. phil. habil. et Dr. h. c. **Carl Ludwig Paal**  
(1860 – 1935)  
Químico austriaco

[http://research.uni-leipzig.de/catalogus-professorum-lipsiensium/leipzig/Paal\\_111/](http://research.uni-leipzig.de/catalogus-professorum-lipsiensium/leipzig/Paal_111/)

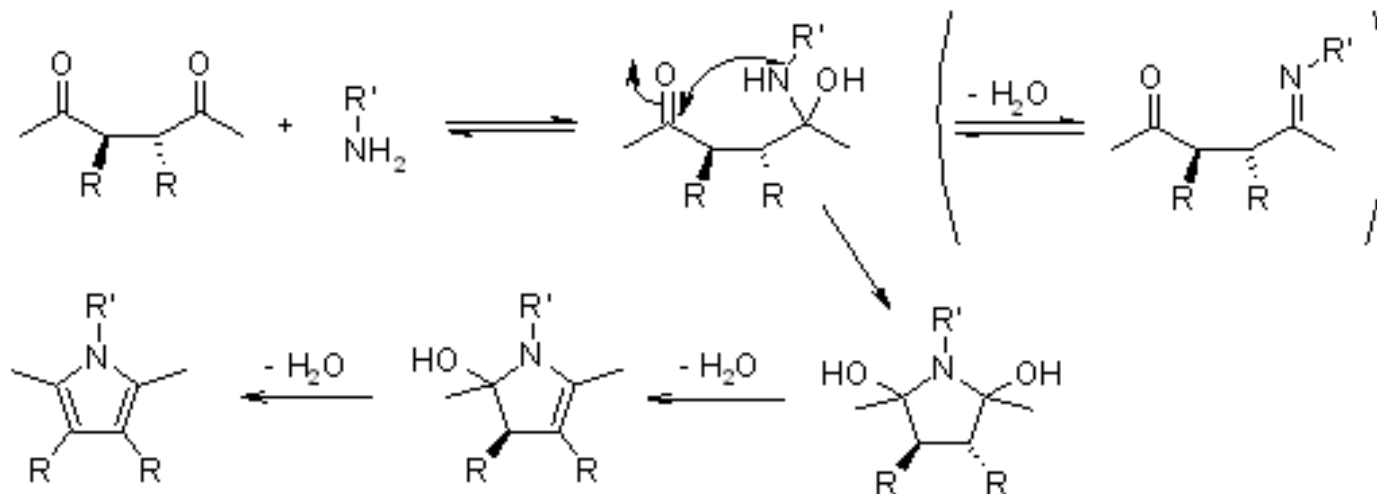
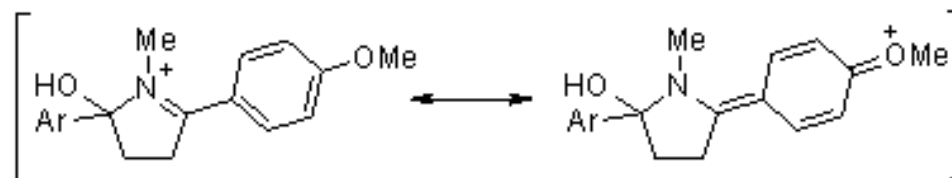


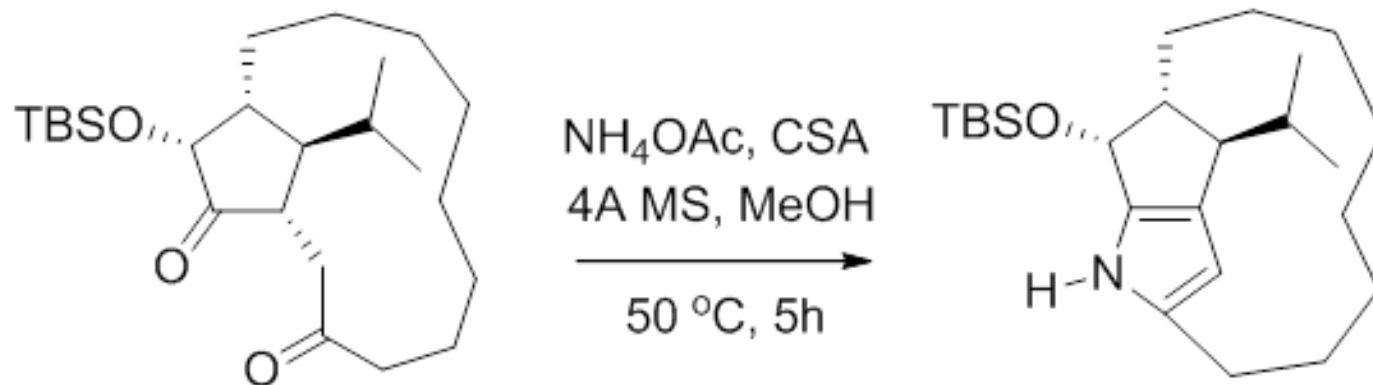
Venkataraman Amarnath has shown (J. Org. Chem., **1991**, 56, 6924) that *meso*- and *dl*-3,4-diethyl-2,5-hexanediones cyclize at unequal rates, and that the stereochemical configuration of the unchanged dione is preserved during the reaction. Any mechanism such as the following one that involves the formation of an enamine before the rate-determining step - the cyclization - must be ruled out.





estabilización

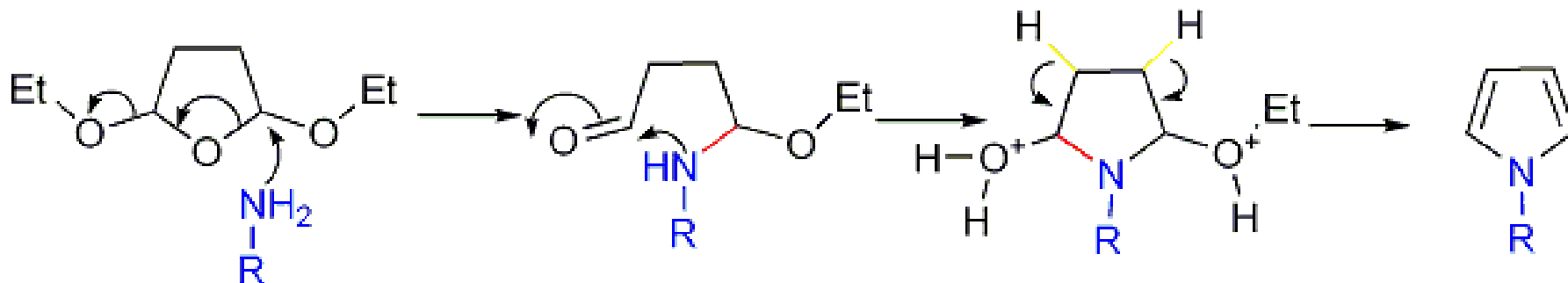
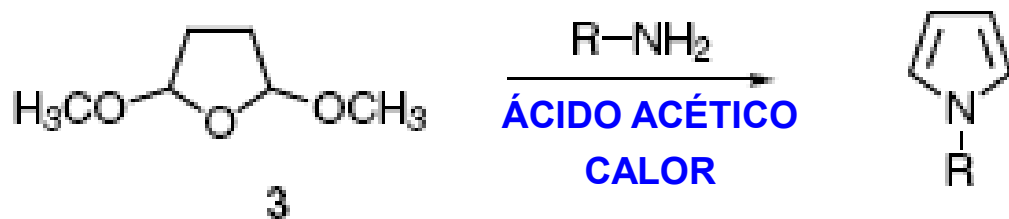




Trost, B. M.; Doherty, G. A. *Journal of the American Chemical Society*, **2000**, 122 (16), 3801–3810

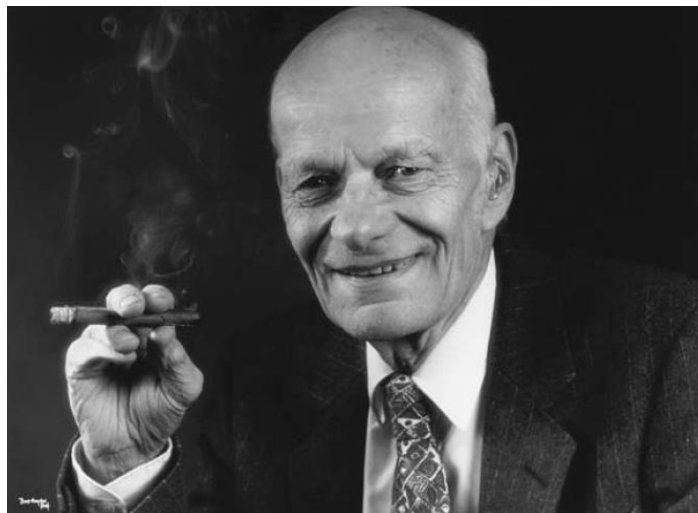


## Reacción de Clauson-Kaas



Clauson-Kaas N., Tyle Z., *Acta Chem. Scand.*, **1952**, 6, 667.  
Elming N., Clauson-Kaas N., *Acta Chem. Scand.*, **1952**, 6, 867.



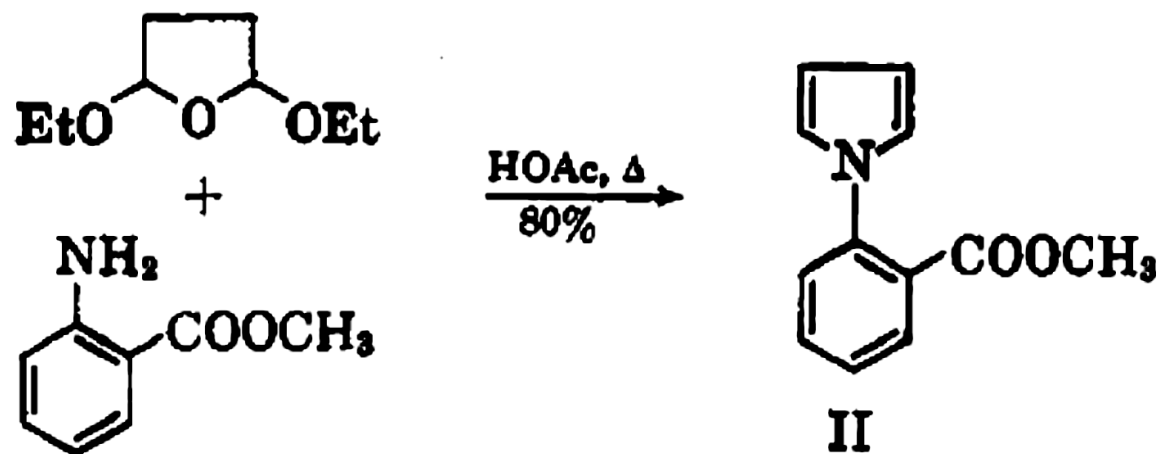


Niels Clauson-Kaas  
(1917-2003)



# N-Functionally Substituted Pyrroles

A. D. JOSEY AND E. L. JENNER

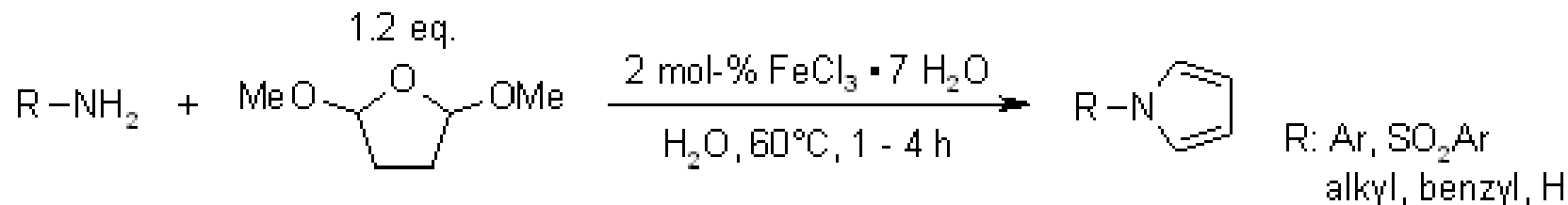


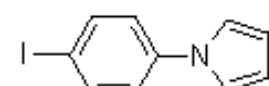
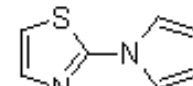
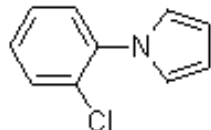
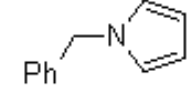
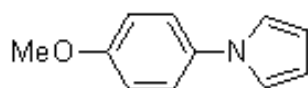
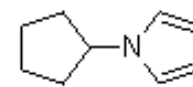
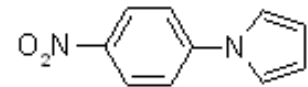
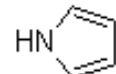
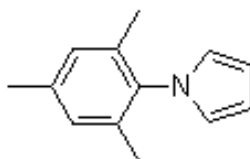
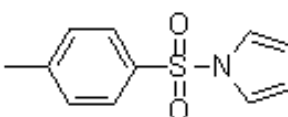
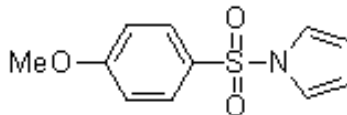
*J. Org. Chem.*, 1962, 27 (7), pp 2466–2470



# Iron-Catalyzed Inexpensive and Practical Synthesis of N-Substituted Pyrroles in Water

N. Azizi, A. Khajeh-Amiri, H. Ghafari, M. Bolourtchian, M. R. Saidi, *Synlett*, **2009**, 2245-2248

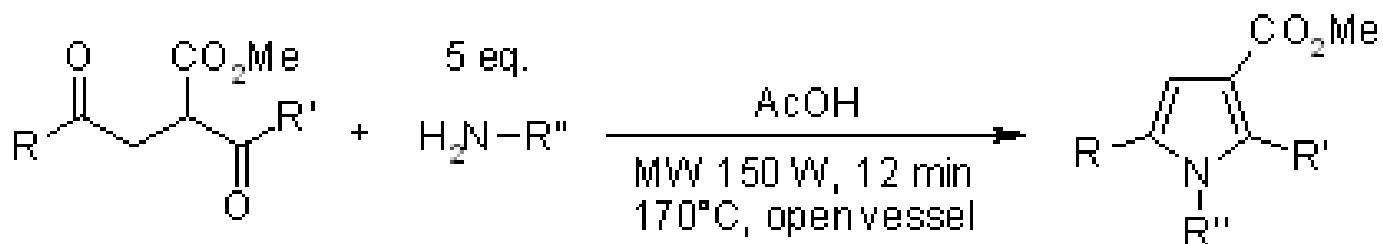


product	yield (% , isol.)	product	yield (% , isol.)
	98		80
	95		78
	90		80
	90		82
	85		85
			78



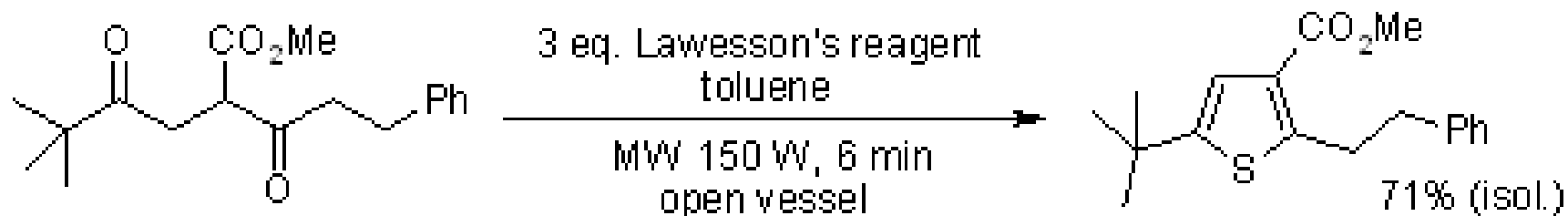
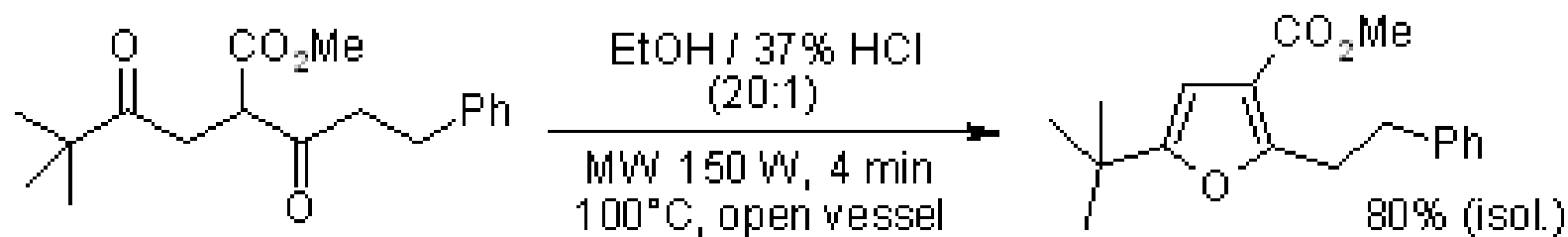
# Microwave-Assisted Paal-Knorr Reaction - Three-Step Regiocontrolled Synthesis of Polysubstituted Furans, Pyrroles and Thiophenes

G. Minetto, L. F. Raveglia, A. Segá, M. Taddei, *Eur. J. Org. Chem.*, **2005**, 5277-5288.



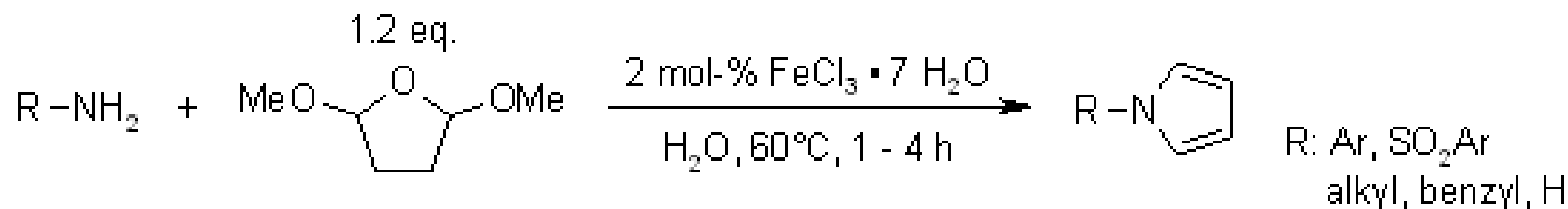
Product	Yield (% <sub>isol.</sub> )	Product	Yield (% <sub>isol.</sub> )	Product	Yield (% <sub>isol.</sub> )
	88		77		79
	82		88		79

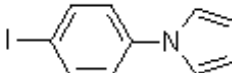
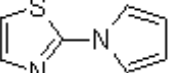
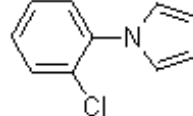
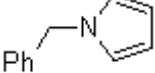

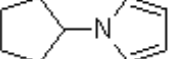

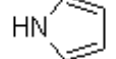
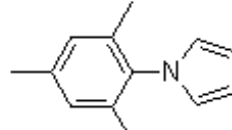
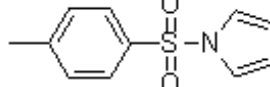
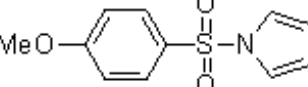




# Iron-Catalyzed Inexpensive and Practical Synthesis of N-Substituted Pyrroles in Water

N. Azizi, A. Khajeh-Amiri, H. Ghafuri, M. Bolourtchian, M. R. Saidi, *Synlett*, **2009**, 2245-2248

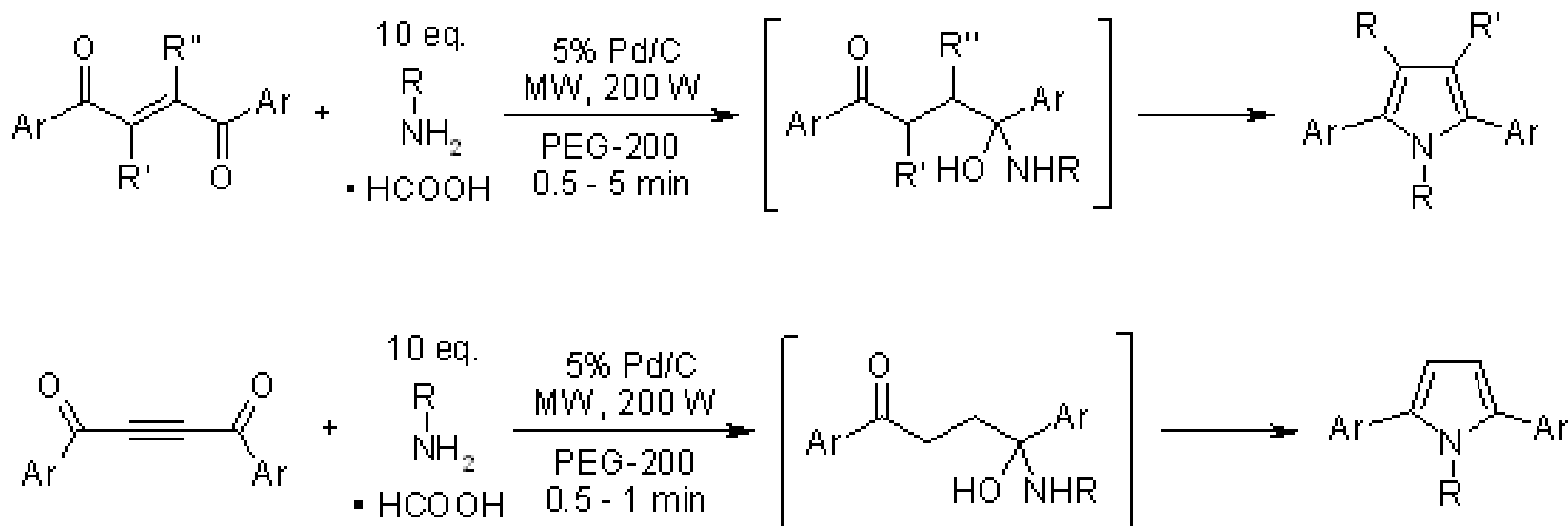


product	yield (% , isol.)	product	yield (% , isol.)
	98		80
	95		78
	90		80
	90		82
	85		85
			78



# Microwave mediated facile one-pot synthesis of polyarylpyrroles from but-2-ene- and but-2-yne-1,4-diones

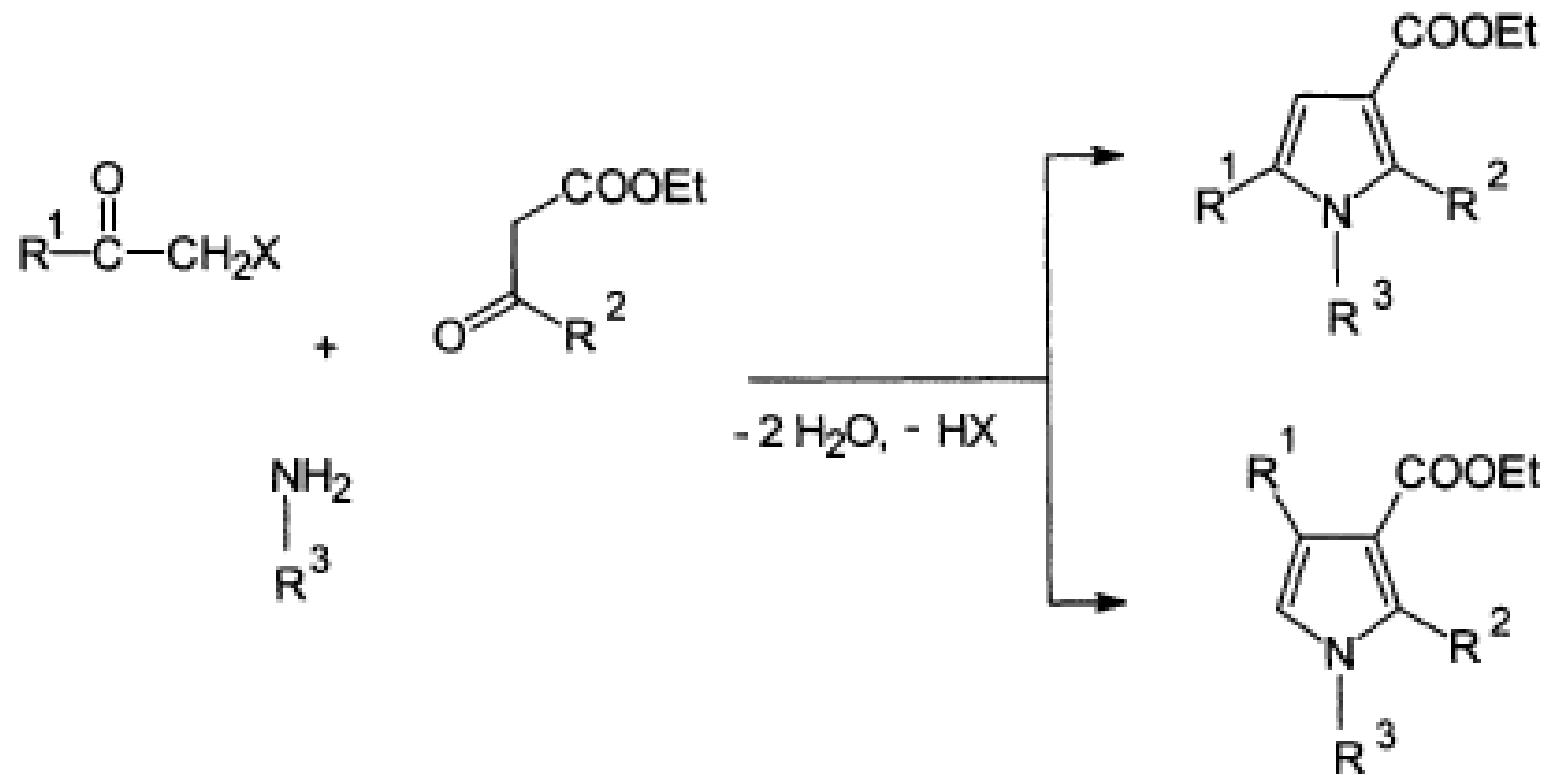
H. S. P. Rao, S. Jothilingam, H. W. Scheeren, *Tetrahedron*, **2004**, *60*, 1625-1630.

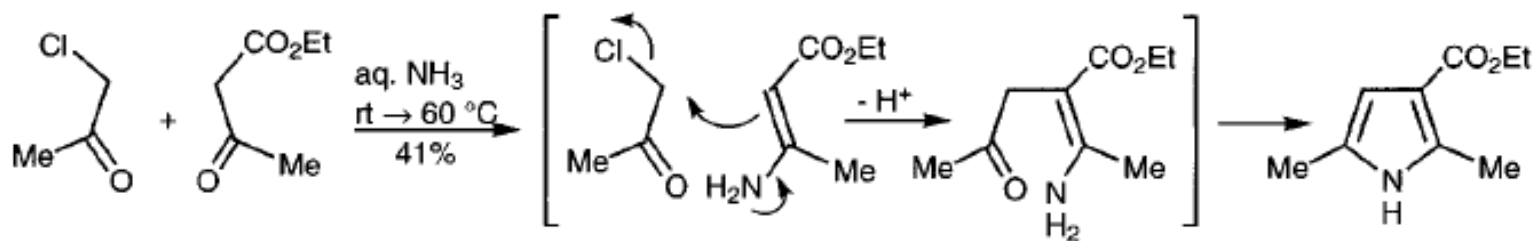
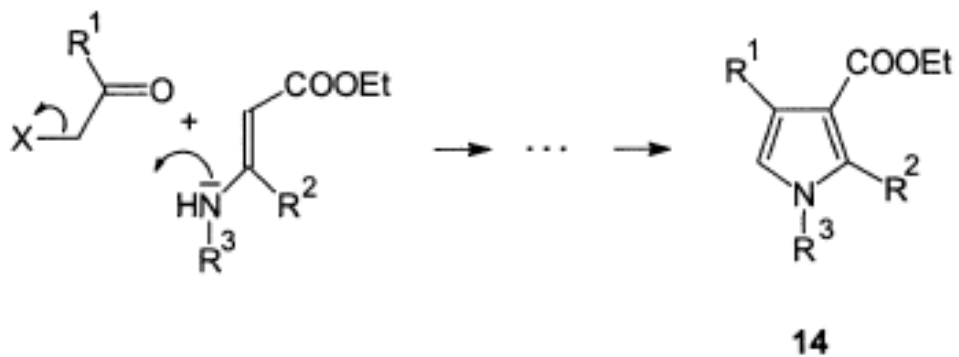
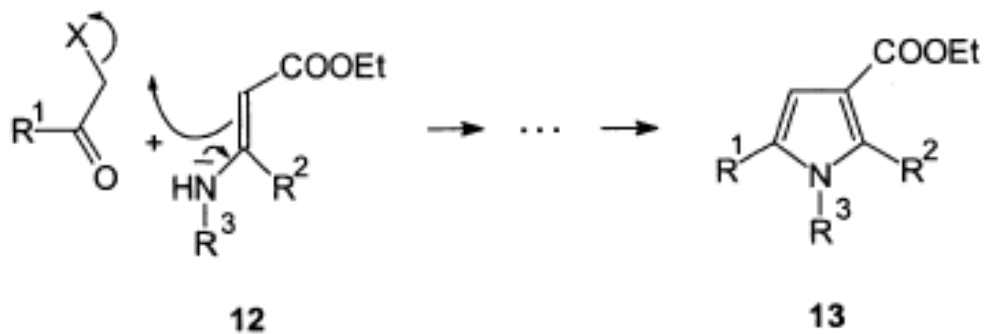


substrate	RNH <sub>2</sub>	t (min)	yield (% , isol.)
	NH <sub>3</sub>	0.5	92
	NH <sub>3</sub>	1.5	85
	Bu-NH <sub>2</sub>	2.0	56
	NH <sub>3</sub>	0.5	92
	NH <sub>3</sub>	1.0	91
	Bu-NH <sub>2</sub>	1.0	60
	Ph-NH <sub>2</sub>	1.0	61
	NH <sub>3</sub>	1.0	95

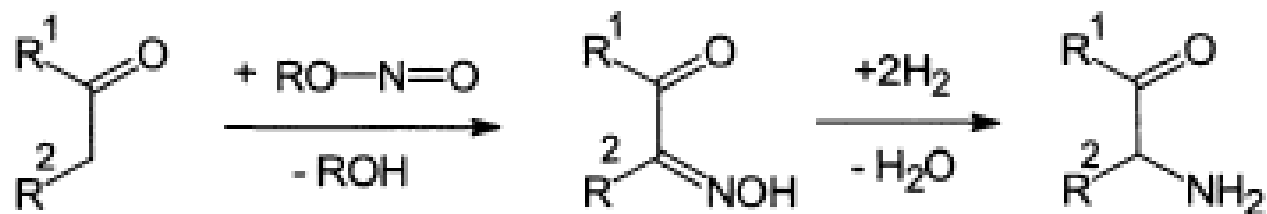
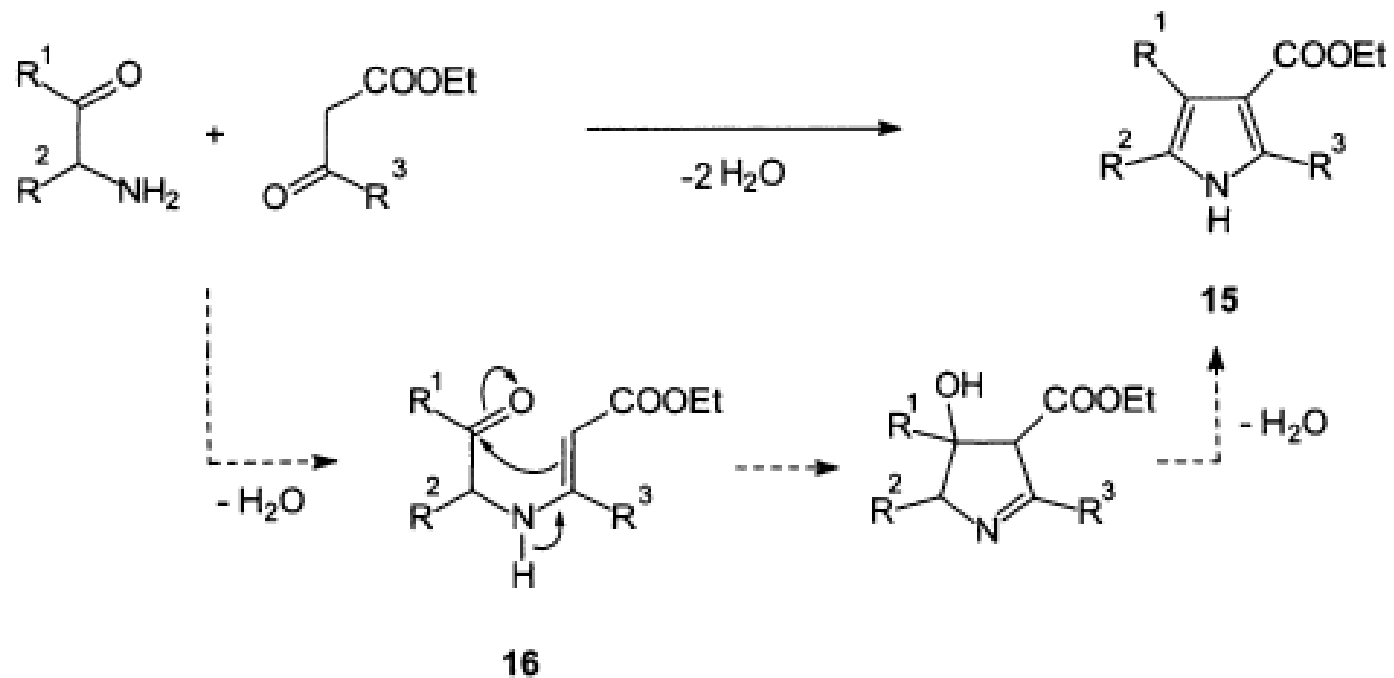


## SÍNTESIS DE HANTZSCH





# SÍNTESIS DE KNORR



## Ludwig Knorr †.

Von Prof. DRUGS, Bochum a./W.

(Eingeg. 28. 1921)

Erstbildd und sozusagen erfüllt die Nachricht von Hinscheiden Ludwig Knorrs den großen Kreis seiner Freunde, Schüler und Verehrer. Wie es auch den Mitwirkenden kein Geheimnis, daß die Gesundheit des, sind so billigen Mannes, der die Stellung eines Oberleitenden hatte, leider schon erschüttert war, so hatten wir doch alle die Hoffnung, daß er sich wieder kräftigen und nach manchen Jahre den Seiten und der Wissenschaft, in der er über alles hing, erlauben könnte. Und wenn er selbst in vertrieben Kreis einmal solchen ersten Gedankens Ausdruck gab, so verjagte doch die sonstige Harmonie, die sein inneres Wesen durchschleuderte, bald seine Züge wieder so, daß jeder gerne noch einen Tag, hellen Lebensabend vor ihm ausgeschreit schon möchte. Es ist anders gekommen.

Eine glanzvolle Epoche chemischen Fortschritts blüht alljährlich aus, die des Münchener Laboratoriums unter Adolf Hantzsch mit seinen unzahlbaren Schülern und Mitarbeitern: Emil Fischer, H. von Perlmann, Wilhelm König, Eduard Buchner, Ludwig Knorr, Johannes Thiele und nach manchen anderen Namen verknüpfen diese Zeit erfolgreichster synthetischer Arbeit auf organischem Gebiet: — wie diese von ihnen hat das Gedächtnis vorzeitig überleben, und wie manchen hat der Krieg und seine Erschütterungen und Folgen hinterlassen. Auch Ludwig Knorr hat durch den Krieg und seine Folgen seelisch und körperlich schwer gelitten. Vier Jahre und ein Schilddrüsenwaden im Felde strahlen und er selbst hat im Herbst 1911 sich mit jugendlicher Begierde dem Nationaldienst zur Verfügung gestellt, eine Nationalkommission organisiert und nach Frankreich geführt. Die damit verbundenen Strapazen und Anforderungen überlegen indes seine Kräfte, so daß er schließlich krank von den Fronten heimkehrte und erst nach langem Erholungszeit sich an den durch den Krieg gestellten chemischen Aufgaben beteiligen konnte. Als dann das Unglück der Revolution über uns hereinbrach, warf ihn dieser Schlag schwer nieder; er hat sich nur völlig von ihm erholt. So leben wir und den Zeiten die letzten Jahre viele vergessene Stunden gebracht, in denen seine so glückliche, harmonische Welt- und Lebensanschauung sich wohl schwer durchzusetzen mußte. In Genuß aber war sie doch unbesiegt, denn sie war der Kern seines ganzen Wesens, und alle, die ihn näher kennen, empfinden den Zauber, den irgend diese frischen und warmen Persönlichkeit. Wer in diesen 50 Jahren in dem Chemie studierte, nahm Teil daran, daß das Fach durch eine hochstrebende, sympathische und edle Persönlichkeit vertreten war, er nahm nicht nur chemisches Wissen und Können mit auf den Lebensweg, sondern eine Bereicherung seines Lebensinhalts, die den lebendigen Verkehr mit dem Lehrer entspringt. Was Knorr selbst über dies

Verhältnis von Lehrer und Schüler darbot, sagen folgende schöne Worte von ihm (1910):

„Das Glücklichste auf meine 50 Semester Dozententum ist in jeder Hinsicht ein ungünstiger, und wenn ich nochmals vor die Wahl gestellt würde, ich würde mich wieder für diese Laufbahn entscheiden, denn ich habe den Beruf des Universitätslehrers für den schönsten, den es gibt. Sein Hauptvergnügen ist der erforschende Verkehr mit der Jugend; ihm verbinde ich es, wenn ich vom Mediziner und Optiker meines reinerer Jahre ein ganzes Teil mir bis heute bewahrt habe.“

In diesen Worten liegt wirklich ein großes Stück von ihm. Jeder empfindet, wie sie mit dem Jüngling wirken wollten. Und so ist es kein Zufall, daß auch seine wissenschaftlichen Arbeiten den 50-er und 60-er Jahren von Idealismus und Optimismus getragenen Forscher erkennen lassen.

Nehmen wir die Arbeiten der Erlanger und Würzburger Zeit: die synthetischen Versuche mit dem Acetylacetone und verwandten Verbindungen, sie sind Entdeckungspfeiler auf Unbekanntes, von denen er mit ruhiger Güte und Geduld die arbeitsreich und wertvollsten Dinge herangeht. Dann die Morphinderarbeiten: mit vielen Fortschritten dreißig Jahre lang durchgeführt, mit wechselvollem Enthusiasmus und manchen Irrgängen. Es ist hier nicht der Platz, sie näher zu beleuchten, es sind der Aufgabe und Probleme zu viel und die professionellen Verhältnisse dieser Alkoholdruppe verschieden. Sie sind heute hinsichtlich einer resoluten Aufklärung und der Totalanalyse. Knorr ist nicht müde geworden, immer neues, wertvolles experimentelles Material beizubringen und in originellen Kombinationen sich eine Vorstellung von dem Aufbau dieser komplizierten Pflanzenstoffe zu machen. Kollidie die durch chemische Konstitution unzugänglich waren Forschungen auf dem Tautomeriegebiet. Hier galt es nicht nur jahrelang anstrengende geliebte Konstitutionsaufgaben zu lösen, sondern ihr Licht legt außerdem in einem gewissen künstlerischen Geiz, das ihm aufgedrückt ist. In glücklicher Ergänzung mit anderen, auf diesem Gebiet erfolgreich arbeitenden Forschern, wie W. Wiedemann, Clausen, K. H. Meyer, Hantzsch u. a. hat Ludwig Knorr uns über unzähligen Einblick in das Wesen dieser interessanten Körperklassen der organischen Chemie verschafft.

Es muß anderer Gerechtigkeit vorbehalten bleiben, diese wissenschaftlichen Leistungen zusammenfassend zu verzeichnen. Hier sei nur nochmals der tiefen Trauer Ausdruck gegeben, daß dieses reiche Leben vor der Zeit ausklingen mußte, und dem unendlichen Dank über, denn es so viel gegeben hat.

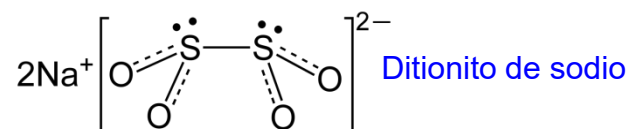
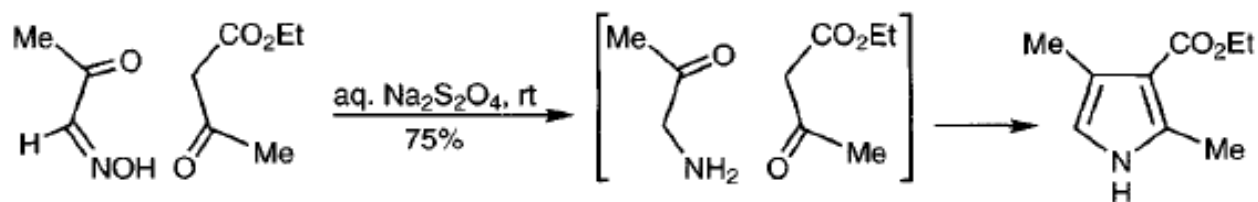
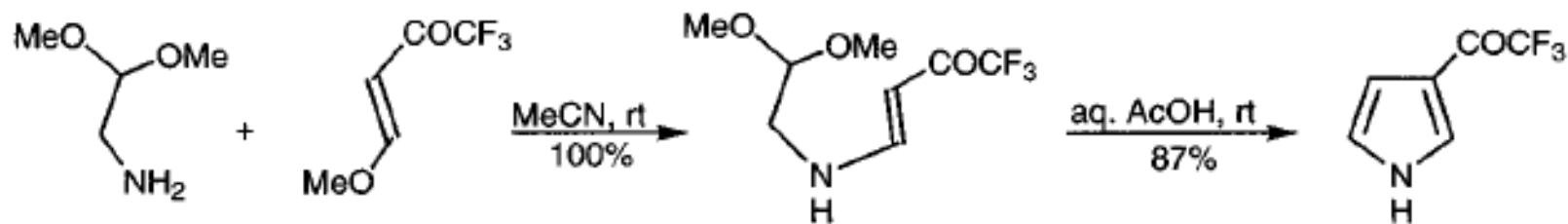
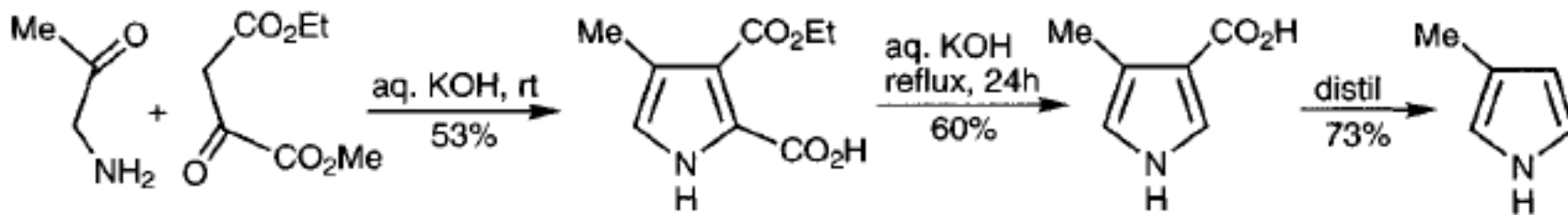
[S. 124.]

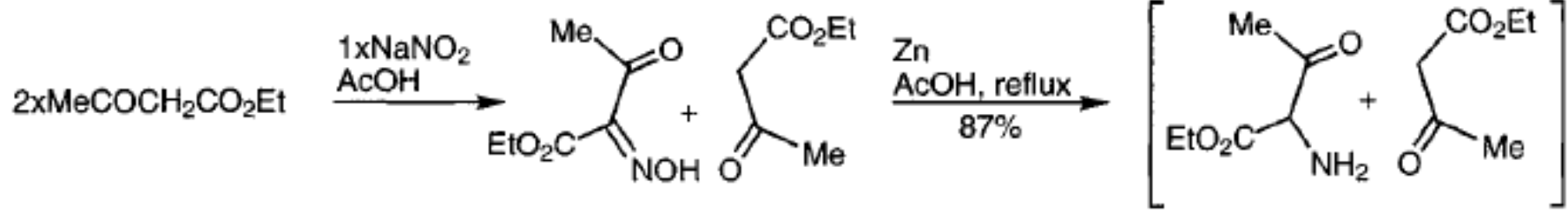


*L. Knorr*

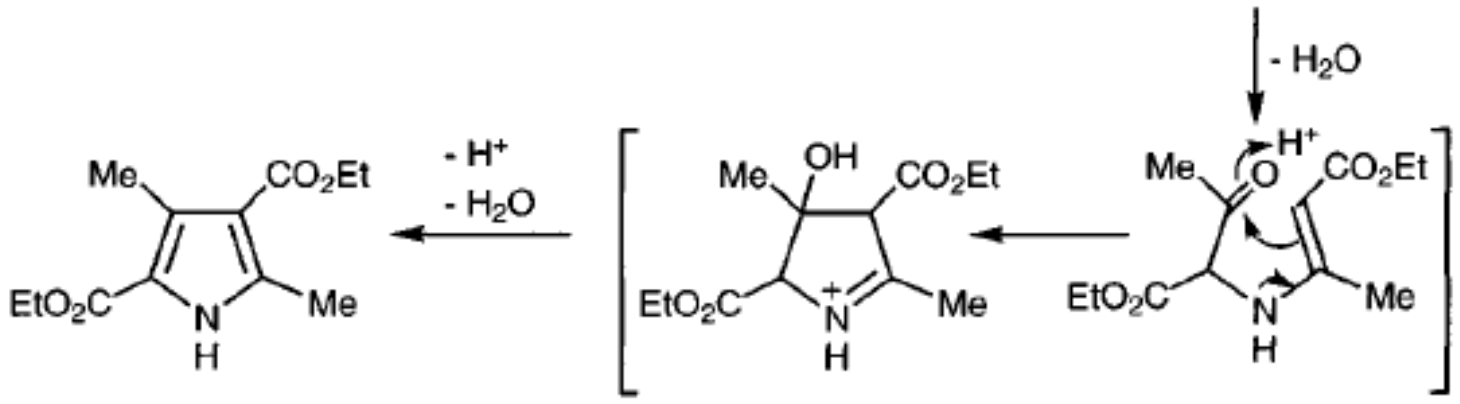
Ludwig Knorr (1859 – 1921) Químico alemán





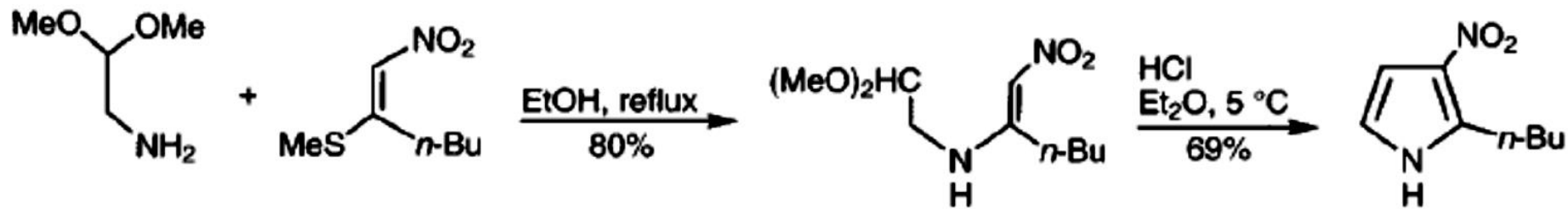
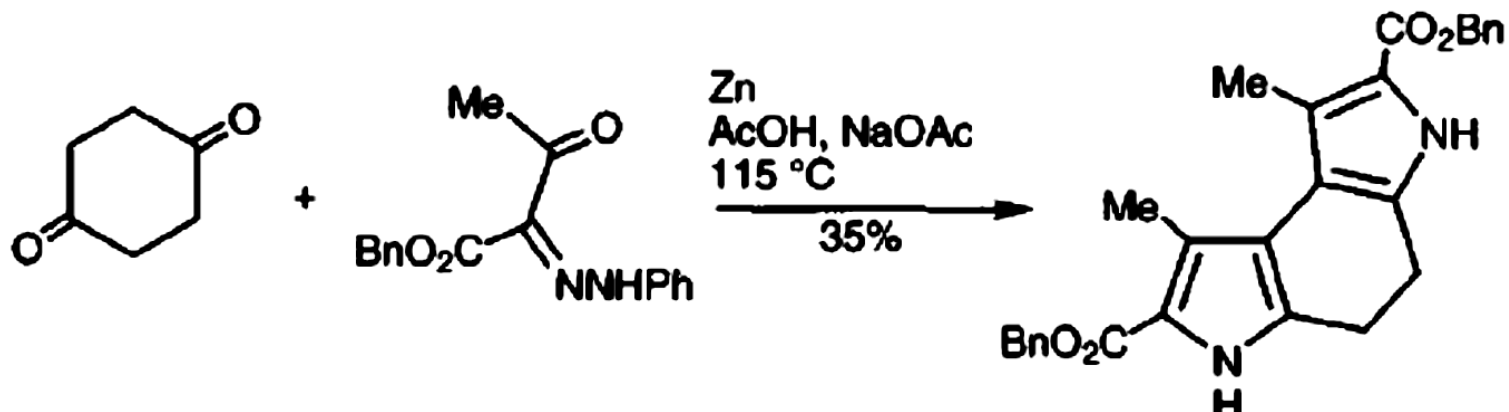


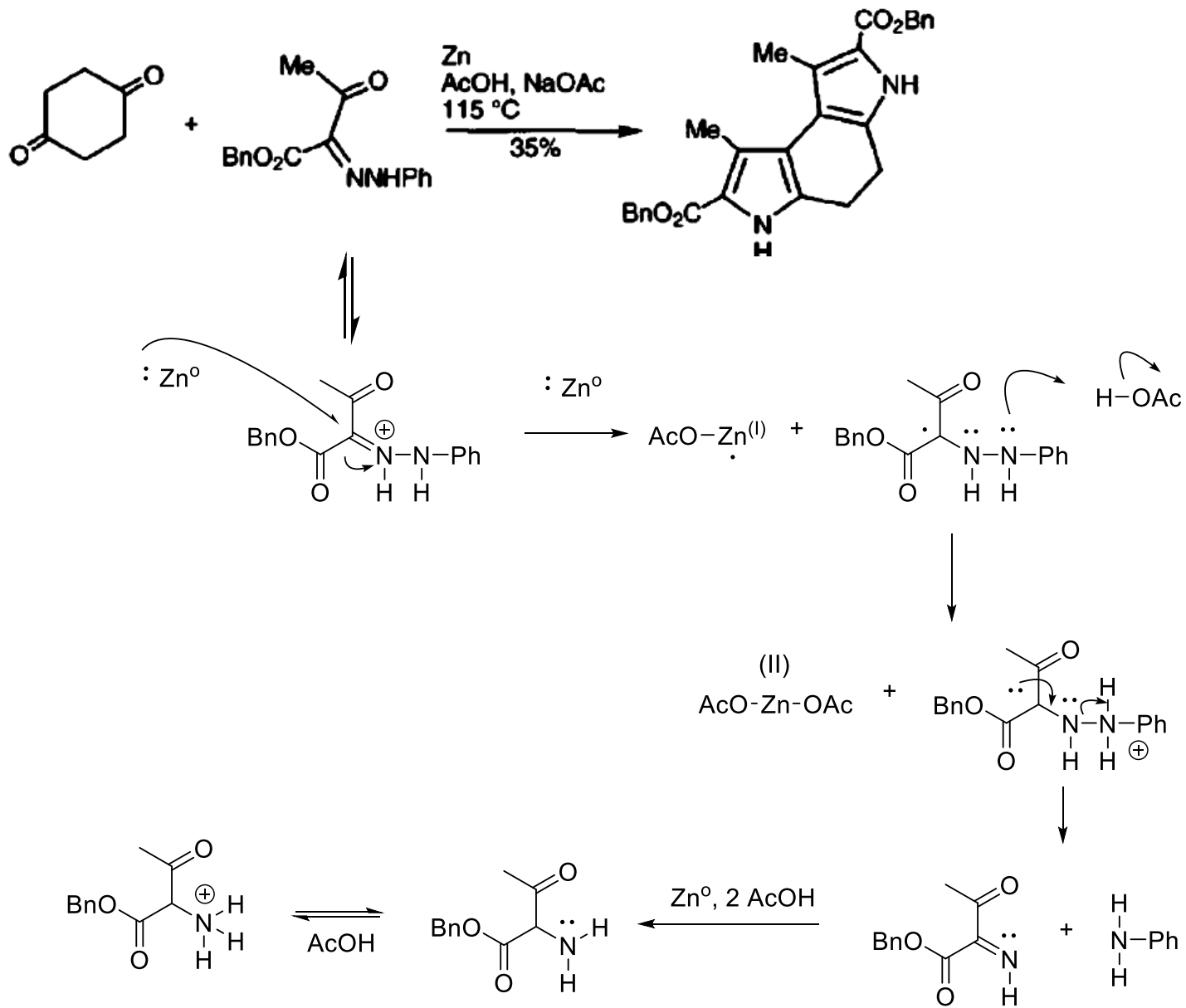
Pirrol de Knorr:



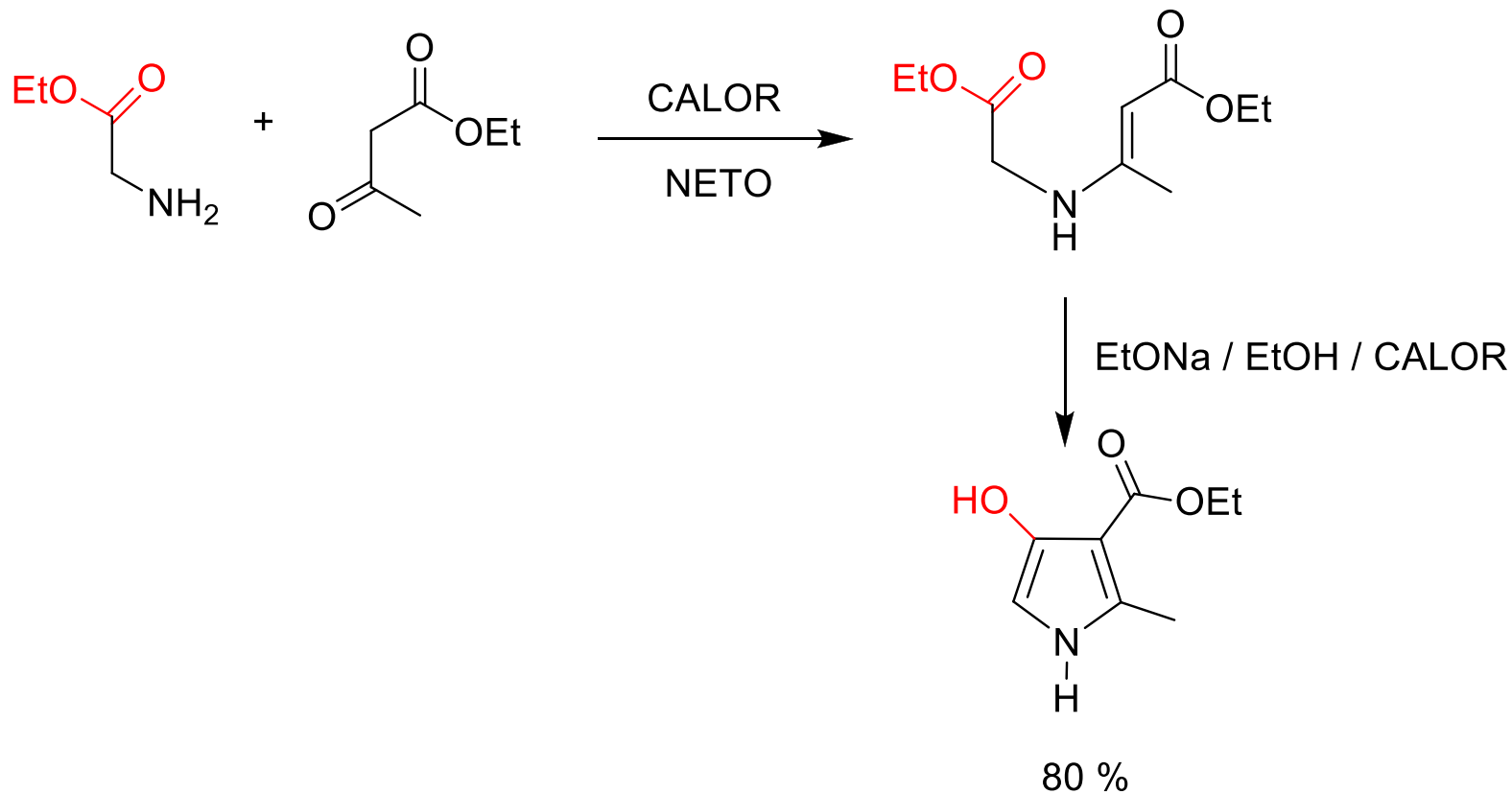
2,4-Dietoxicarbonil-3,5-dimetilpirrol







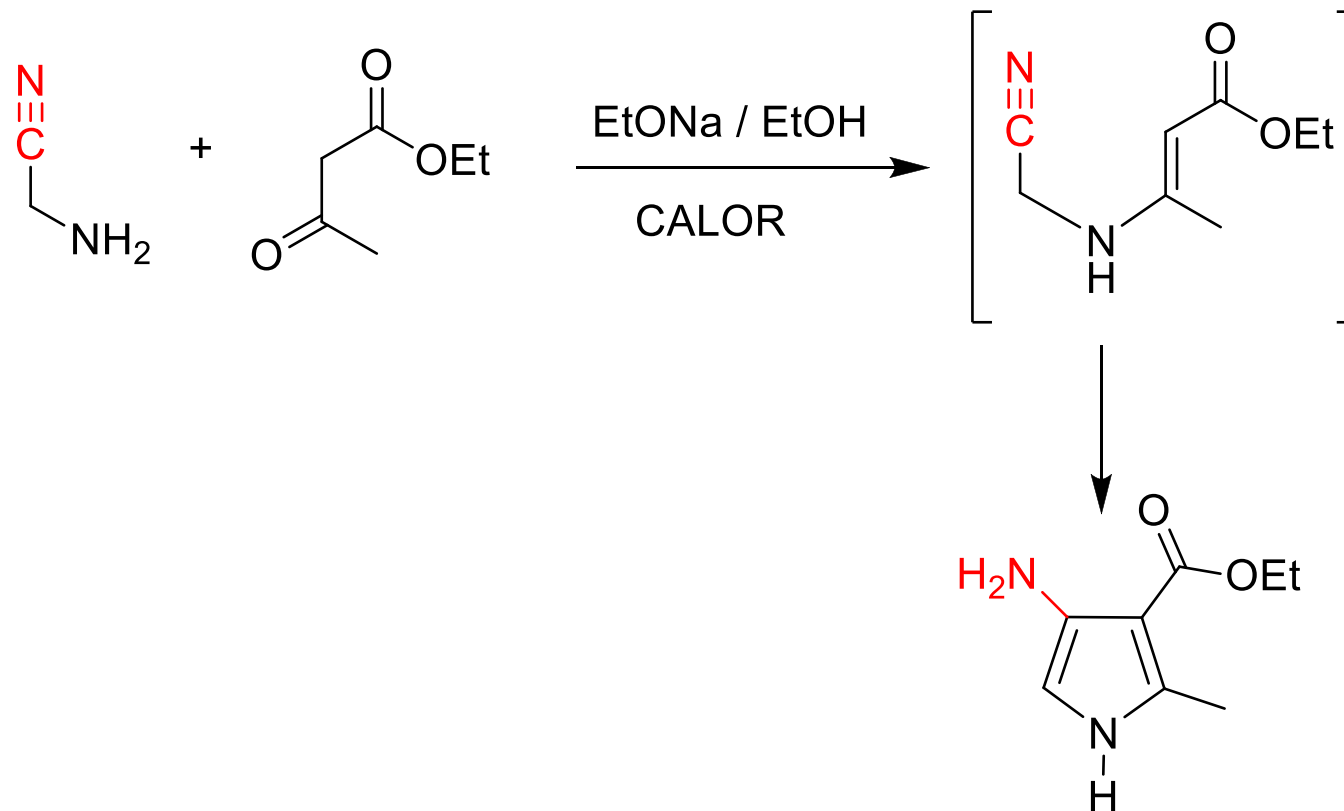
## VERSATILIDAD DE LA REACCIÓN DE KNORR



**Hidroxipirroles**

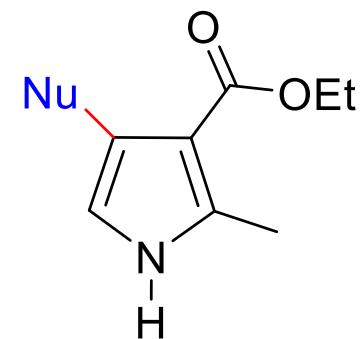
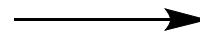
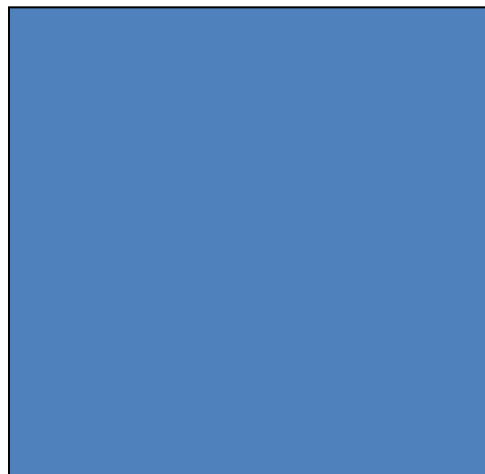
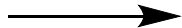
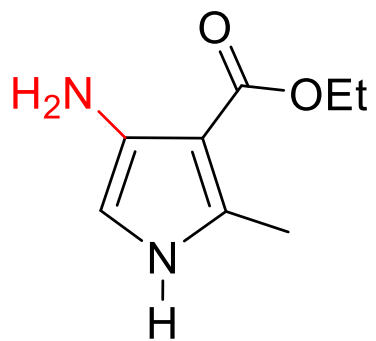


## VERSATILIDAD DE LA REACCIÓN DE KNORR



**Aminopirroles**

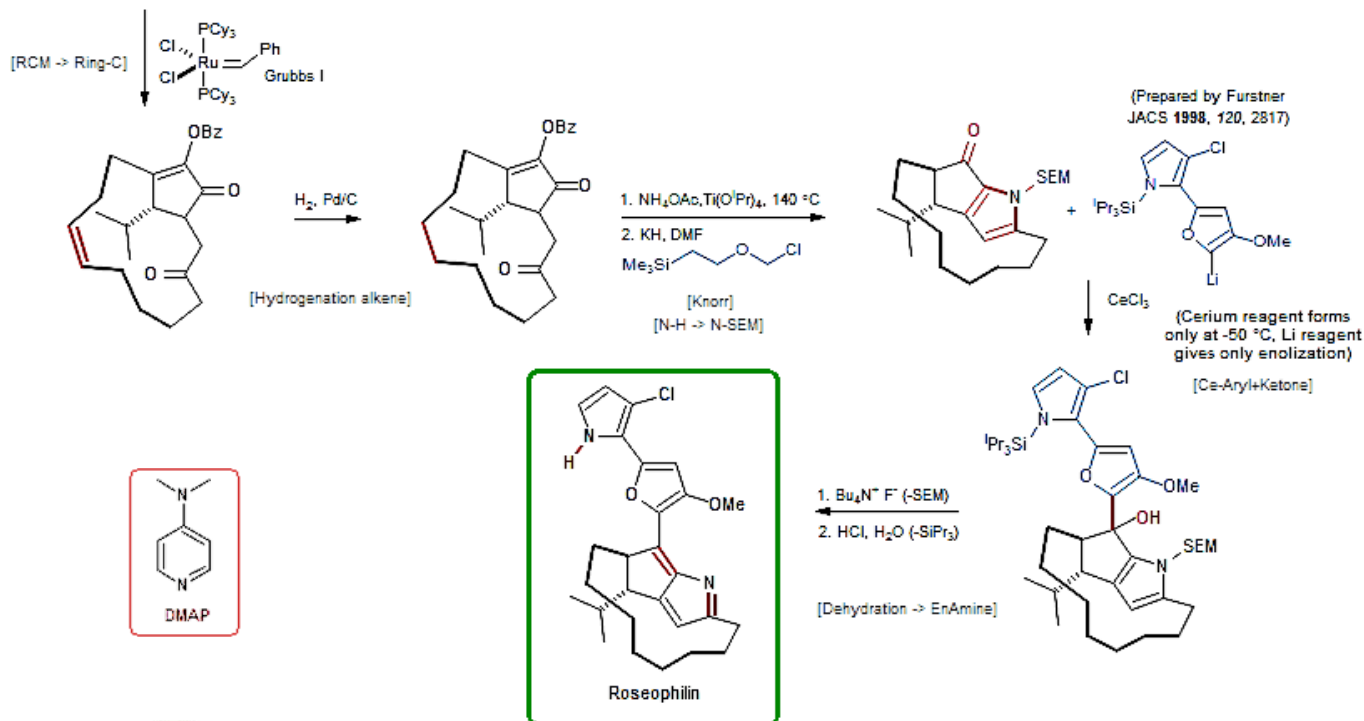
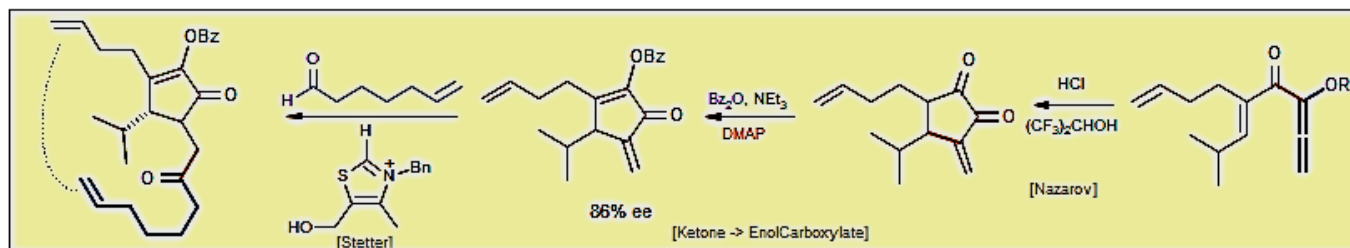
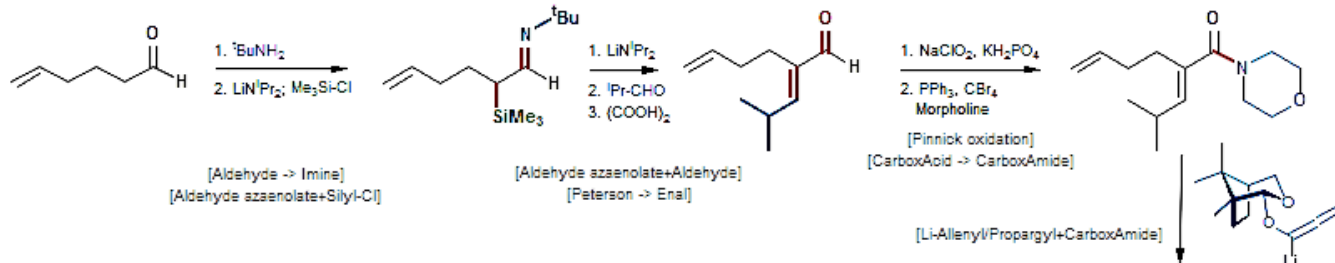




# Roseophilin

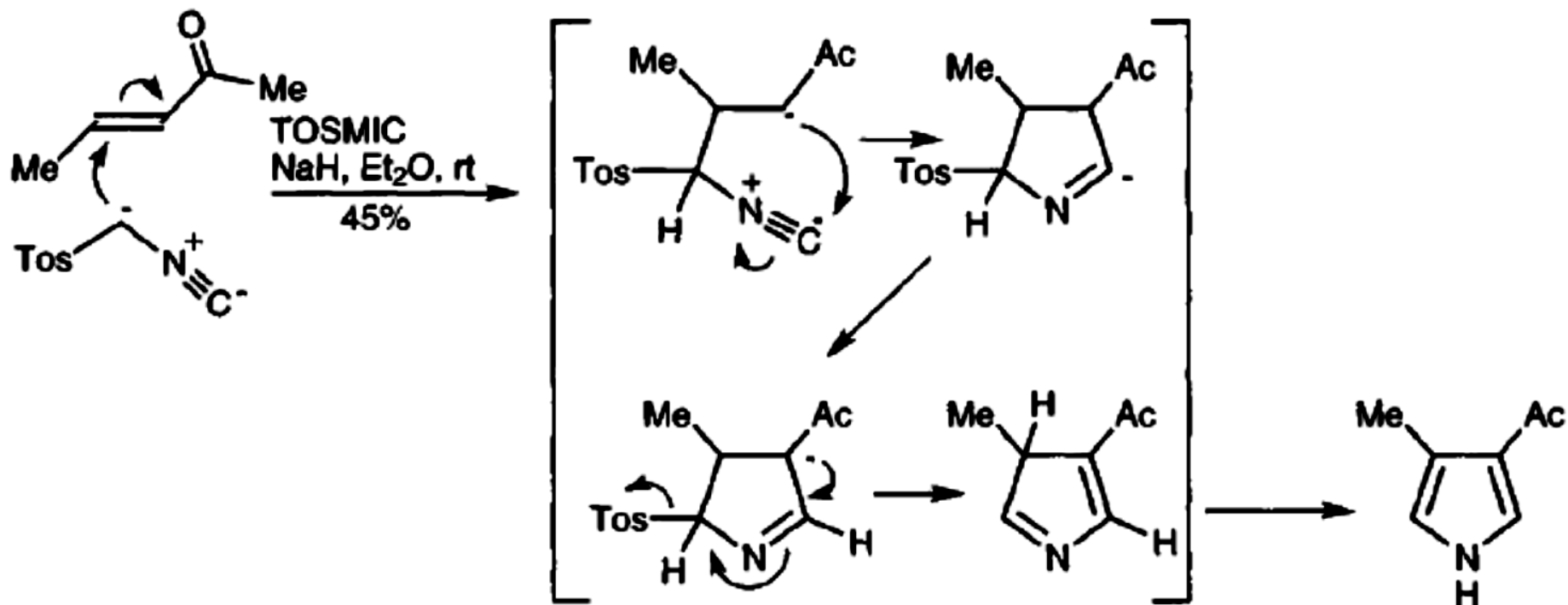
01-18

Harrington, P. E.; Tius, M. A. *J. Am. Chem. Soc.* 2001, 123, 8509-8514.



# SÍNTESIS DE van LEUSEN

A.M. van Leusen (Holanda)



SÍNTESIS DE van LEUSEN

Pirroles, imidazoles y Oxazoles

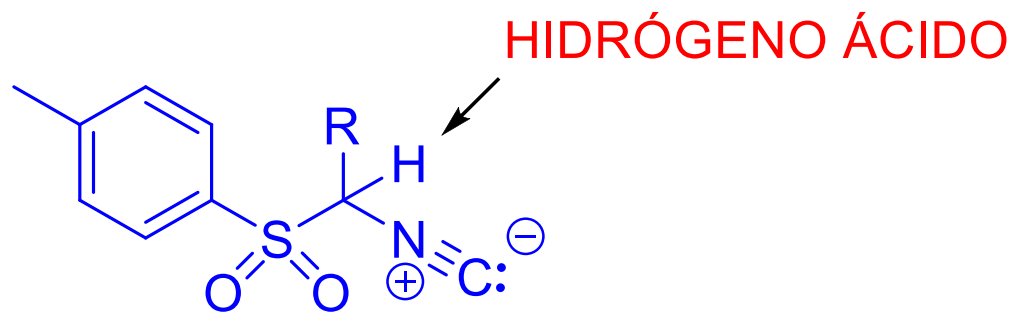
A. M. van Leusen, J. Wildeman, O. H. Oldenziel, *J. Org. Chem.* **1977**, 42, 1153.

A. M. van Leusen, *Heterocycl. Chem.* **1980**, 5, S-111

A. D. van Leusen, A. M. van Leusen, *Org. React.* **2003**, 57, 419

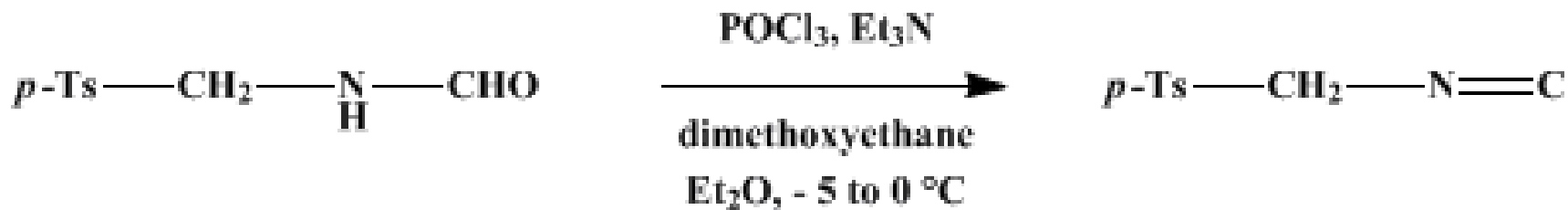
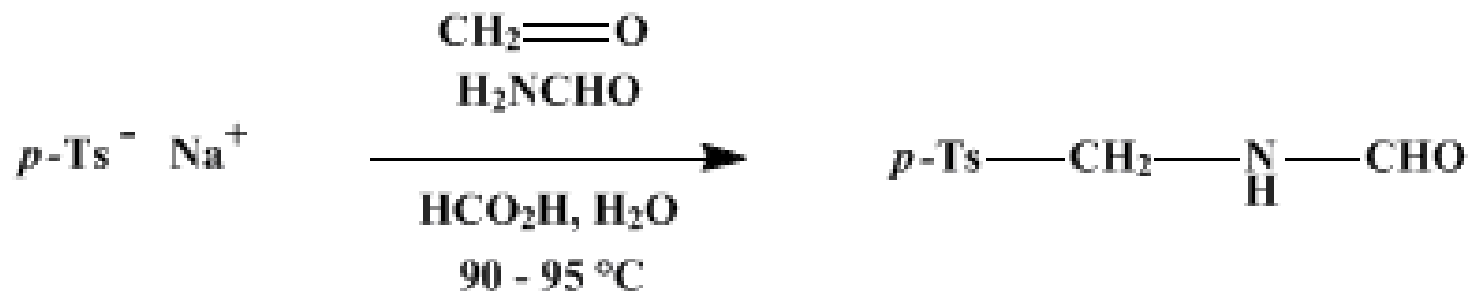


# TOSMIC:



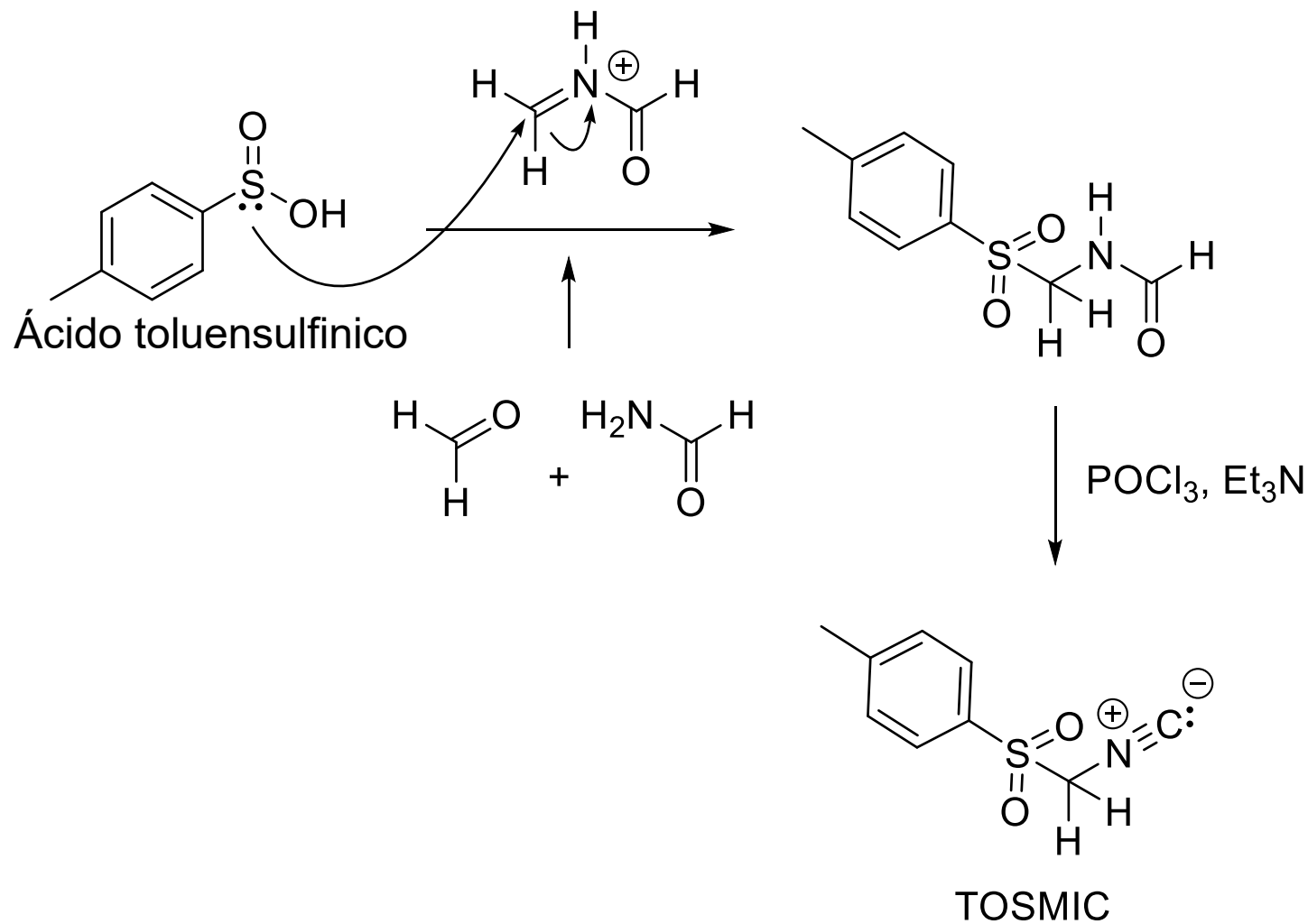
GRUPO SULFONILO

GRUPO ISONITRILO



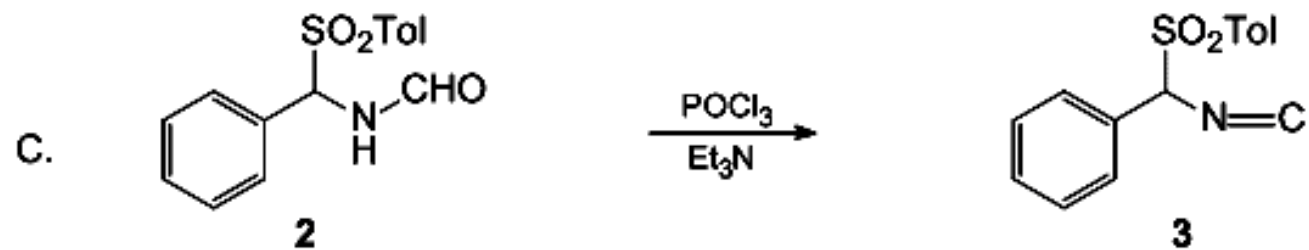
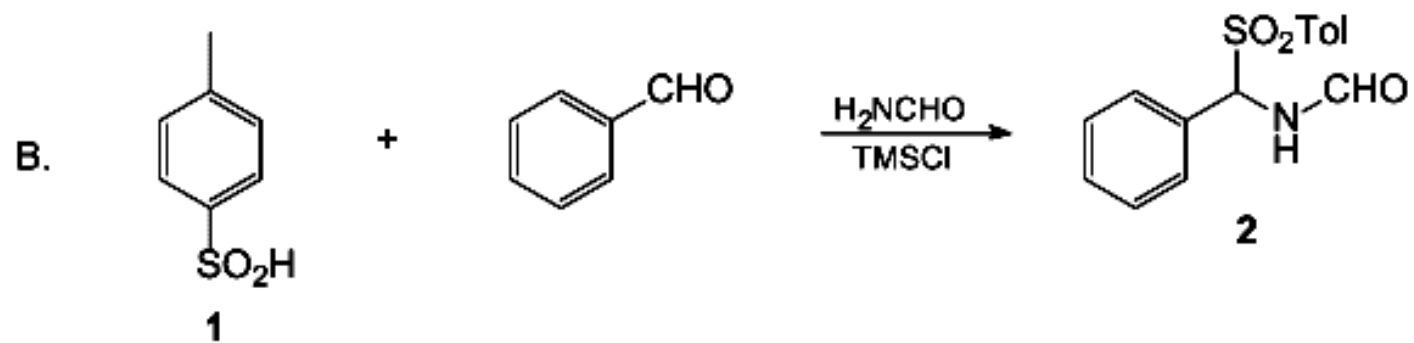
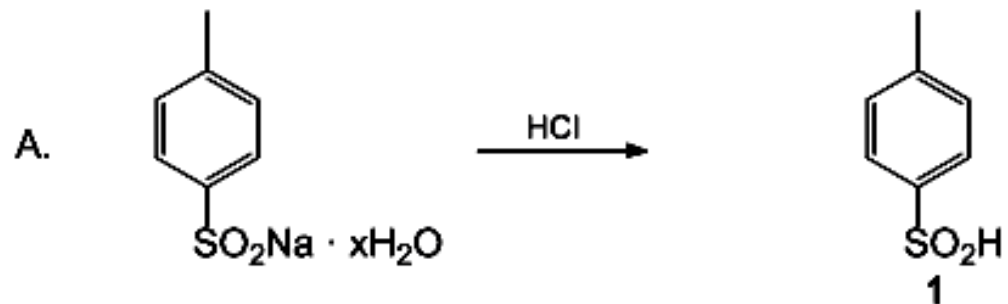
Org. Synth. 1977, 57, 102

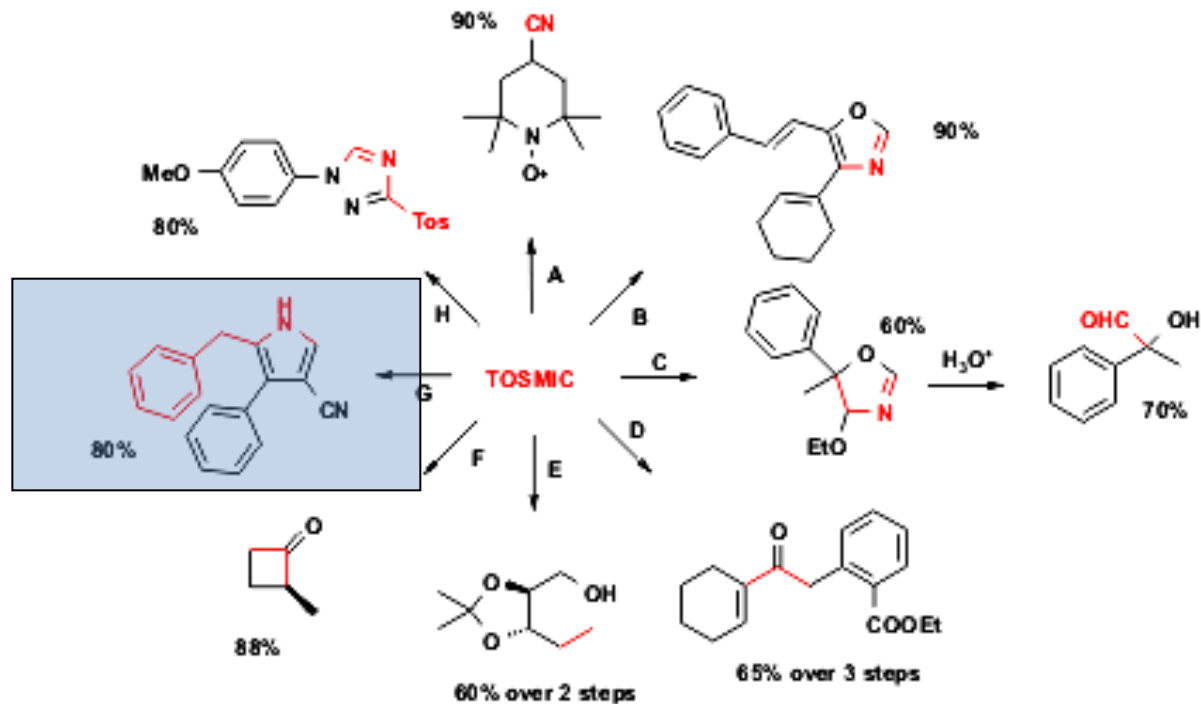




A.M. Van Leusen, *org. Synth.*, 1977, 57, 102.





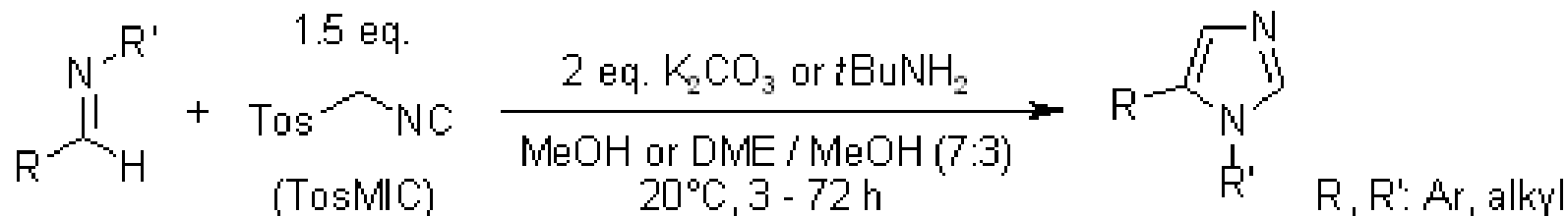


TOSMIC es una molécula muy versátil, un sintón, que permite llevar a cabo muchas reacciones útiles. En las fórmulas de los productos, las partes de color rojo muestran las porciones del producto que se originan a partir del TOSMIC que se usa como reactivo.

- A** (Cianación reductiva selectiva de cetonas): TOSMIC, *t*-BuOK;
- B** (Formación del anillo de oxazol): 1. TOSMIC condensación con ciclohexanona, 2. aldehído cinámico, 2 eq. *n*-BuLi (-70 a 0 °C, 2 h);
- C** (Formación de 4-alcoxi-2-oxazolina): 1. acetofenona, TOSMIC, EtOH; 2. H<sub>3</sub>O<sup>+</sup>;
- D** (Formación de cetonas  $\alpha,\beta$ -insaturadas sustituidas): 1. TOSMIC condensación con ciclohexanona, 2. bromuro de bencilo, *t*-BuOK, DME; 3. H<sub>3</sub>O<sup>+</sup>;
- E** (TOSMIC como reactivo conectivo, reducción): 1. yoduro de alquilo, TOSMIC, PTC, 2. Li, NH<sub>3</sub>(liq.);
- F** (TOSMIC como reactivo conectivo, hidrólisis): 1. TOSMIC, dialquilación 2. H<sub>2</sub>SO<sub>4</sub> (50%), sulfolano, 20 a 100 °C, 2 h;
- G** (pirroles a partir de aceptores de Michael): **TOSMIC bencil-sustituído, NaH, acrilonitrilo;**
- H** (Formación de triazol): sal de diazonio, TOSMIC, K<sub>2</sub>CO<sub>3</sub>, DMSO, MeOH, H<sub>2</sub>O, -10 °C.



**Chemistry of sulfonylmethyl isocyanides. 12. Base-induced cycloaddition of sulfonylmethyl isocyanides to carbon,nitrogen double bonds. Synthesis of 1,5-disubstituted and 1,4,5-trisubstituted imidazoles from aldimines and imidoyl chlorides**



product	base	MeOH / DME	t (h)	yield (%, isol.)	product	base	MeOH / DME	t (h)	yield (%, isol.)
	K <sub>2</sub> CO <sub>3</sub>	7:3	16	82		tBuNH <sub>2</sub>	1:0	20	94
	K <sub>2</sub> CO <sub>3</sub>	7:3	16	43		cHexNH <sub>2</sub>	1:0	17	96
	tBuNH <sub>2</sub>	0:1	20	70		K <sub>2</sub> CO <sub>3</sub>	1:0	20	37

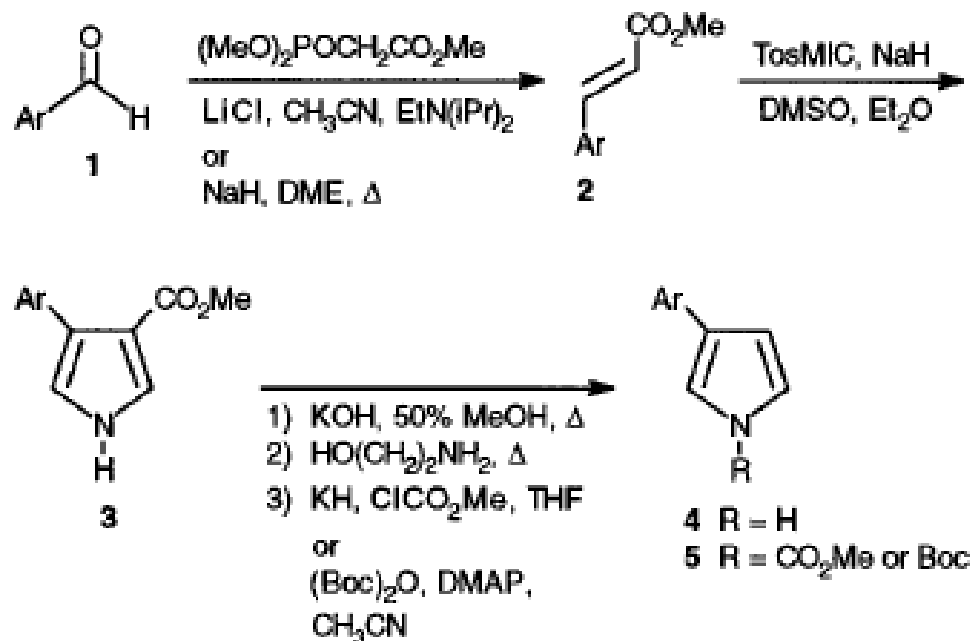
A. M. Van Leusen, J. Wildeman, O. H. Oldenzel, *J. Org. Chem.*, **1977**, *42*, 1153-1159



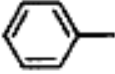
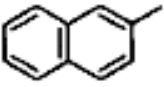
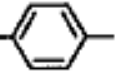
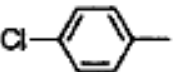
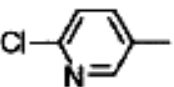
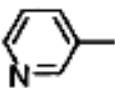

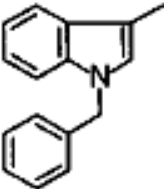
# An Efficient Method for the Synthesis of 3-Arylpyrroles

Neville P. Pavri and Mark L. Trudell\*<sup>†</sup>

*J. Org. Chem.* 1997, 62, 2649–2651



**Table 1. Synthesis of 3-Arylpyrrole Derivatives**

entry	Ar	3 (%) <sup>a</sup>	4 (%) <sup>a</sup>	5 (%) <sup>a</sup>
a		70	82	
b		60	67	
c	Me- 	64	63	88 <sup>b</sup>
d	Cl- 	60	81	84 <sup>b</sup>
e	Cl- 	68	70	86 <sup>c</sup>
f		64	65	
g		60	60	80 <sup>b</sup>
h		48	70	

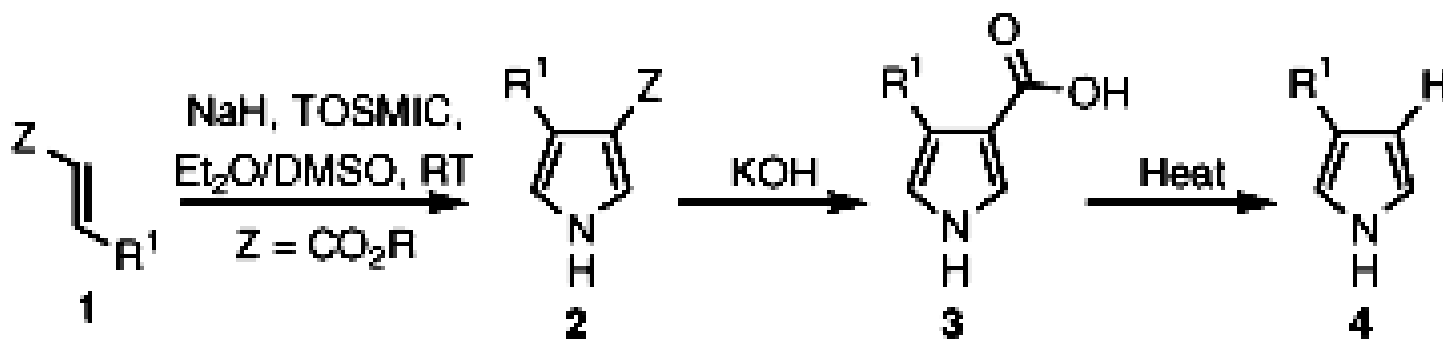


# One-Step Synthesis of 3-Aryl- and 3,4-Diaryl-(1*H*)-Pyrroles Using Tosylmethyl Isocyanide (TOSMIC)

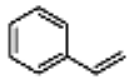
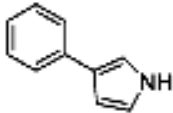
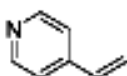
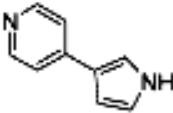
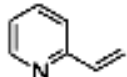
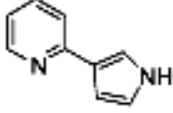
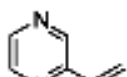
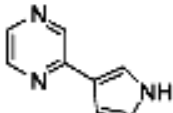
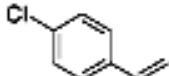
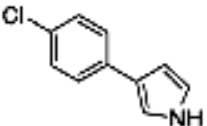
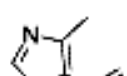
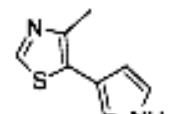
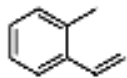
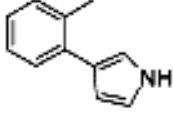
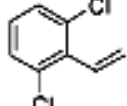
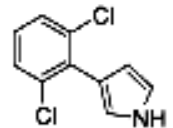
Nicholas D. Smith,\* Dehua Huang, and Nicholas D. P. Cosford

ORGANIC  
LETTERS

2002  
Vol. 4, No. 20  
3537–3539



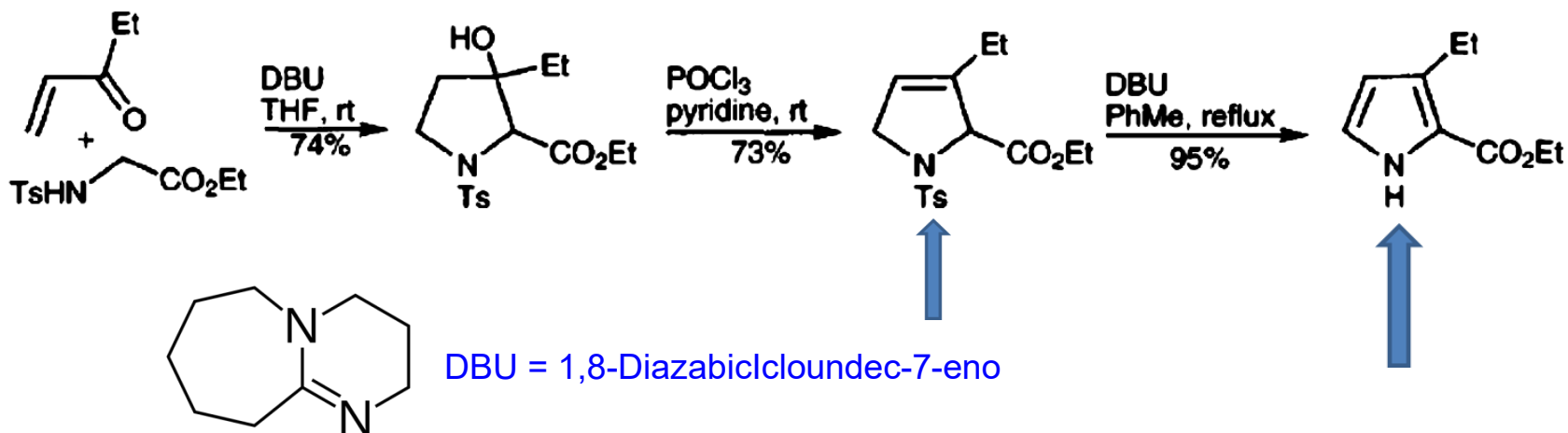
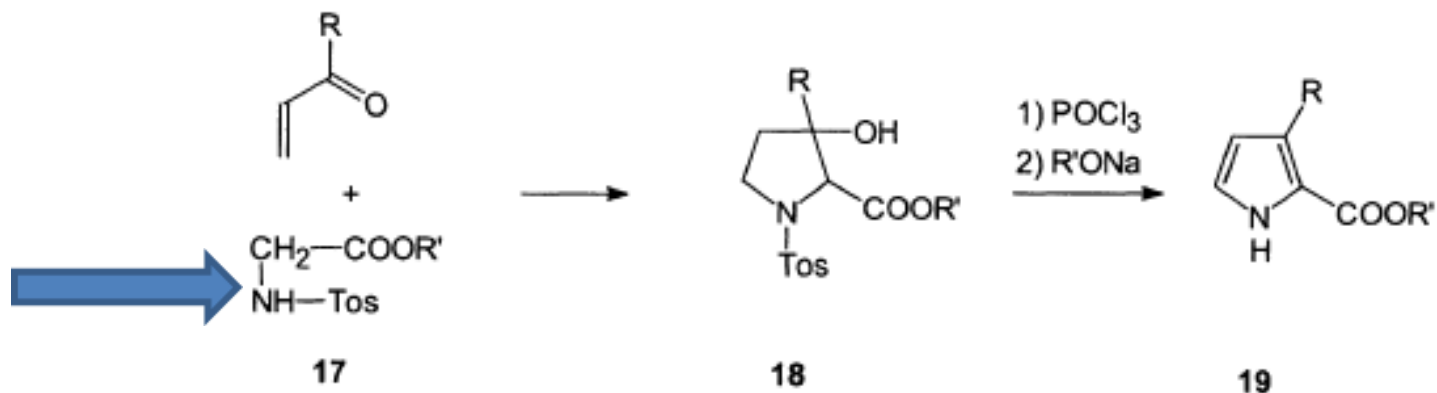
**Table 1.** Synthesis of 3-Aryl Pyrroles Using TOSMIC<sup>a</sup>

entry	substrate	product	T°C/time	yield <sup>b</sup>
1			50°C/18h	47%
2			25°C/2h	67%
3			25°C/2h	74%
4			25°C/1h	76%
5			50°C/6h	58%
6			50°C/2h	39%
7			75°C/2h	44%
8			100°C/18h	48%

<sup>a</sup> TOSMIC (1.3 equiv), NaOtBu (2 equiv), DMSO, *T* in °C. <sup>b</sup> Isolated yield after chromatography.



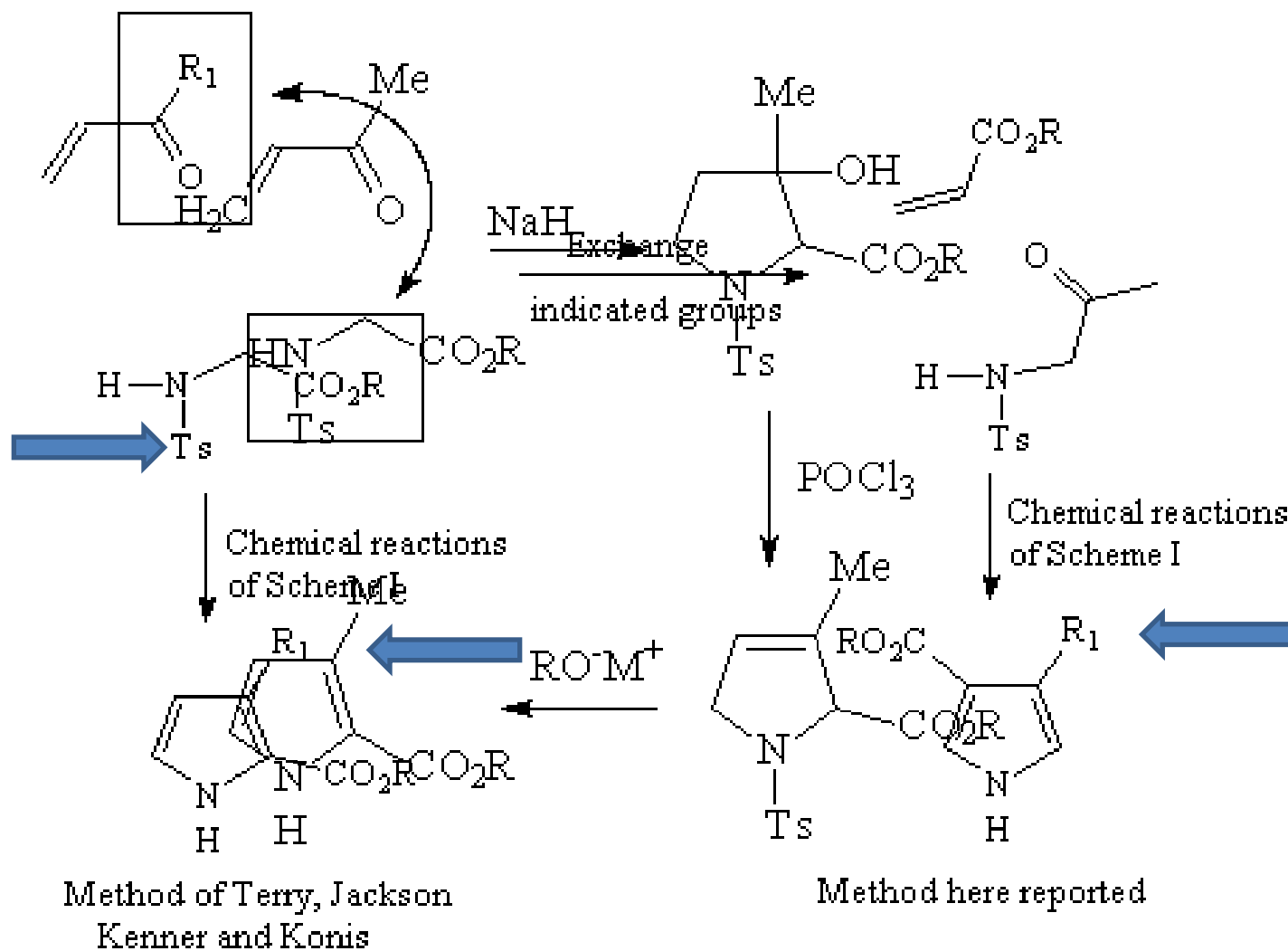
# SÍNTESIS DE TERRY

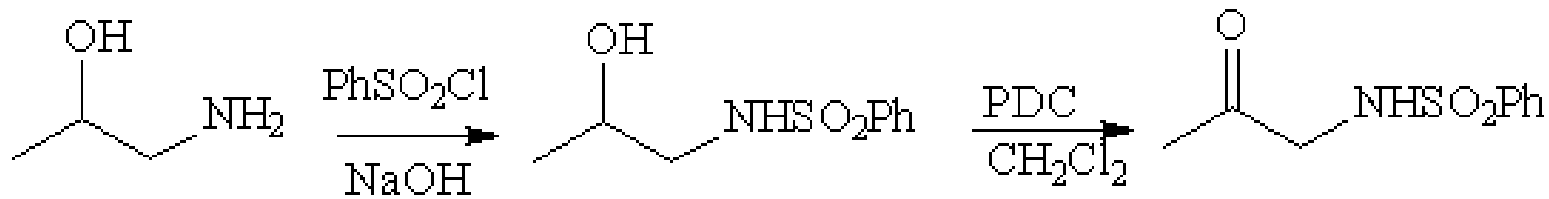


Terry, W.G.; Jackson, A.H., Kenner, G.W.; Konis G., *J. Chem. Soc.*, 1965, 4389

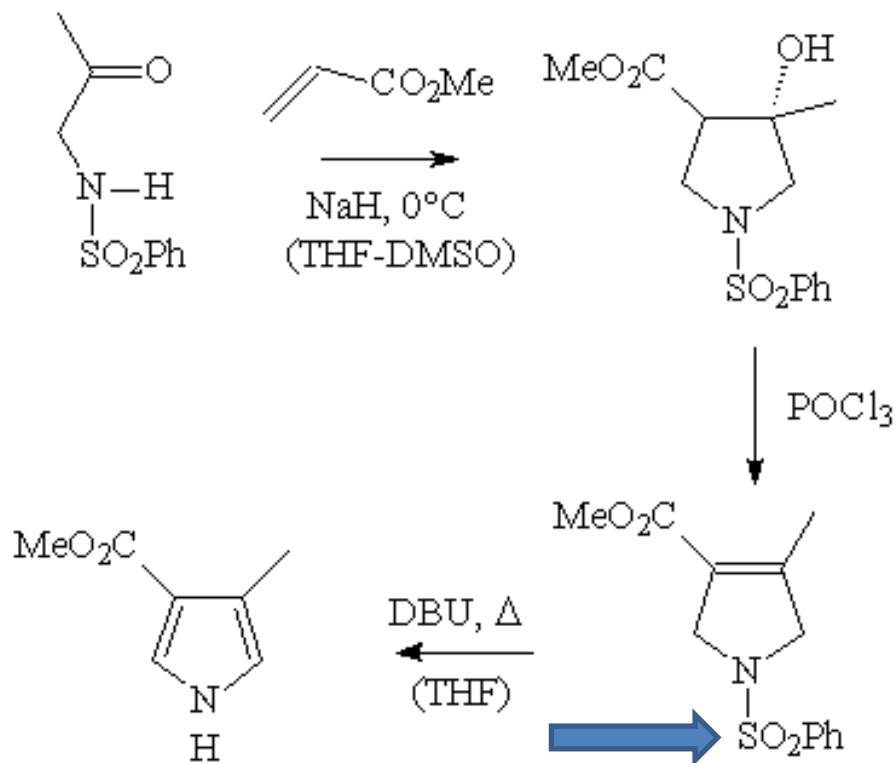


A simple modification to improve the generality of Terry's 3,4-disubstituted pyrrole synthesis  
 G. Fernando Cortés, J. Z. Gustavo Avila and G. Luis Angel Maldonado





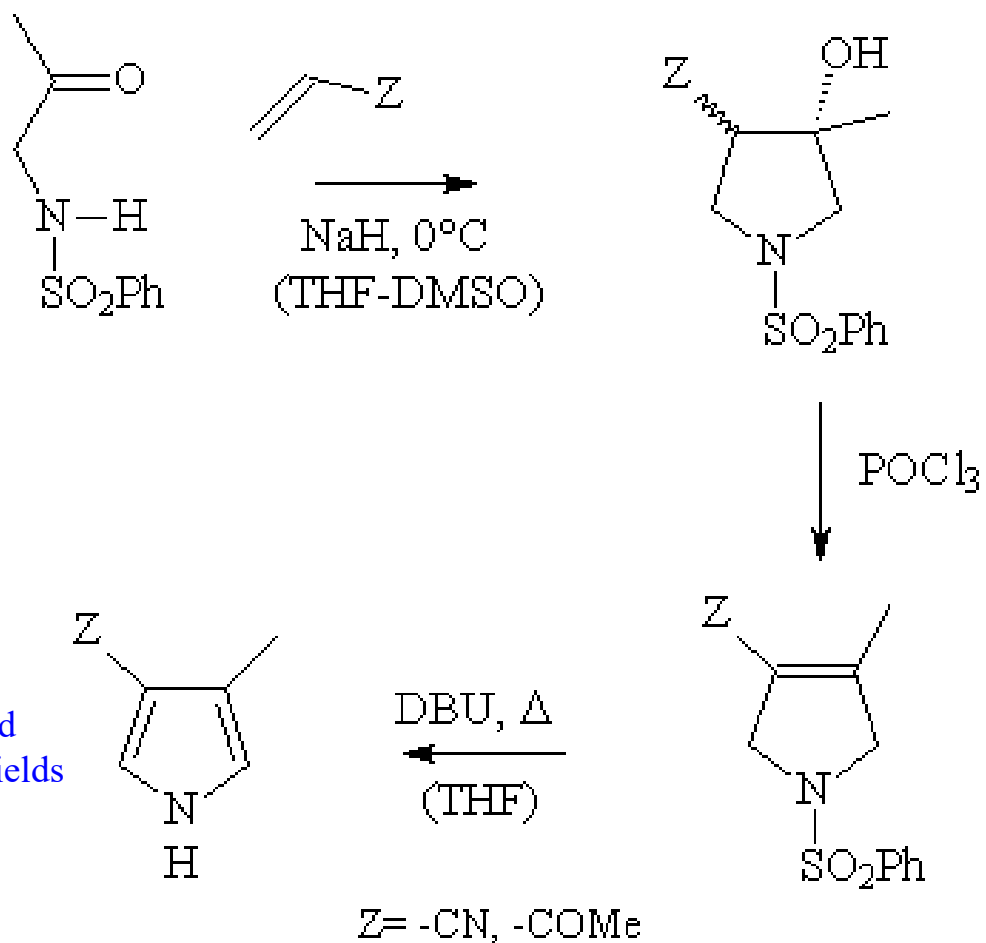
85% overall yield



Pyrrole in ~ 40% overall yield

<https://www.ch.ic.ac.uk/ectoc/echet96/papers/117/index.htm>

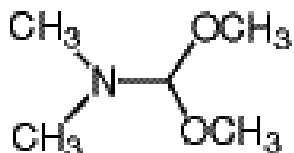
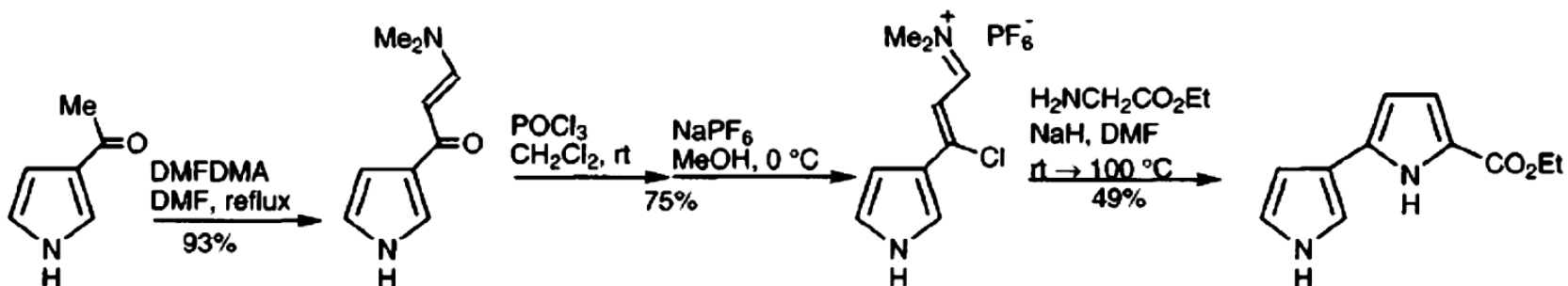
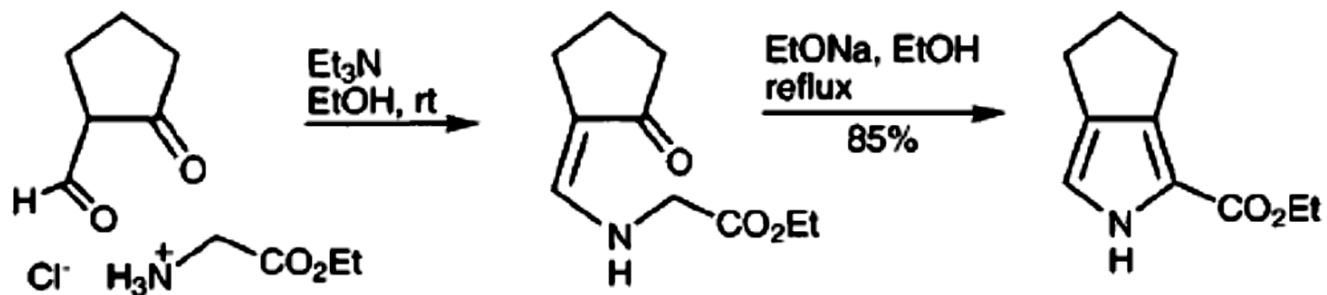




4-Methyl-3-substituted  
 pyrroles in comparable yields  
 (~ 35-40% overall )

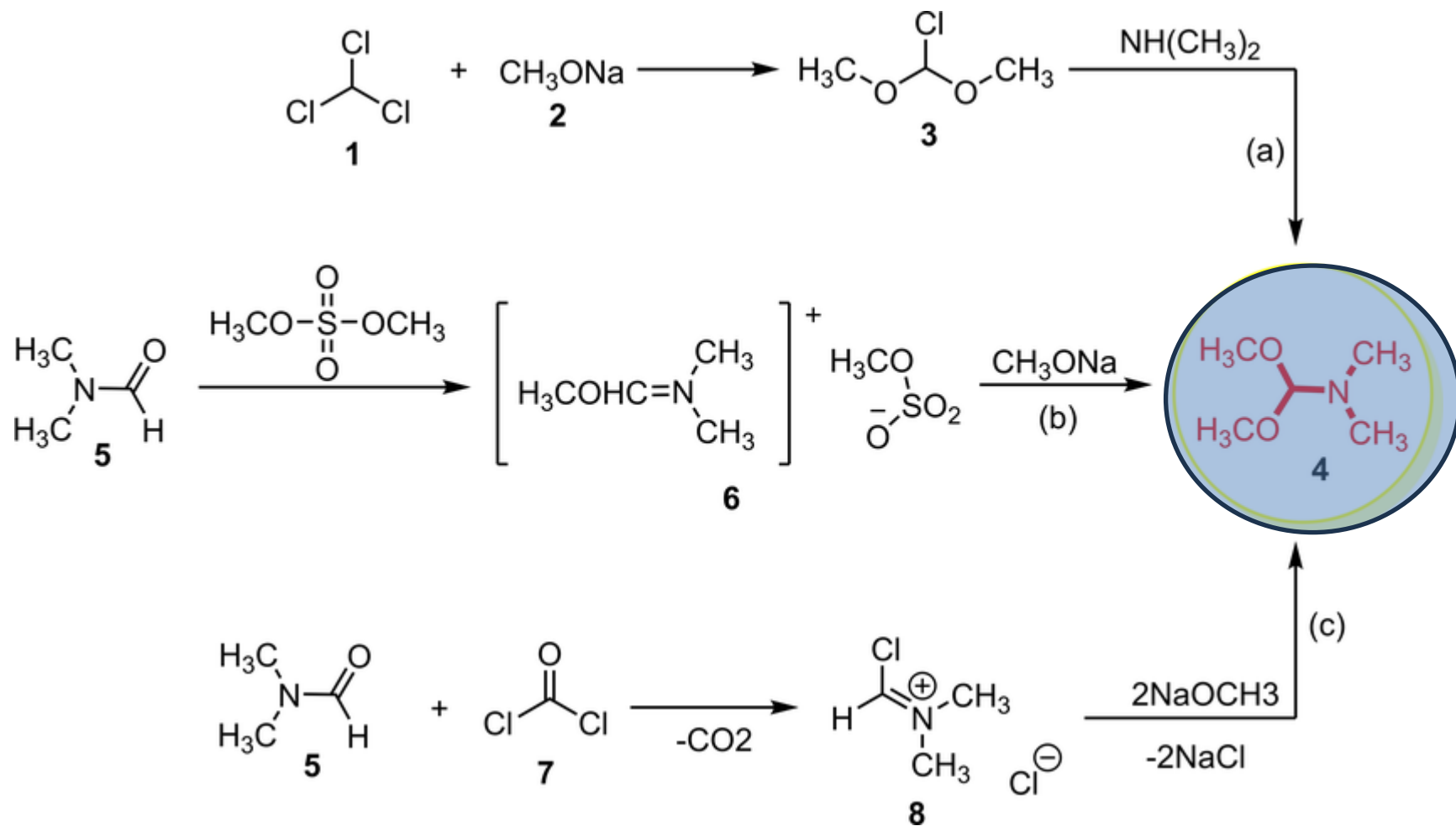


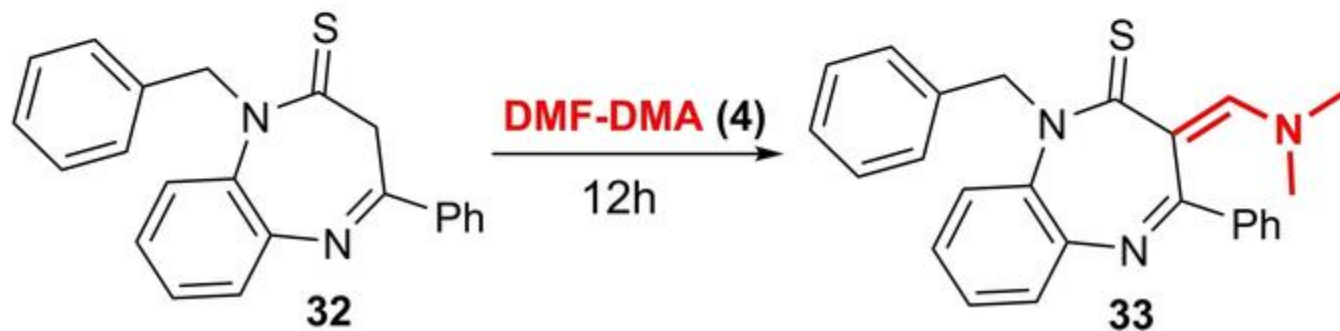
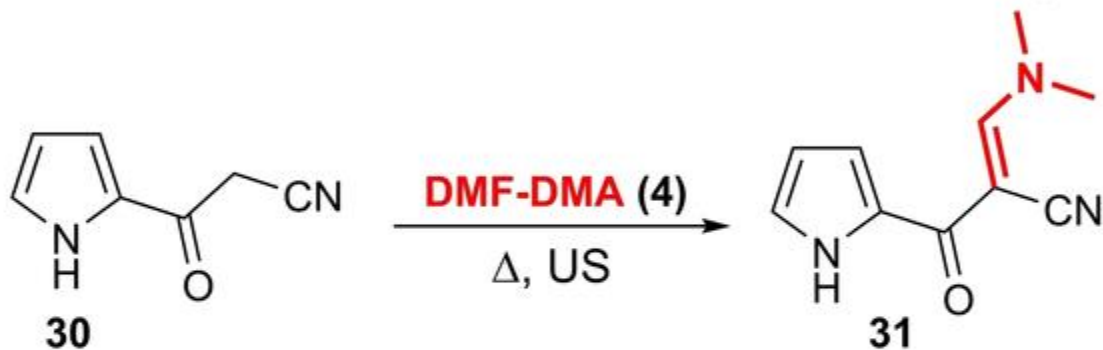
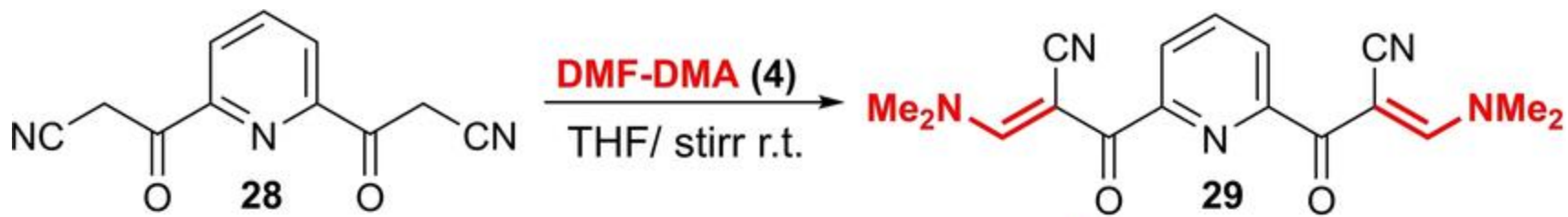
## A PARTIR DE COMPUESTOS 1,3-DICARBONÍlicos Y ÉSTERES DE LA GLICINA

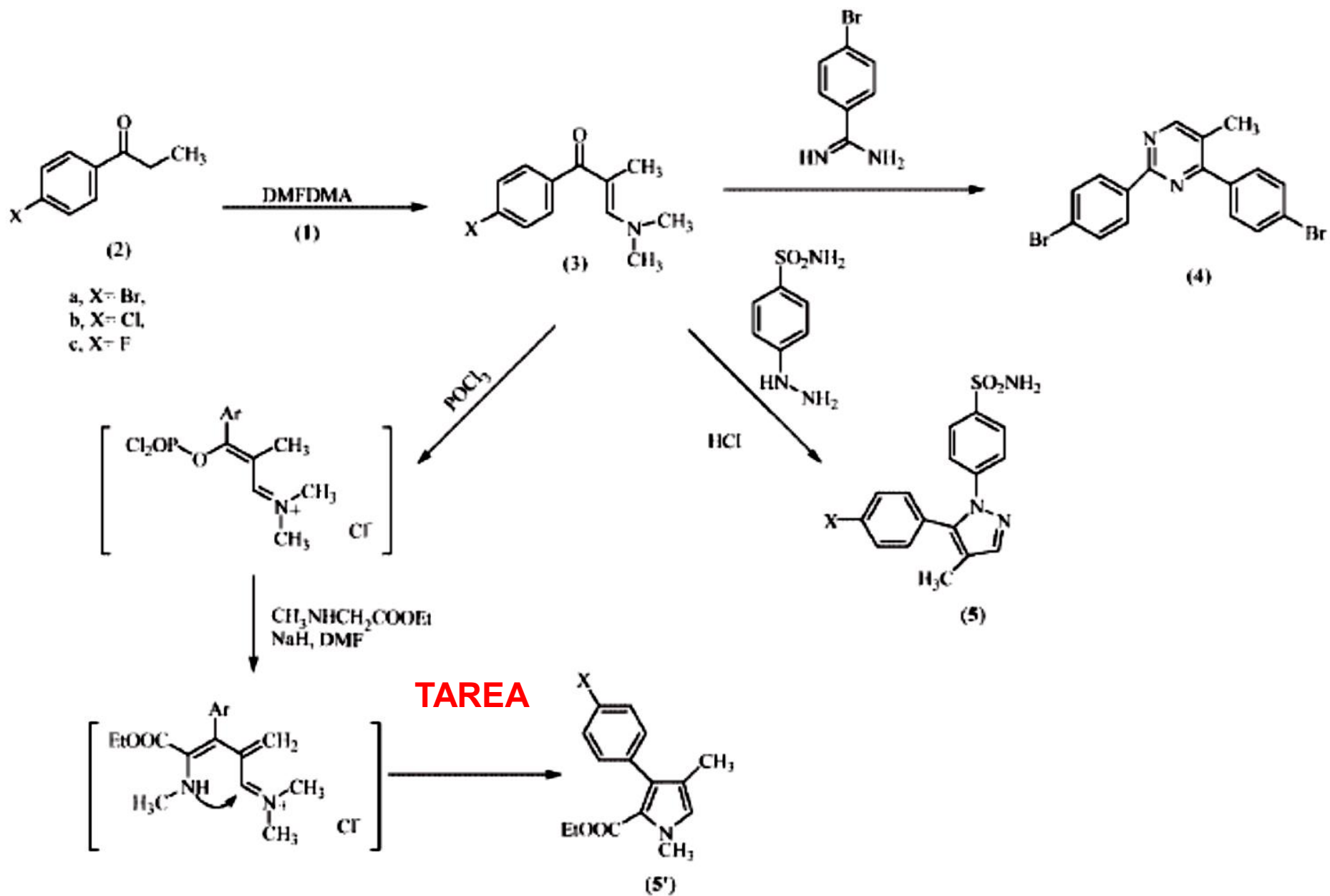


*N,N*-Dimethylformamide  
Dimethyl Acetal

# *N,N*-Dimethylformamide Dimethyl Acetal (DMADMF)



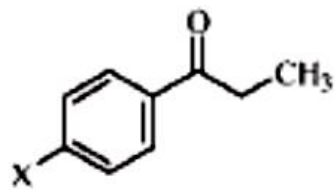




F. A. Abu-Shanab, S. M. Sherif, and S. A. S. Mousa

Journal of Heterocyclic Chemistry 2009, 46, 801-827



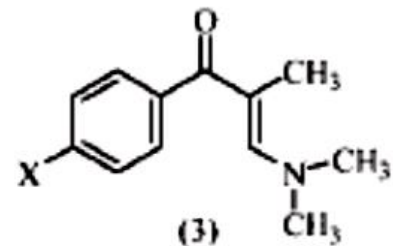


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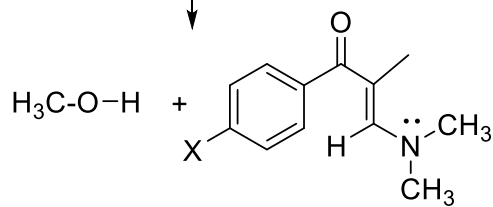
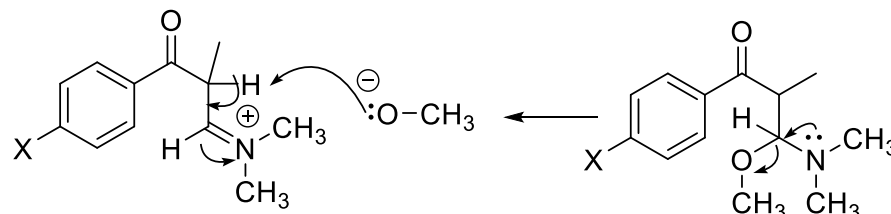
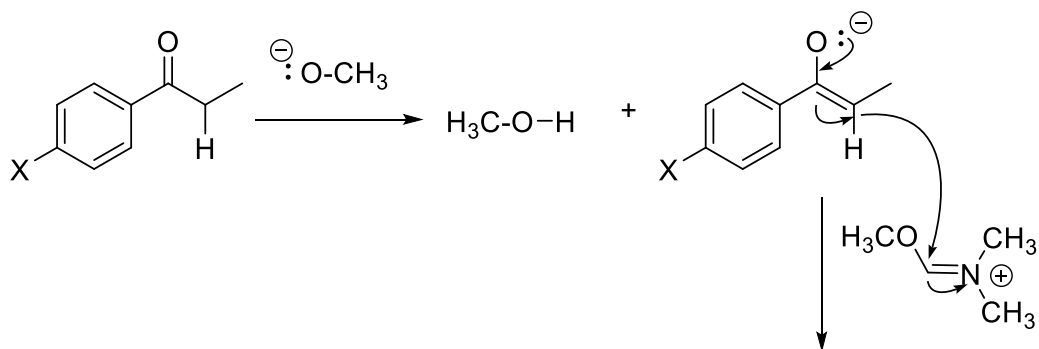
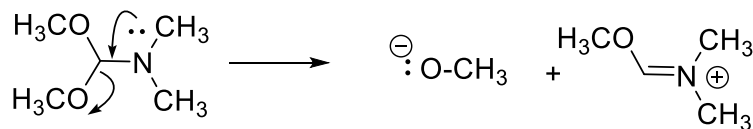
a, X = Br,  
b, X = Cl

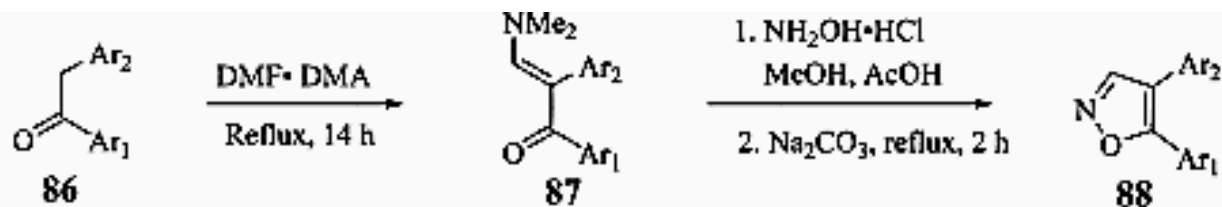
DMFDMA

(1)

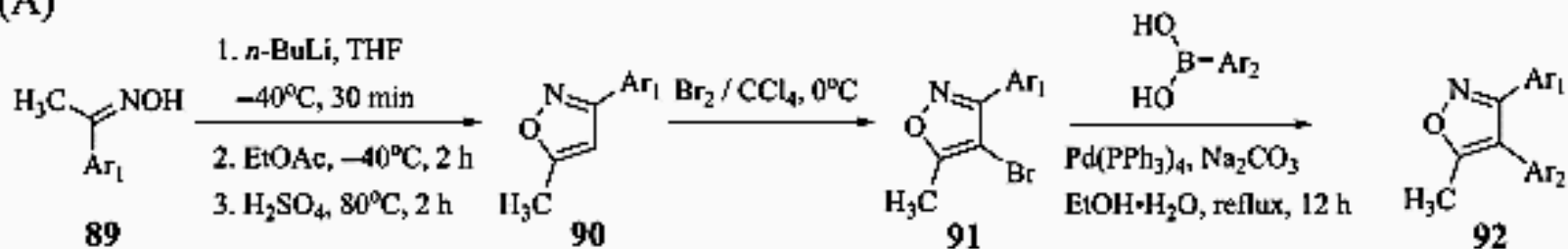


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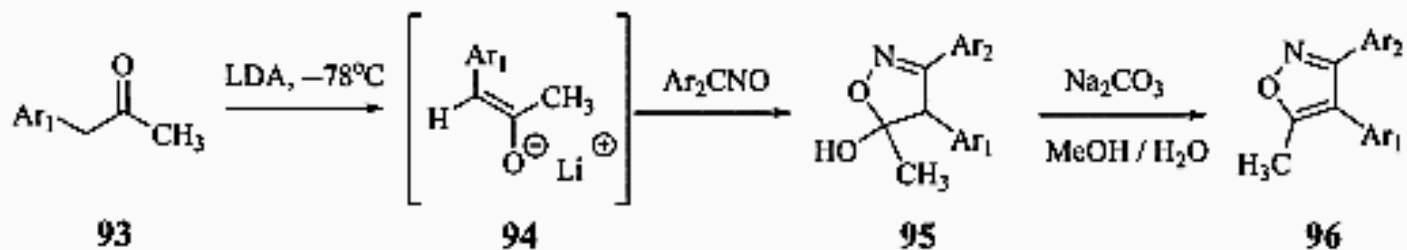




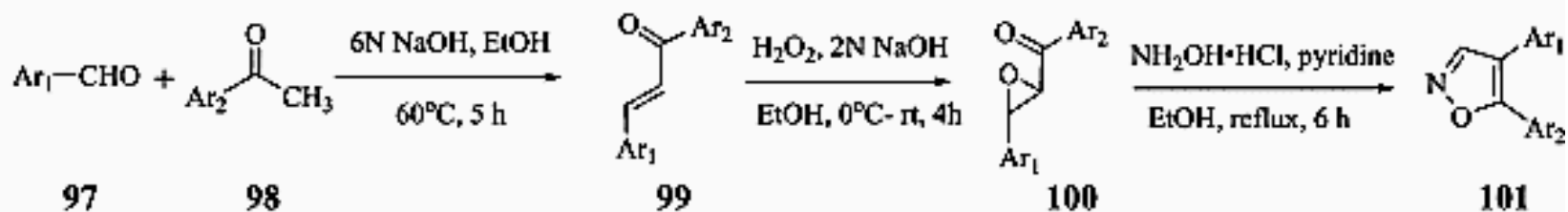
(A)



(B)



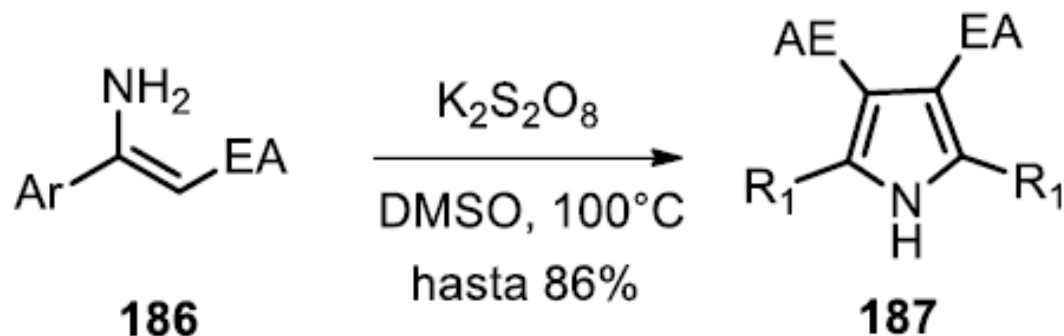
(C)



(D)



A) Gao y Guan, 2016



En 2016, Gao y Guan reportaron la síntesis de pirroles polisustituídos **187** a partir de una ciclación oxidativa de enaminas **186** bajo condiciones libres de metales empleando  $K_2S_2O_8$  como único oxidante (**A**).

Gao, P.; Wang, J.; Bai, Z.-J.; Shen, L.; Yan, Y.-Y.; Yang, D.-S.; Fan, M.-J.; Guan, Z.-H. *Org. Lett.* **2016**, *18*, 6074-6077.



El anión radical sulfato ( $\text{SO}_4^{\cdot-}$ ) es un poderoso agente oxidante ( $E^0 = 2.5 - 3.1 \text{ V}$ ) utilizado ampliamente en procesos de oxidación avanzados (AOP) para degradar los contaminantes ambientales en el agua. Generalmente se genera activando persulfato ( $\text{S}_2\text{O}_8^{2-}$ ) mediante calor, luz ultravioleta o metales de transición, ofreciendo una mayor selectividad y una vida útil más larga que el radical hidroxilo ( $\text{HO}\cdot$ ).

Aspectos clave del anión radical sulfato ( $\text{SO}_4^{\cdot-}$ ):

**Métodos de generación:** Formado a través de la escisión del enlace S-S en persulfato, comúnmente usando metales de transición ( $\text{Fe}^{2+}$ ), calor o fotólisis (254 nm).

**Reactividad:**  $\text{SO}_4^{\cdot-}$  es un fuerte agente de transferencia de electrones que reacciona con contaminantes aromáticos y enlaces insaturados mediante oxidación de un solo electrón.

**Aplicaciones ambientales:** Es muy eficaz para descomponer contaminantes orgánicos persistentes, residuos farmacéuticos y colorantes en el tratamiento de aguas residuales.

**Comparación con ( $\text{HO}\cdot$ ):** A diferencia de los radicales hidroxilo, que pueden ser eliminados por los componentes del agua, ( $\text{SO}_4^{\cdot-}$ ) muestra una alta estabilidad en disoluciones acuosas, lo que lo hace más eficaz en matrices específicas.

**Aplicaciones en biología química:** se utiliza en la oxidación fotoquímica rápida de proteínas (FPOP) para investigar la estructura de las proteínas, y a menudo proporciona una mejor cobertura que los radicales hidroxilo.



Anita Kongor, Manthan Panchal, Viren Mehta, Keyur Bhatt, Dehin Bhagat,  
Devayani Tipre, Vinod K. Jain  
Basketing nanopalladium into calix[4]pyrrole as an efficient catalyst for Mizoroki-  
Heck reaction

Arabian Journal of Chemistry

Volume 10, Issue 8, December 2017, Pages 1125-1135

<https://doi.org/10.1016/j.arabjc.2016.06.019>

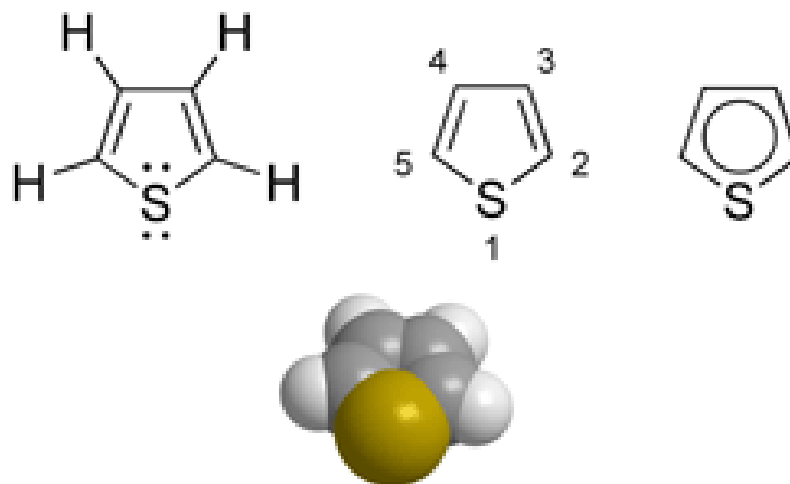
Yukun Cheng, Channing K. Klein and Ian A. Tonks

Synthesis of pentasubstituted 2-aryl pyrroles from boryl and stannyl  
alkynes *via* one-pot sequential Ti-catalyzed [2 + 2 + 1] pyrrole  
synthesis/cross coupling reactions

*Chem. Sci.*, 2020,11, 10236-10242

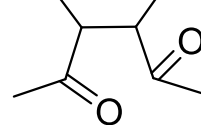
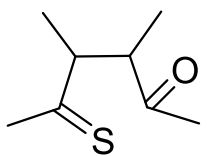
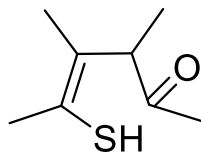
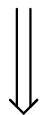
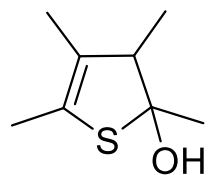


# TIOFENO

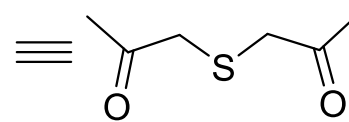
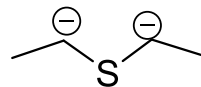
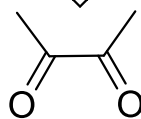
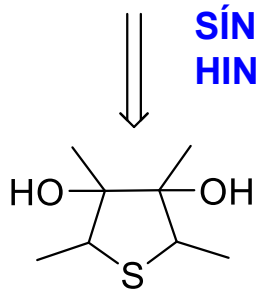


# MÉTODOS DE OBTENCIÓN DE TIOFENO

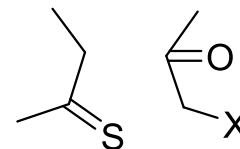
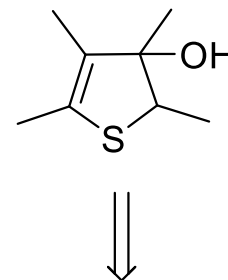
SÍNTESIS DE PAAL-KNORR



SÍNTESIS DE HINSBERGH

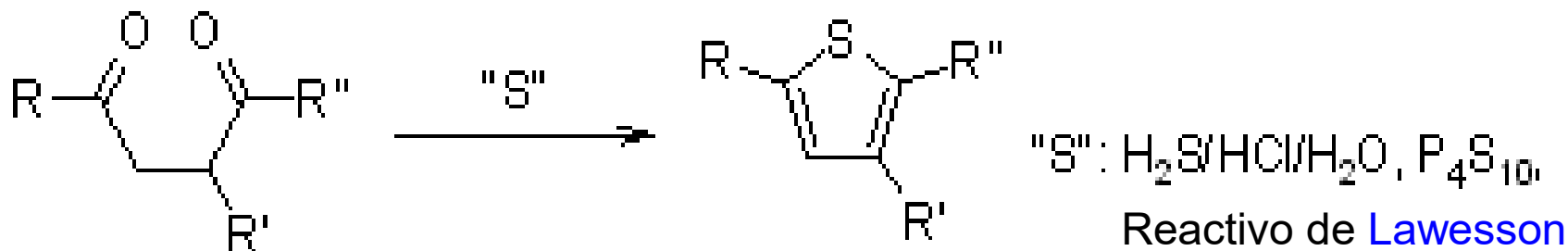


SÍNTESIS DE GEWALD



# Síntesis de Tiofeno de Paal-Knorr

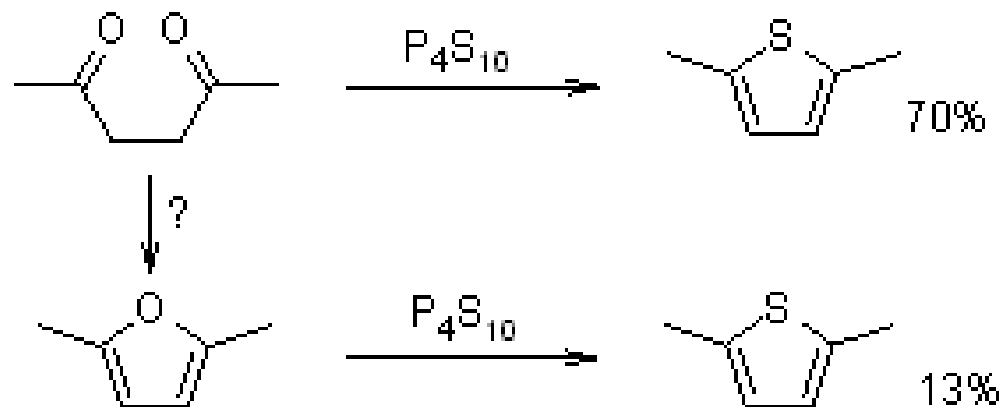
## Síntesis de Tiofeno de Paal ( Carl Paal )



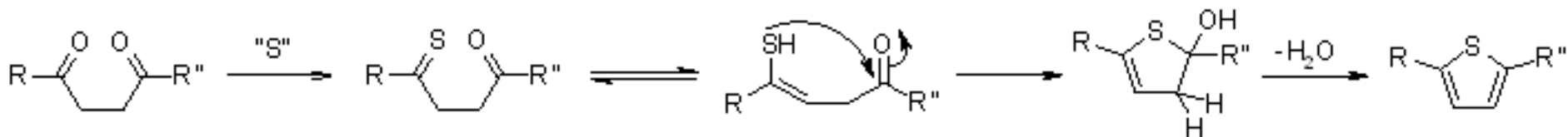
1. Carl Paal: Synthese von Thiophen und Pyrrolderivaten. *Berichte der deutschen chemischen Gesellschaft*. **1885**, 18, Nr. 1, S. 367–371. doi:10.1002/cber.18850180175.
2. Ludwig Knorr.: Einwirkung des Diacetbernsteinsäureesters auf Ammoniak und primäre Aminbasen. *Berichte der deutschen chemischen Gesellschaft*. **1885**, 18, Nr. 1, , S. 299–311. doi:10.1002/cber.18850180154.



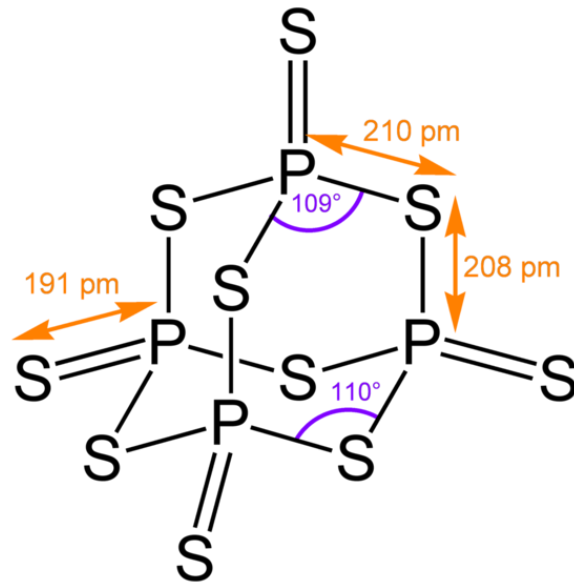
## SÍNTESIS DE PAAL-KNORR

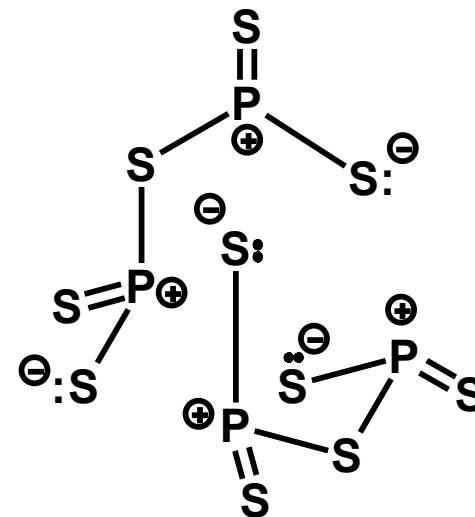
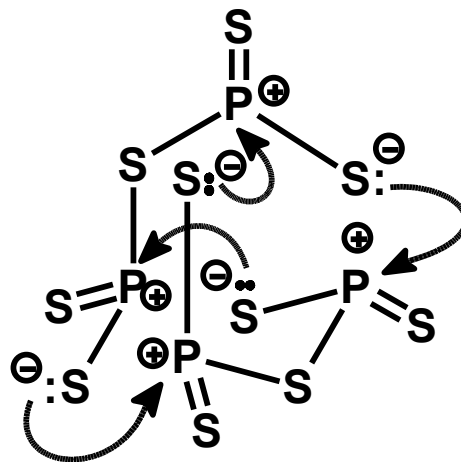
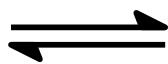
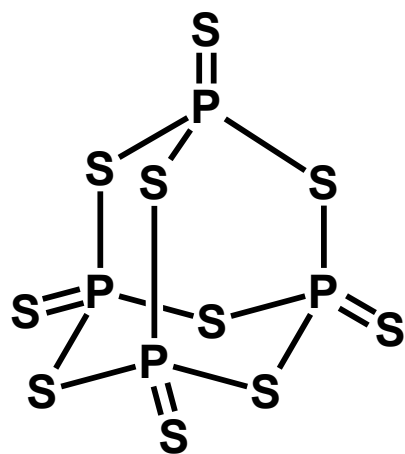


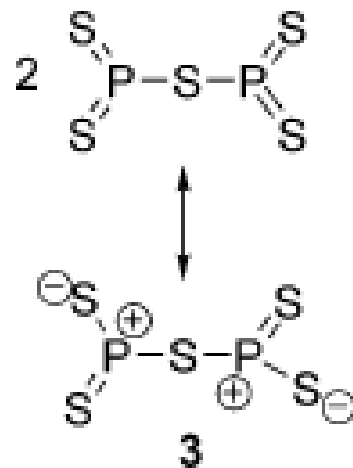
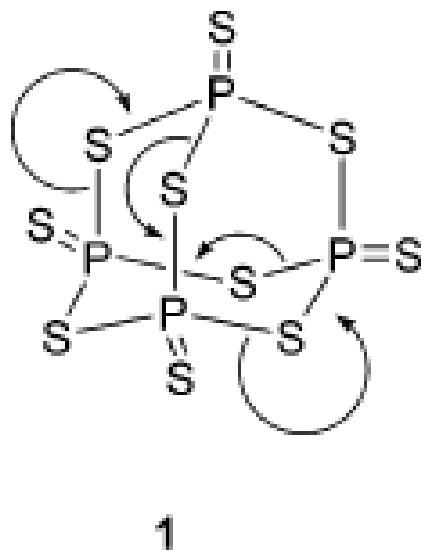
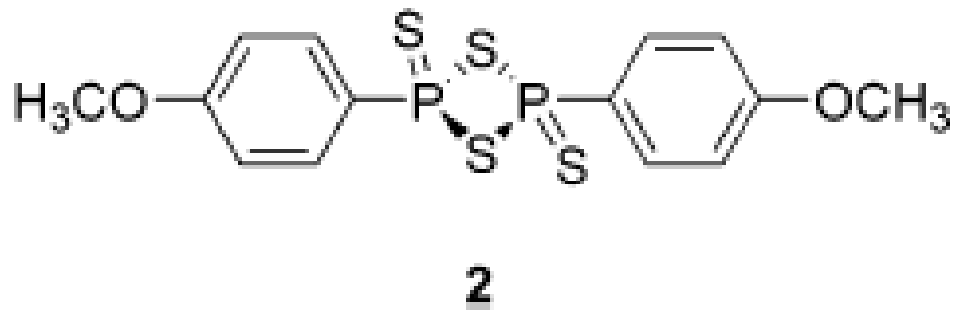
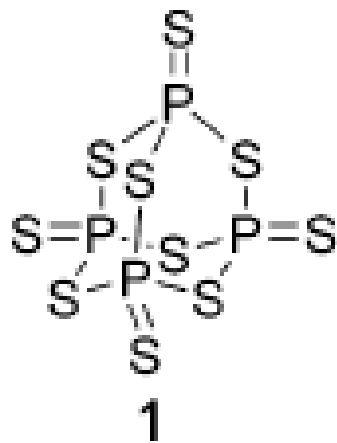
Mecanismo de reacción más probable

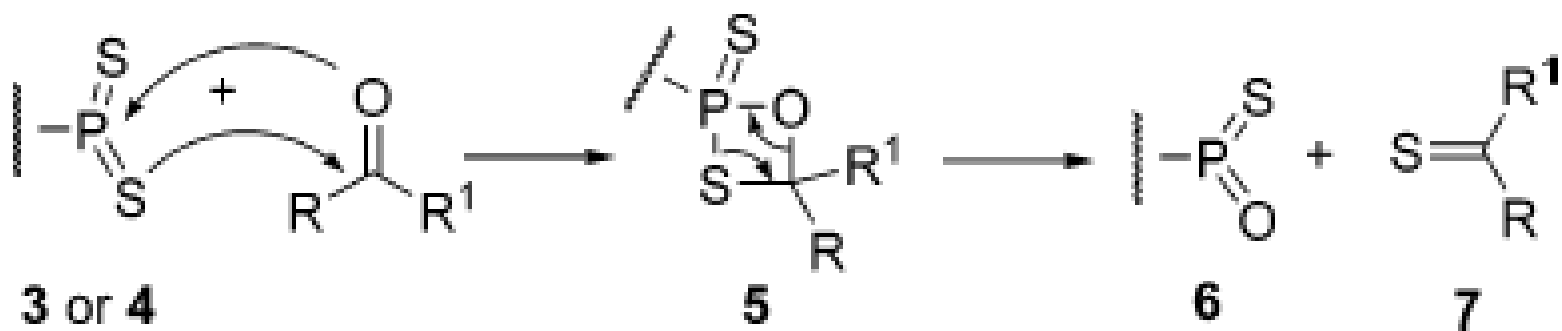
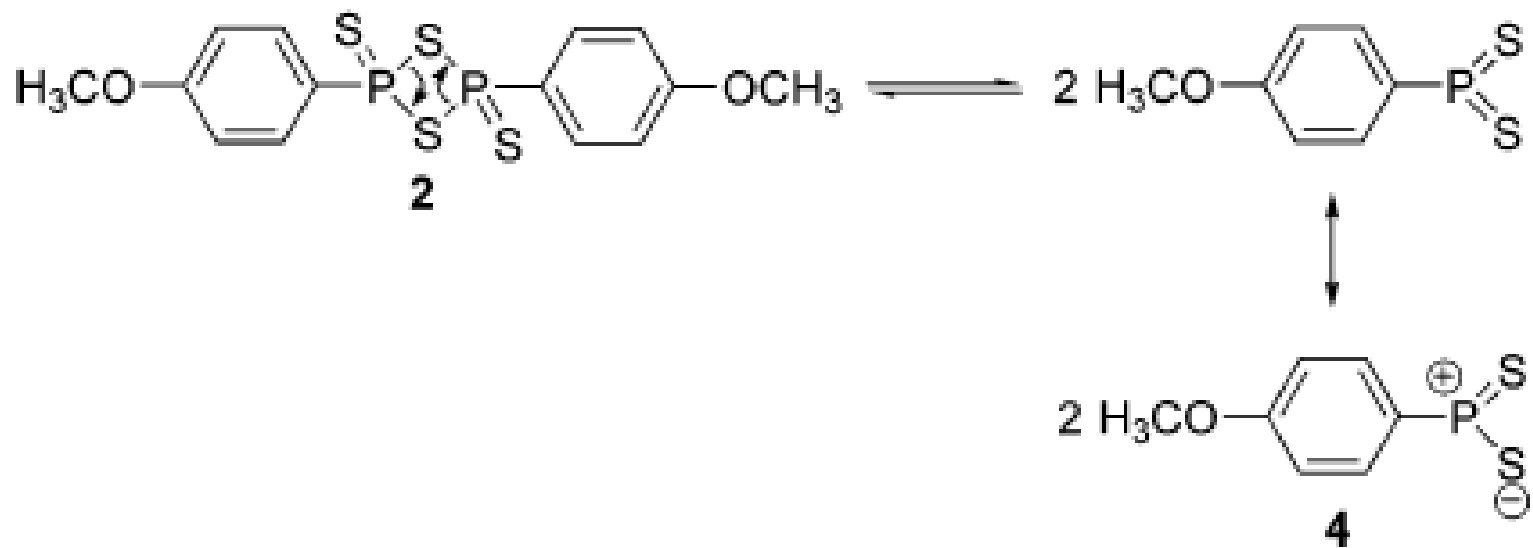


# Pentasulfuro de fósforo

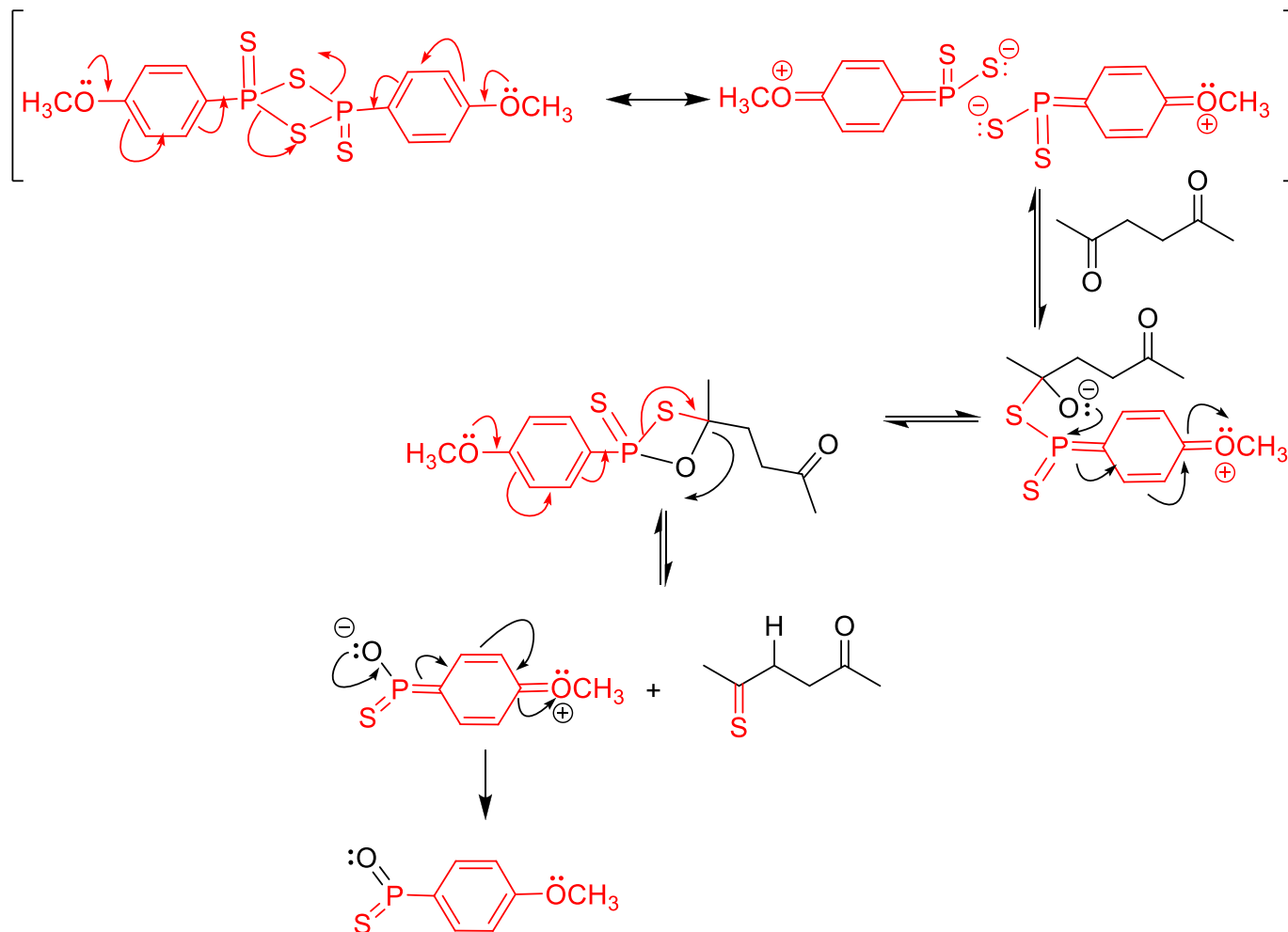


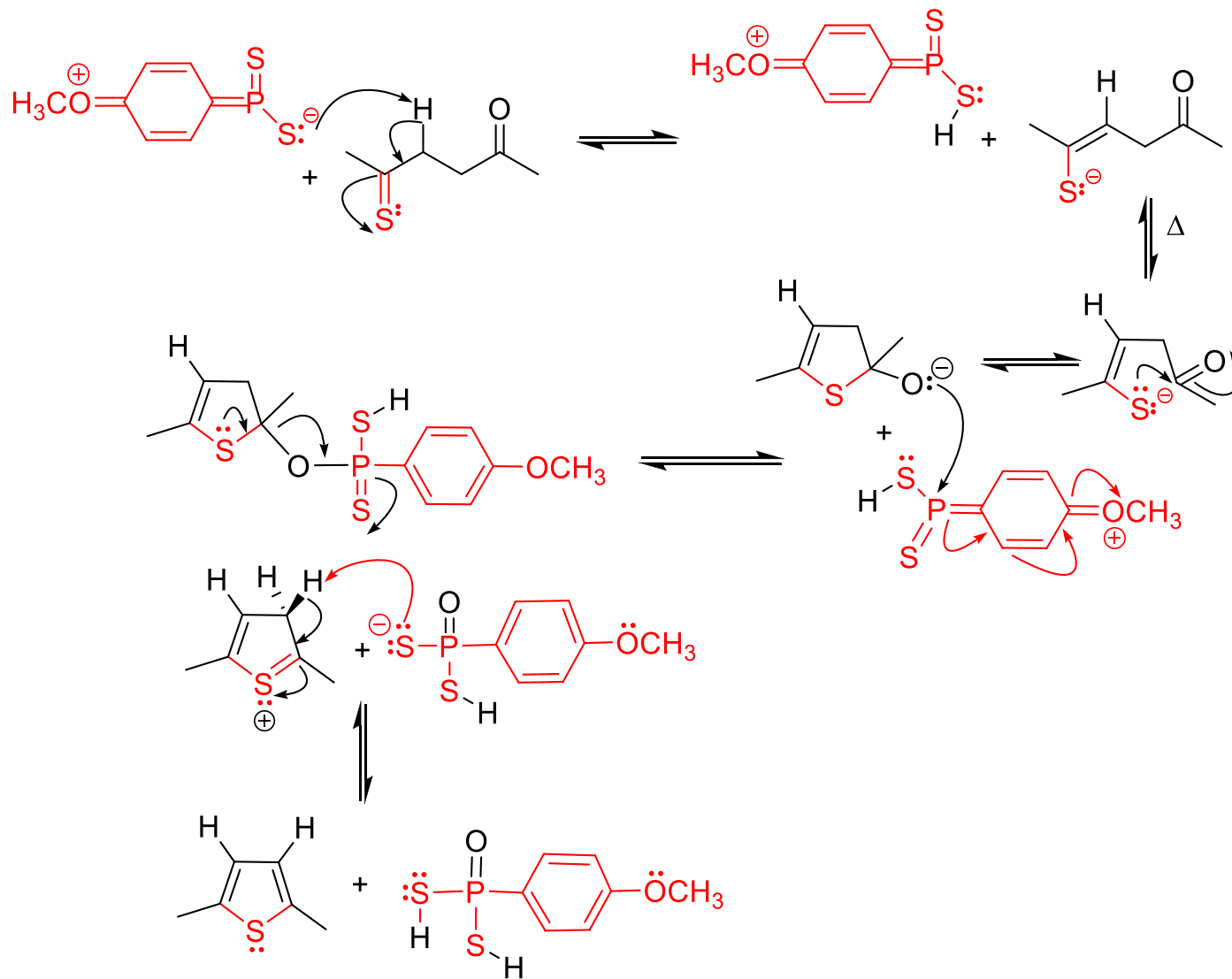






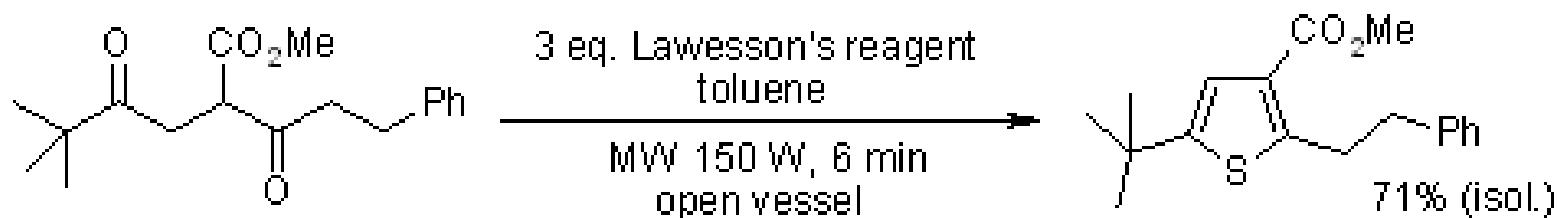
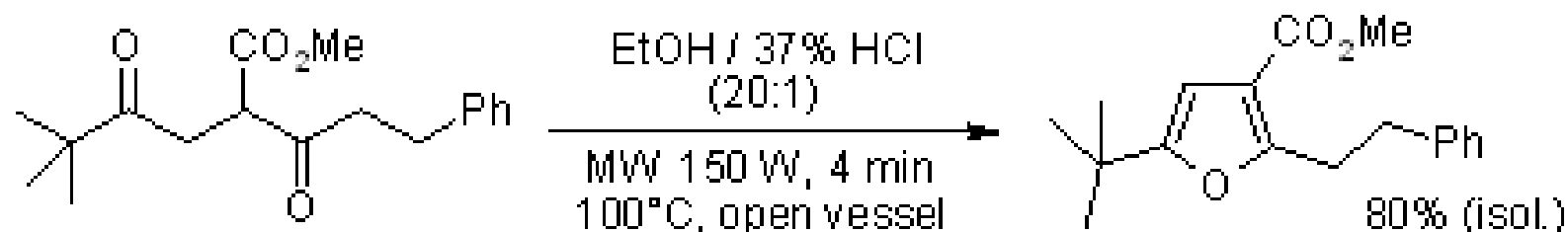
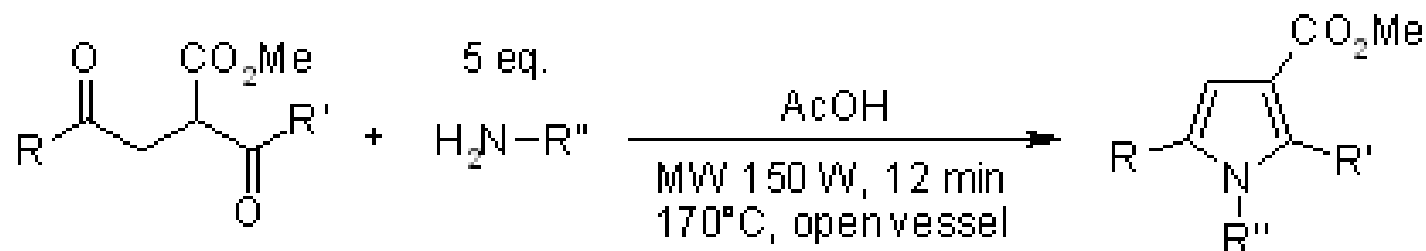
# REACCIÓN CON EL REACTIVO DE LAWESON



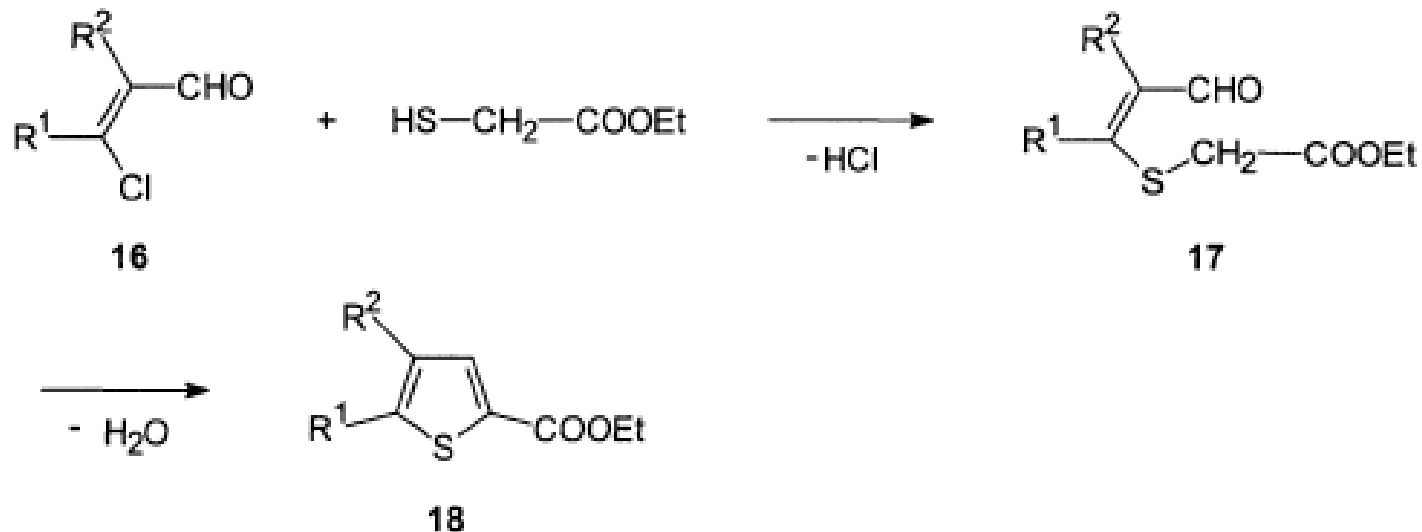


# Microwave-Assisted Paal-Knorr Reaction - Three-Step Regiocontrolled Synthesis of Polysubstituted Furans, Pyrroles and Thiophenes

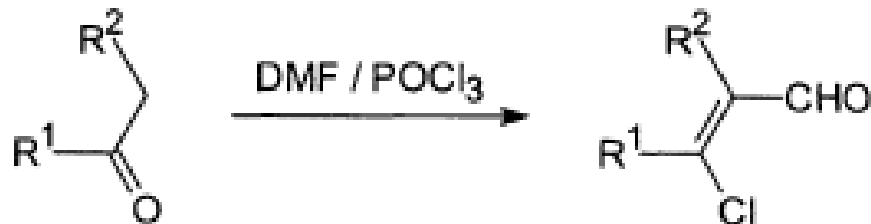
G. Minetto, L. F. Raveglia, A. Segá, M. Taddei, *Eur. J. Org. Chem.*, **2005**, 5277-5288.



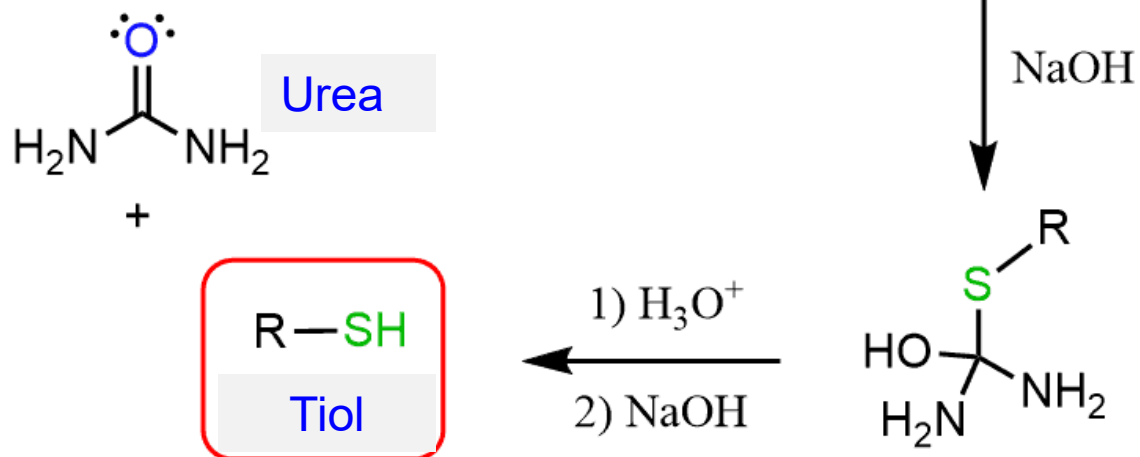
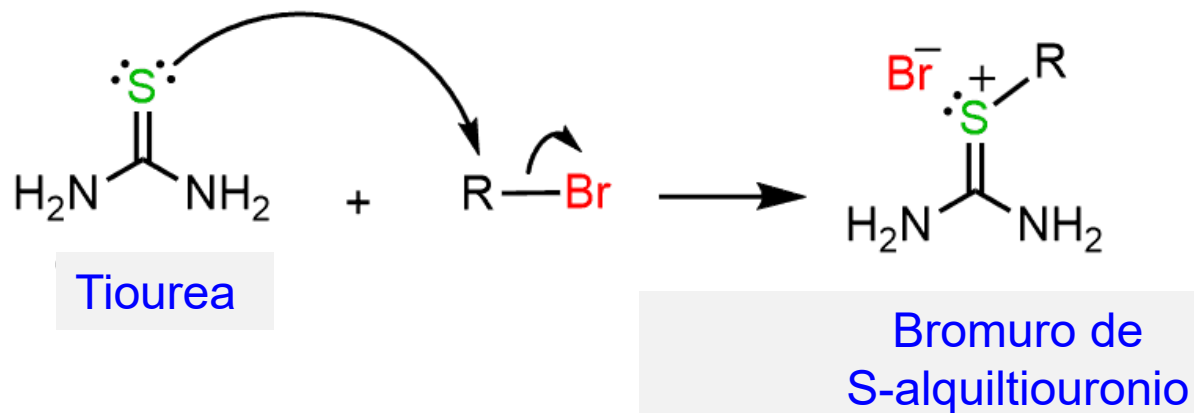
## SÍNTESIS DE FIESSELMANN

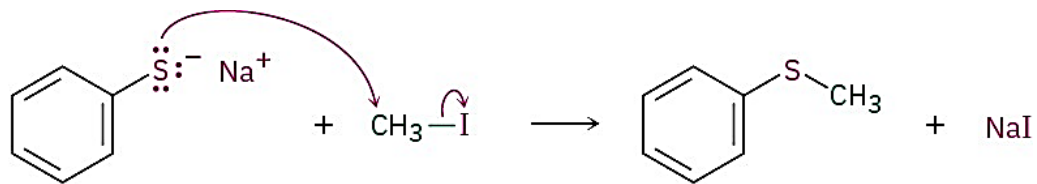


Los sustratos clorovinil aldehídos, se obtienen a partir de cetonas con  $\alpha$ -metilenos, por acción de DMF/ $\text{POCl}_3$  (la reacción de VILSMEIER-HAACK-ARNOLD):



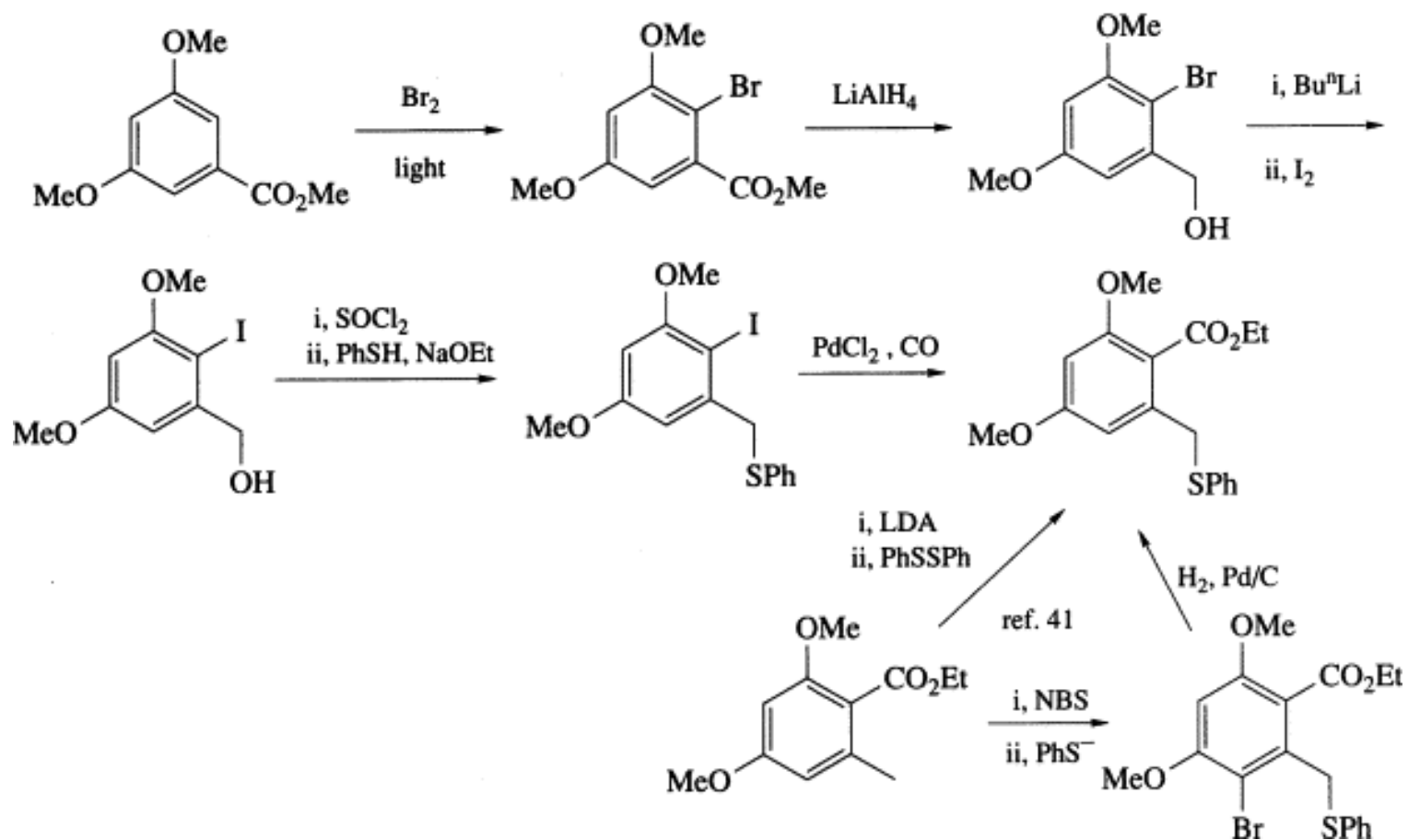
## Síntesis de tioles a partir de tiourea



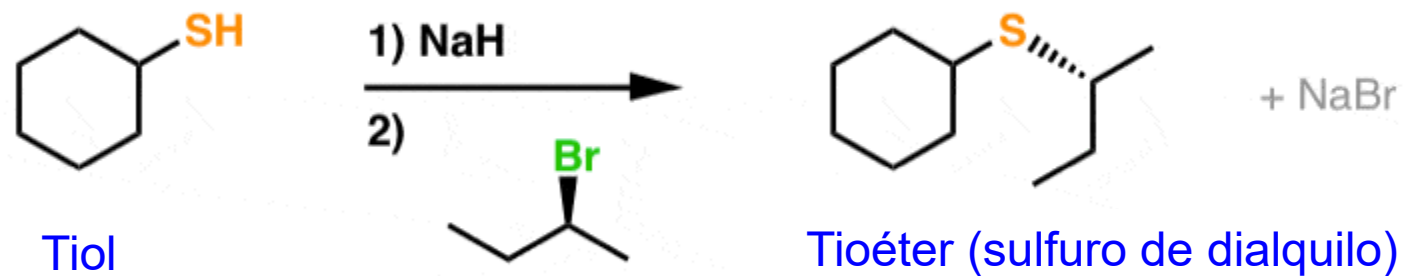


Bencentiolato de sodio

Sulfuro de fenilmetilo  
96 %

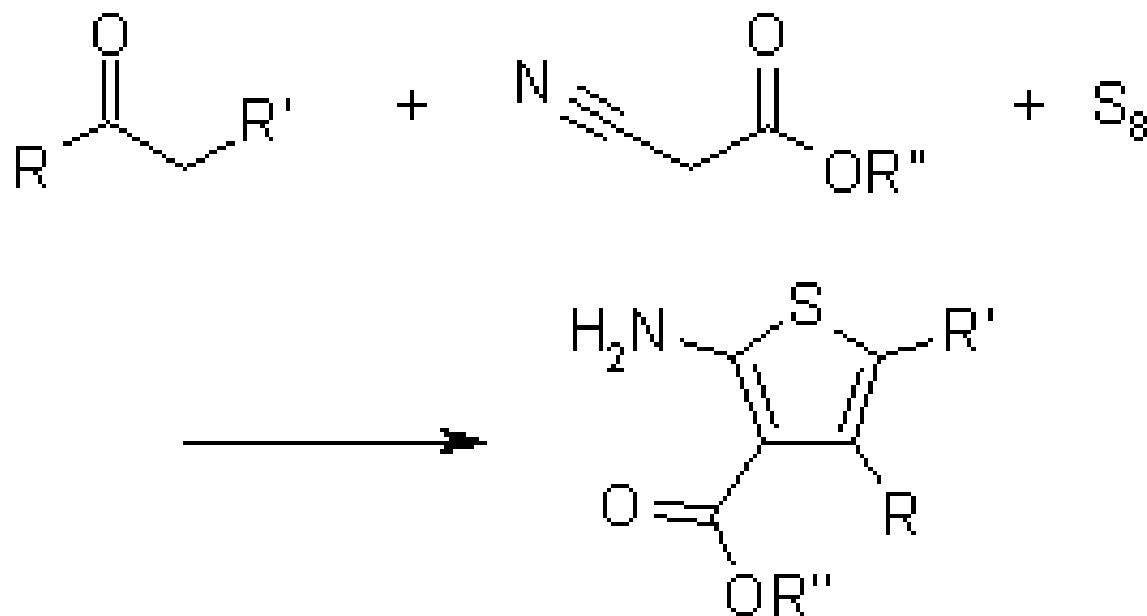


## Síntesis de tioéteres. Similar a la síntesis de éteres de Williamson



**Nota:**  
no hay reacción de eliminación

# Síntesis de Gewald

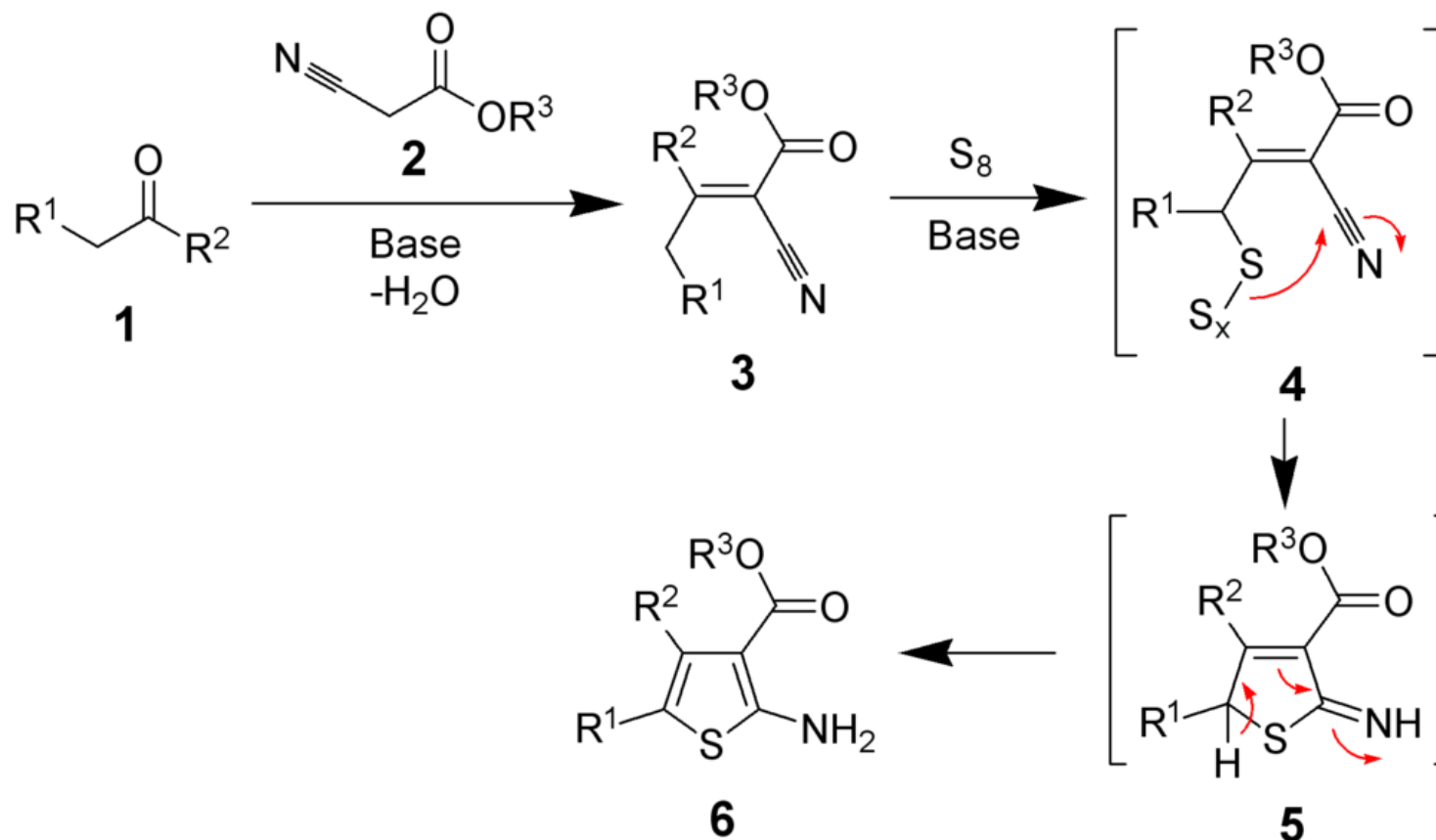


<https://www.organic-chemistry.org/namedreactions/gewald-reaction.shtm>

Gewald, K.; Schinke, E.; Böttcher, H. *Ber.* **1966**, *99*, 94-100



# Mecanismo de la reacción de Gewald



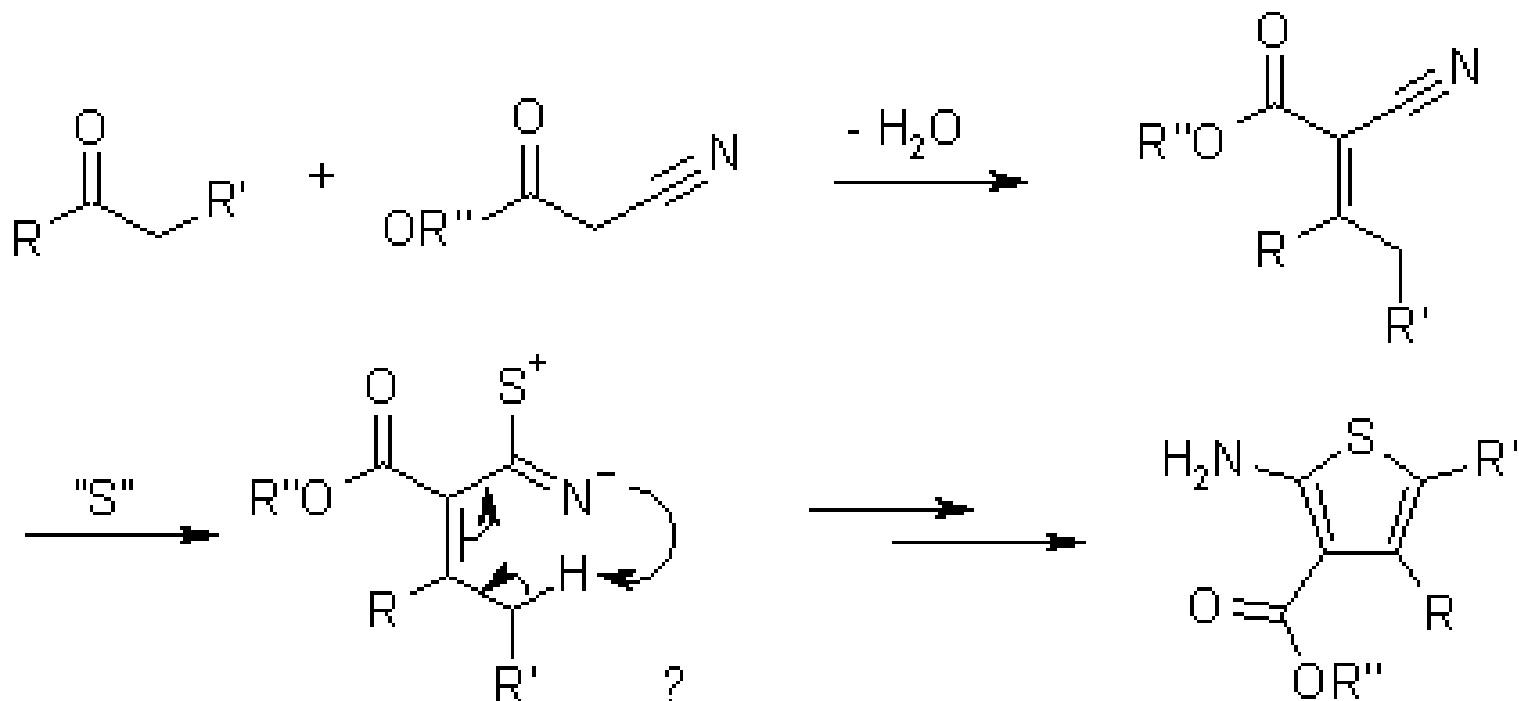
[https://en.wikipedia.org/wiki/Gewald\\_reaction#/media/File:Gewald\\_Reaction\\_Mechanism.png](https://en.wikipedia.org/wiki/Gewald_reaction#/media/File:Gewald_Reaction_Mechanism.png)

Sabnis, R. W.; Rangnekar, D. W.; Sonawane, N. D. *J. Heterocyclic Chem.* **1999**, *36*, 333.



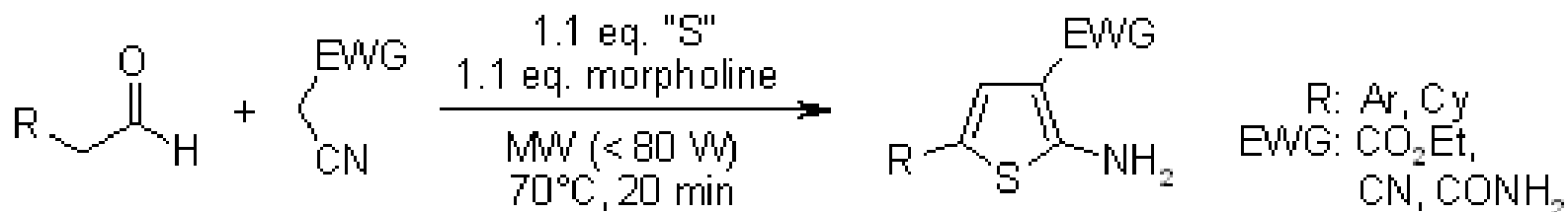
## Mecanismo de la reacción de Gewald

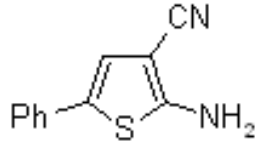
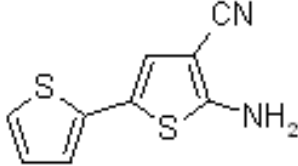
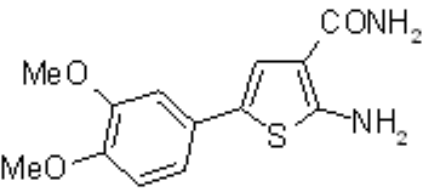
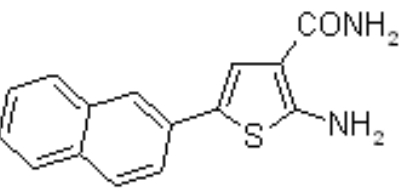
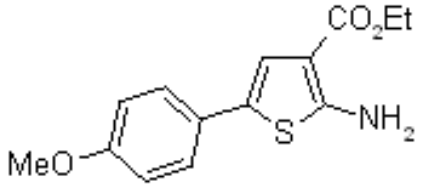
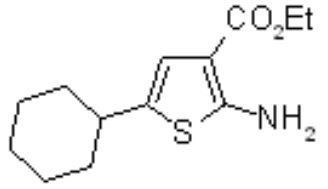
El primer paso del proceso es una condensación de Knoevenagel, pero los siguientes pasos no se conocen con detalle, pero es probable que ocurran de la siguiente manera:



# Microwave-Assisted Synthesis of 5-Substituted 2-Aminothiophenes Starting from Arylacetaldehydes

G. Revelant, S. Dunand, S. Hesse, G. Kirsch, *Synthesis*, **2011**, 2935-2940.

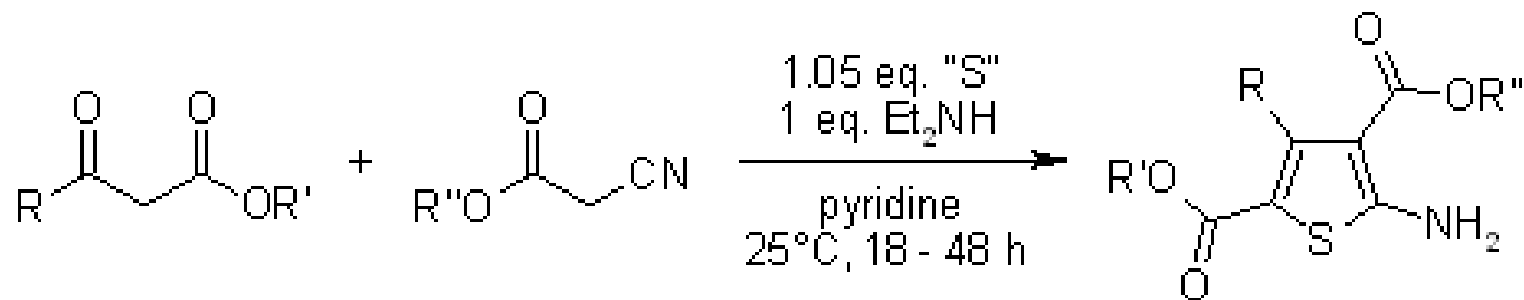


product	yield (% , isol.)	product	yield (% , isol.)
	96		50
	95		74
	50		63



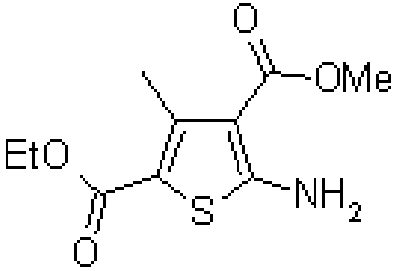
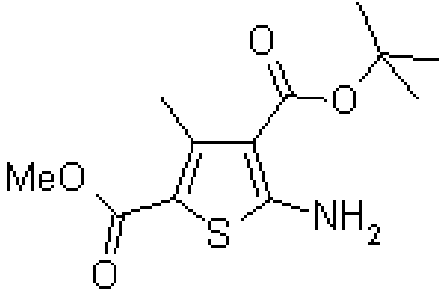
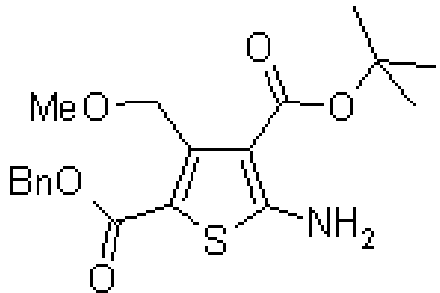
## Practical synthesis of tetrasubstituted thiophenes for use in compound libraries

B. P. McKibben, C. H. Cartwright, A. L. Castelhana, *Tetrahedron Lett.*, **1999**, 5471-5474.

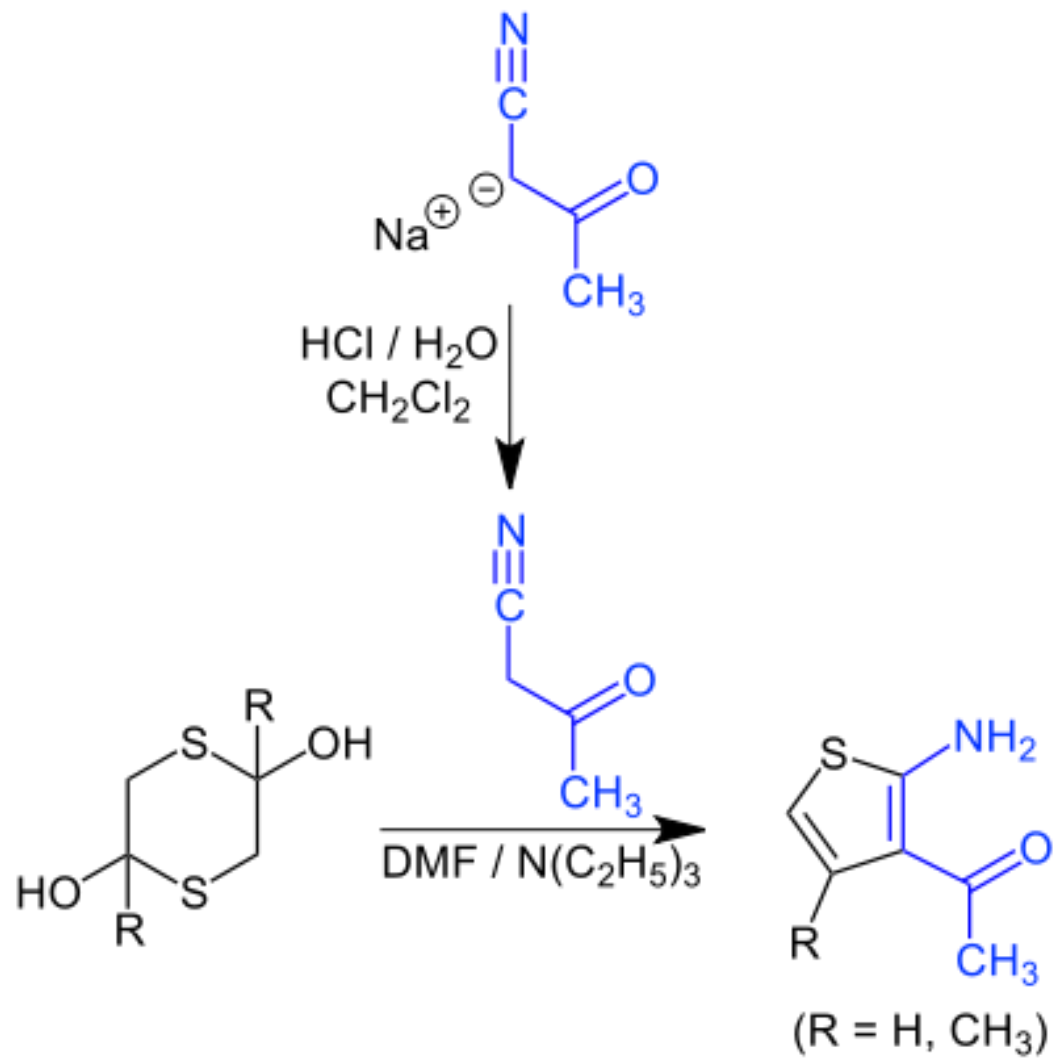


Se han desarrollado condiciones de reacción optimizadas para la reacción de Gewald a temperatura ambiente para obtener tiofenos tetra-sustituidos con buen rendimiento.



Product	t (h)	Yield (%. isol.)
	18	52
	48	69
	48	71



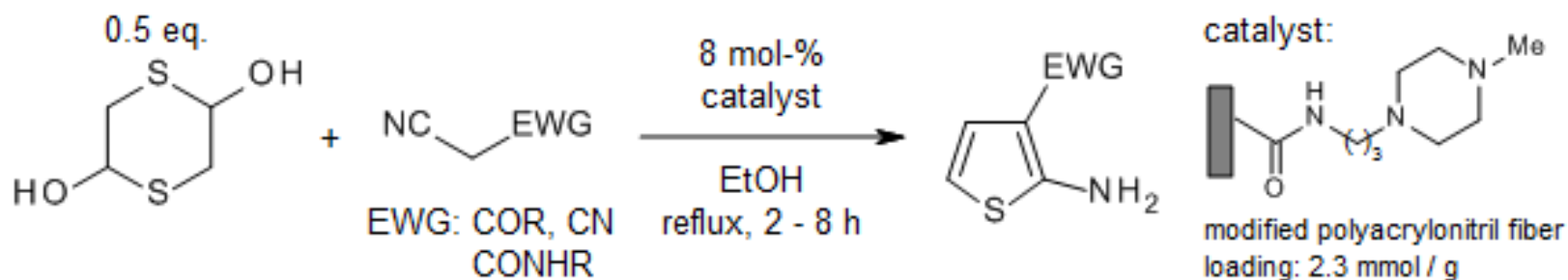


Gernot A. Eller, Wolfgang Holzer *Molecules* **2006**, 11, 371-376



# An Efficient Synthesis of 2-Aminothiophenes via the Gewald Reaction Catalyzed by an *N*-Methylpiperazine-Functionalized Polyacrylonitrile Fiber

L. Ma, L. Yuan, C. Xu, G. Li, M. Tao, W. Zhang, *Synthesis*, **2013**, 45, 45-52.



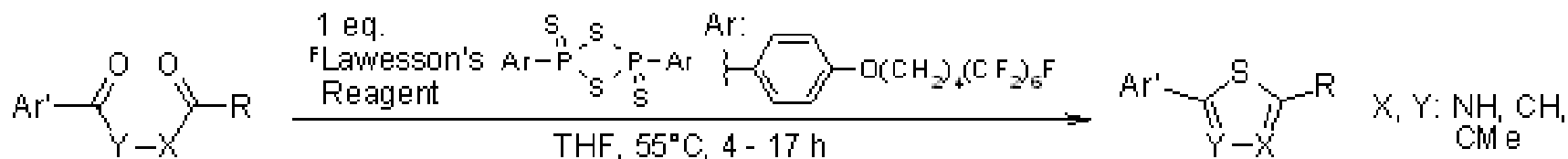
product	run:	t (h)	yield (% , isol.)	product	t (h)	yield (% , isol.)
	1	4	89		6	81
	4	4	87			
	7	4	86		5	85
	10	4	85			
		4	87			

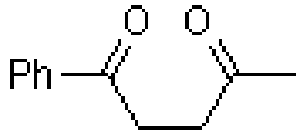
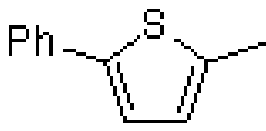
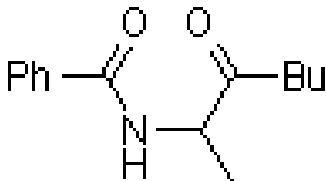
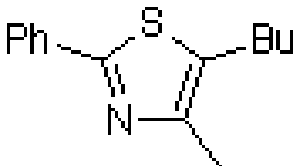
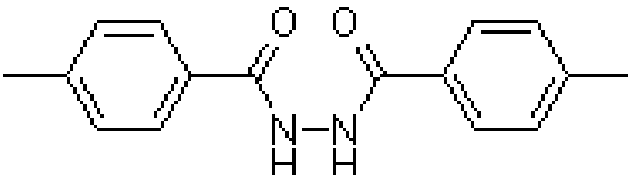
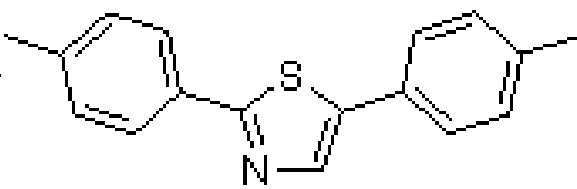


## Thionation Using Fluorous Lawesson's Reagent

Z. Kaleta, B. T Makowski, T. Soos, R. Dembinski, *Org. Lett.*, **2006**, 8, 1625-1628

La tionación de amidas, 1,4-dicetonas, de *N*-(2-oxoalquil)amidas y *N,N'*-acilhidrazinas con el uso del reactivo de Lawesson fluorado dio lugar a las tioamidas, tiofenos, 1,3-tiazoles, y a 1,3,4-tiadiazoles con rendimientos altos

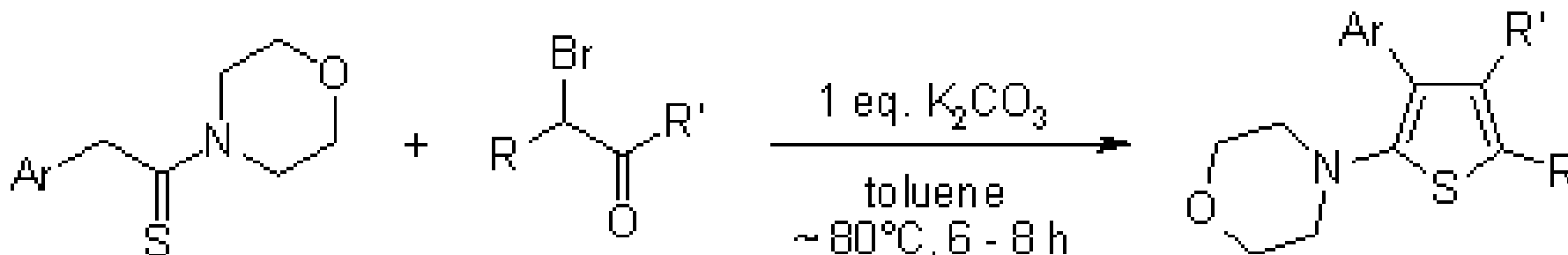


reactant	product	t (h)	yield (% , isol.)
		4	88
		6	48
		6	93



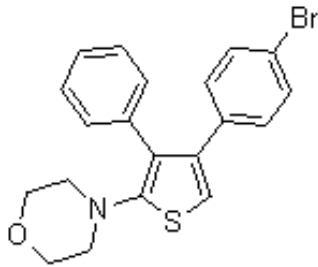
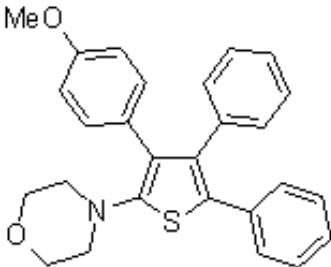
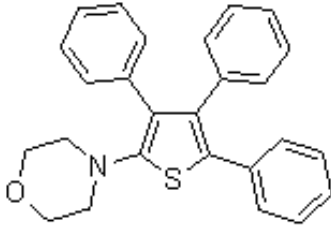
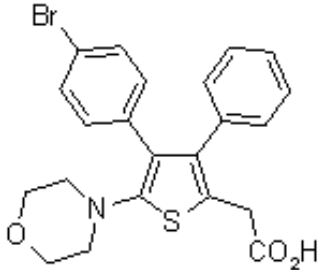
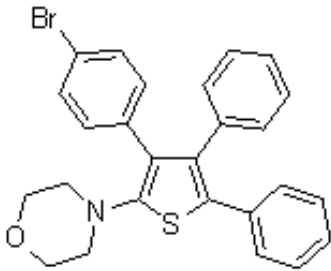
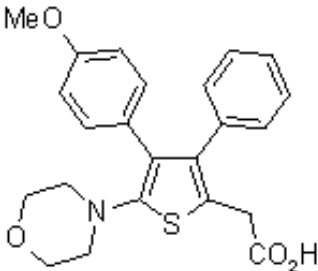
## An efficient and facile one-step synthesis of highly substituted thiophenes

F. Matloubi Moghaddam, H. Zali Bionee, *Tetrahedron*, **2004**, *60*, 6085-6089



Se desarrolló un método eficiente, de un solo paso, para formar tiofenos con una alta sustitución en el anillo, el cual utiliza como materias primas tiomorfólidos y derivados de  $\alpha$ -halocetonas



Product	T (°C)	t (h)	Yield (% , isol.)	Product	T (°C)	t (h)	Yield (% , isol.)
	70	7	75		75	7	69
	75	6.5	80		60	7	60
	80	7	55		55	6	55



# Síntesis de Hinsberg

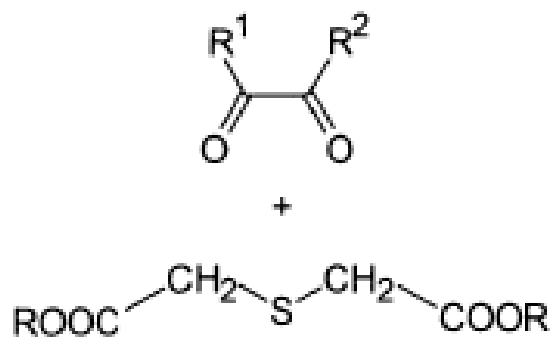


Oscar Hinsberg, Ber. 43, 901 (1910)

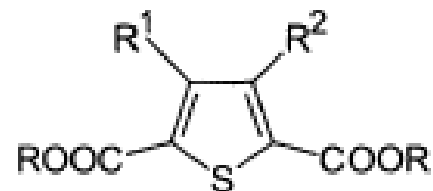
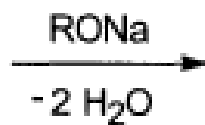
Oscar Heinrich Daniel Hinsberg  
(1857 – 1939)  
Químico alemán



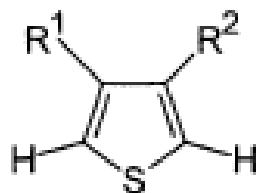
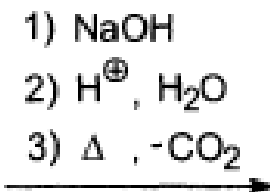
## SÍNTESIS DE HINSBERG



21



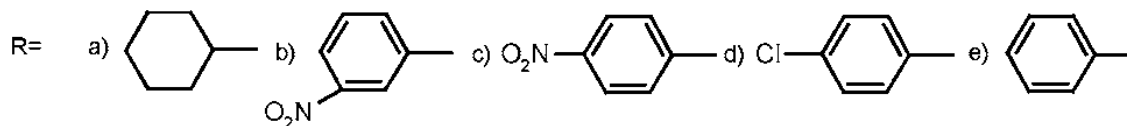
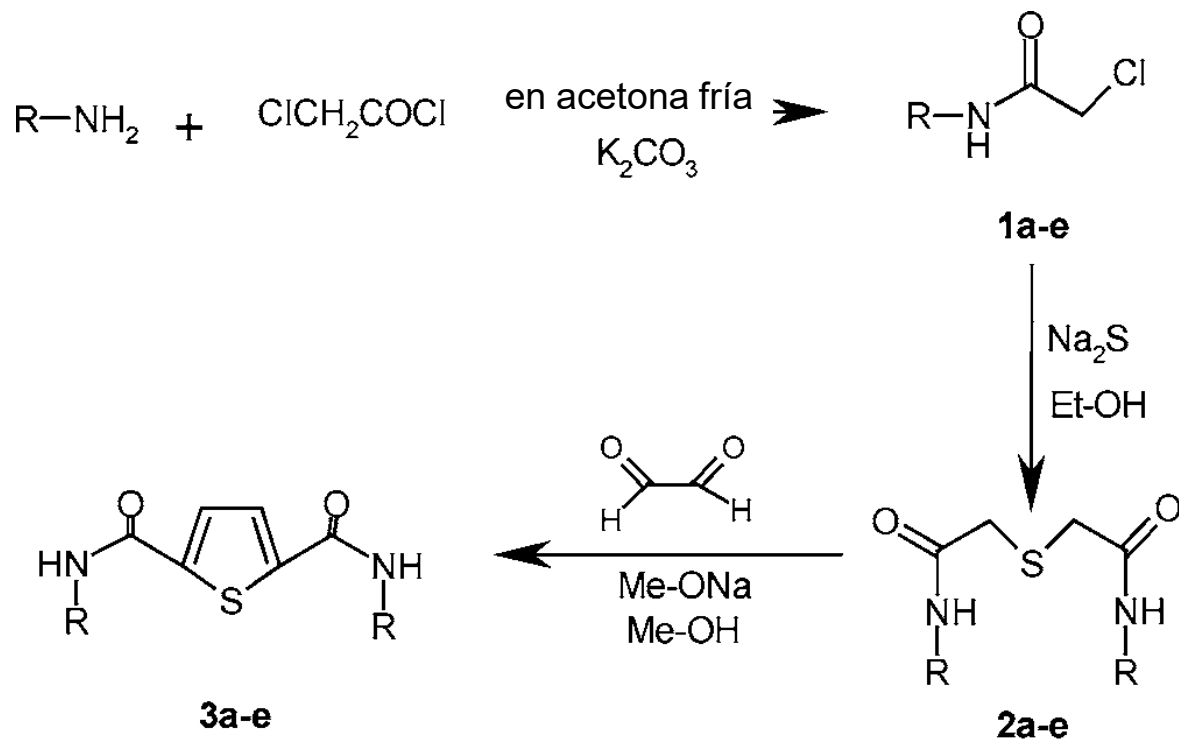
22



23



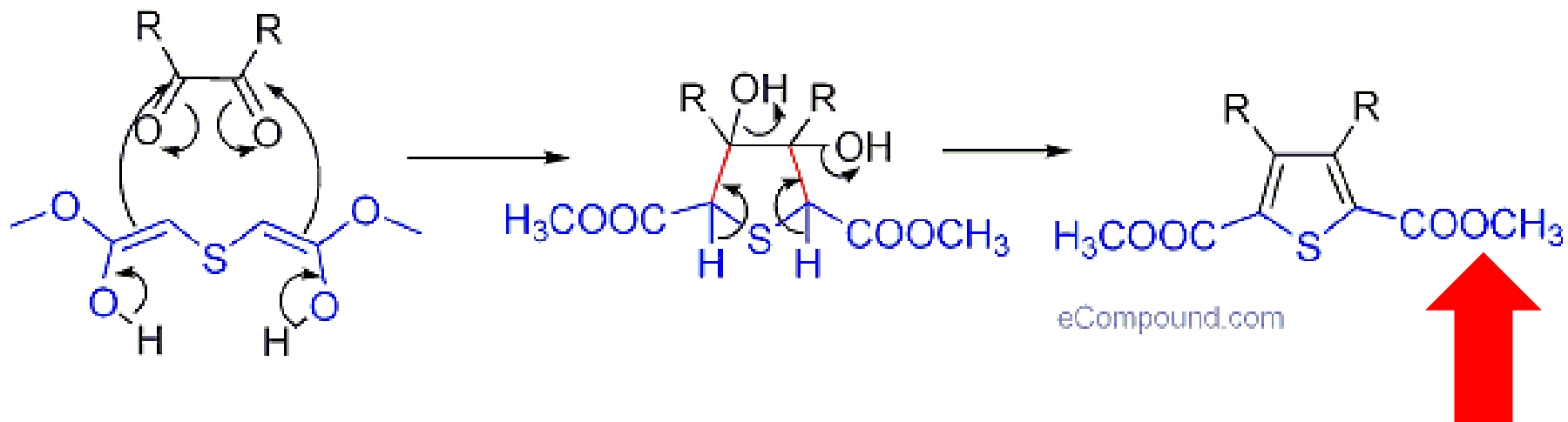
## Bis-aryl(alquil)amidas del ácido tioen-2,5-dicarboxílico



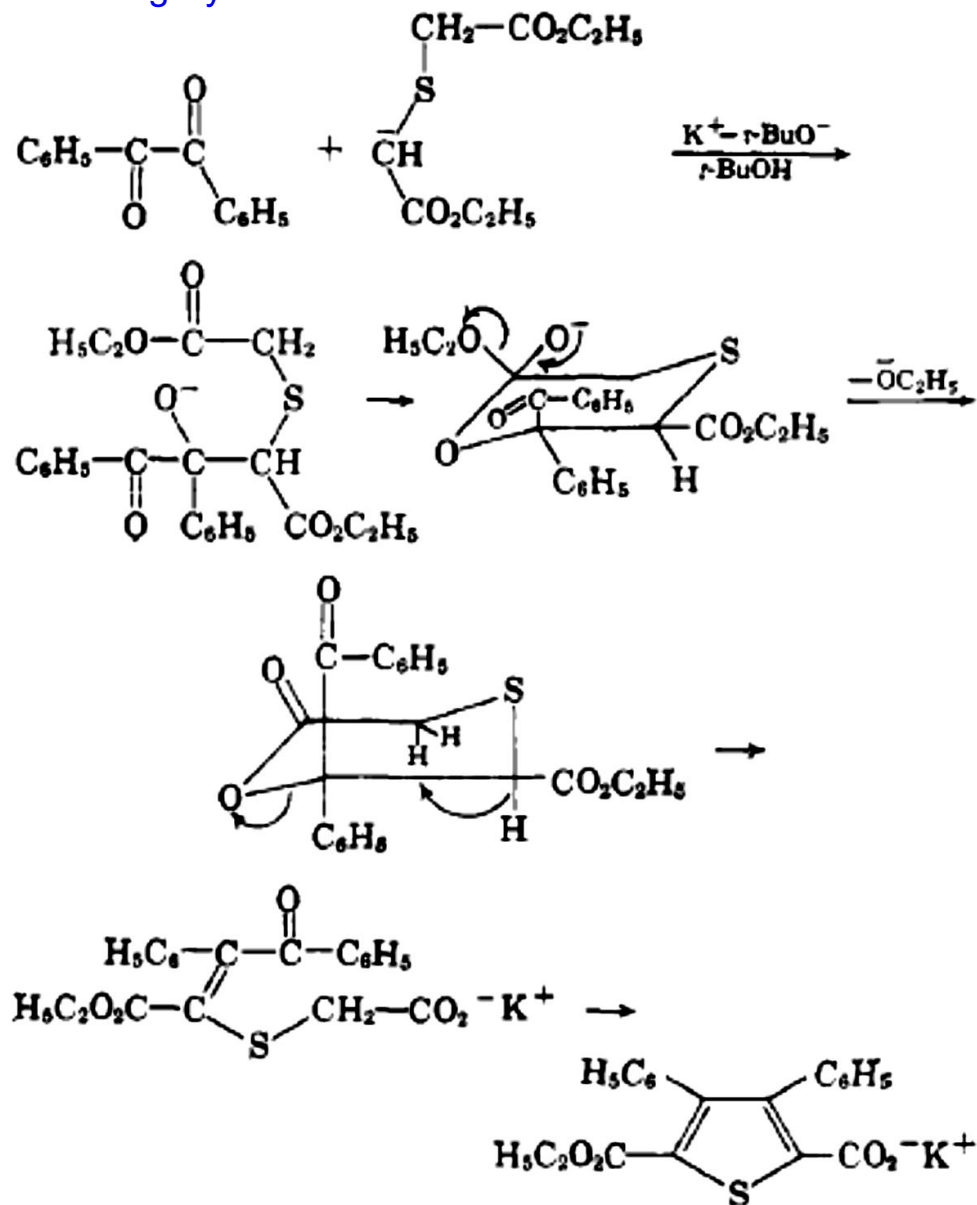
Kopar, M. R.; Cans, A. Z.; Çetin, A.; Heteroatom Chemistry, **2005**, *16*, [6], 503 - 506



## Síntesis de tiofenos de **Hinsberg**



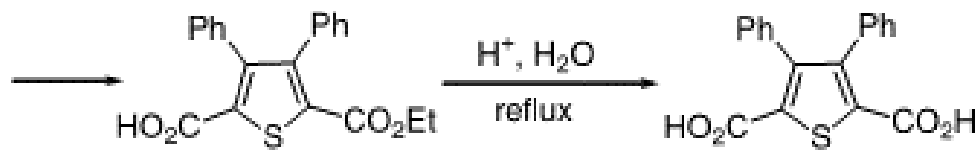
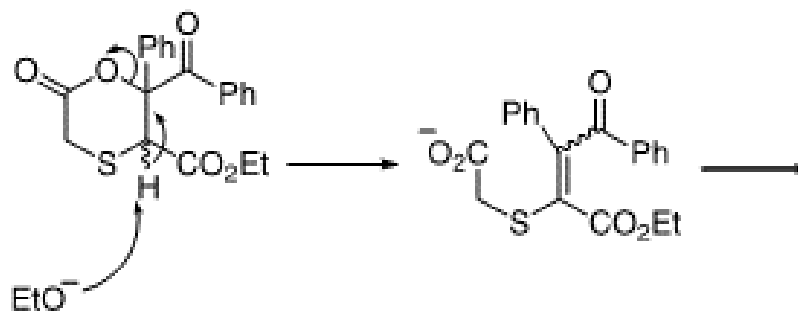
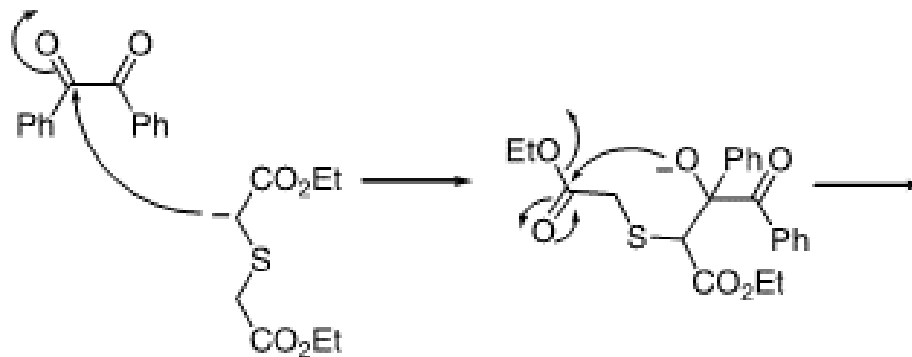
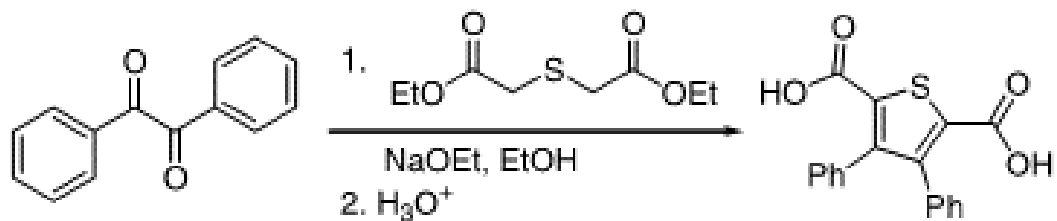
# The Mechanism of the Hinsberg Thiophene Ring Synthesis



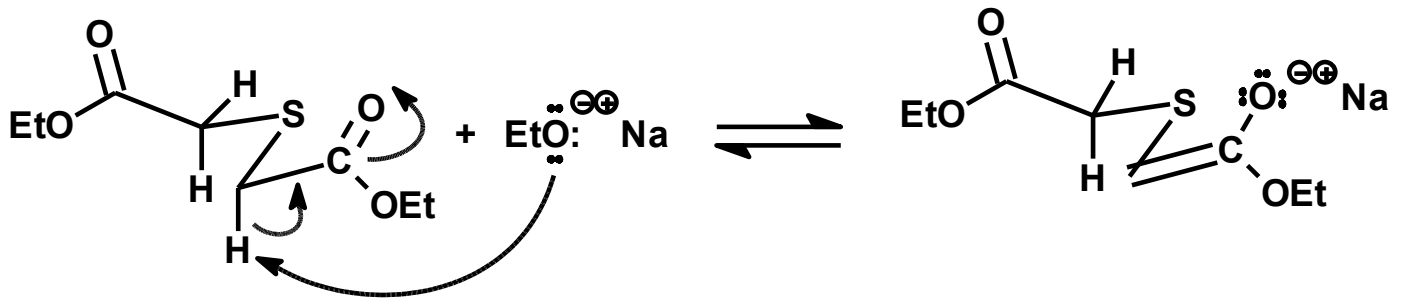
Hans Wynberg and H. J. Kooreman

Journal of the American Chemical Society,  
1965, 87:8, 1739-1742

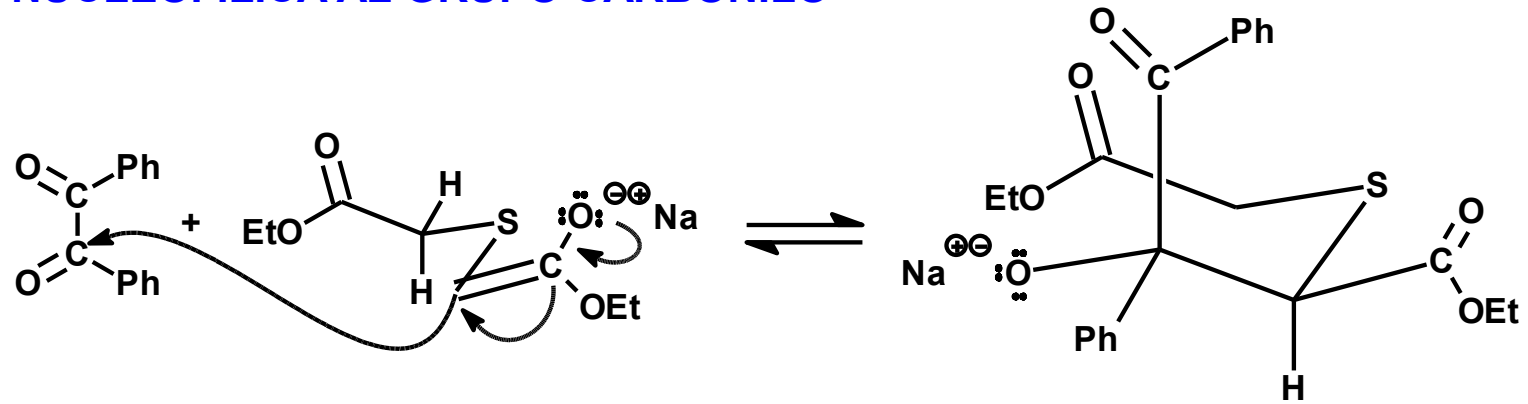




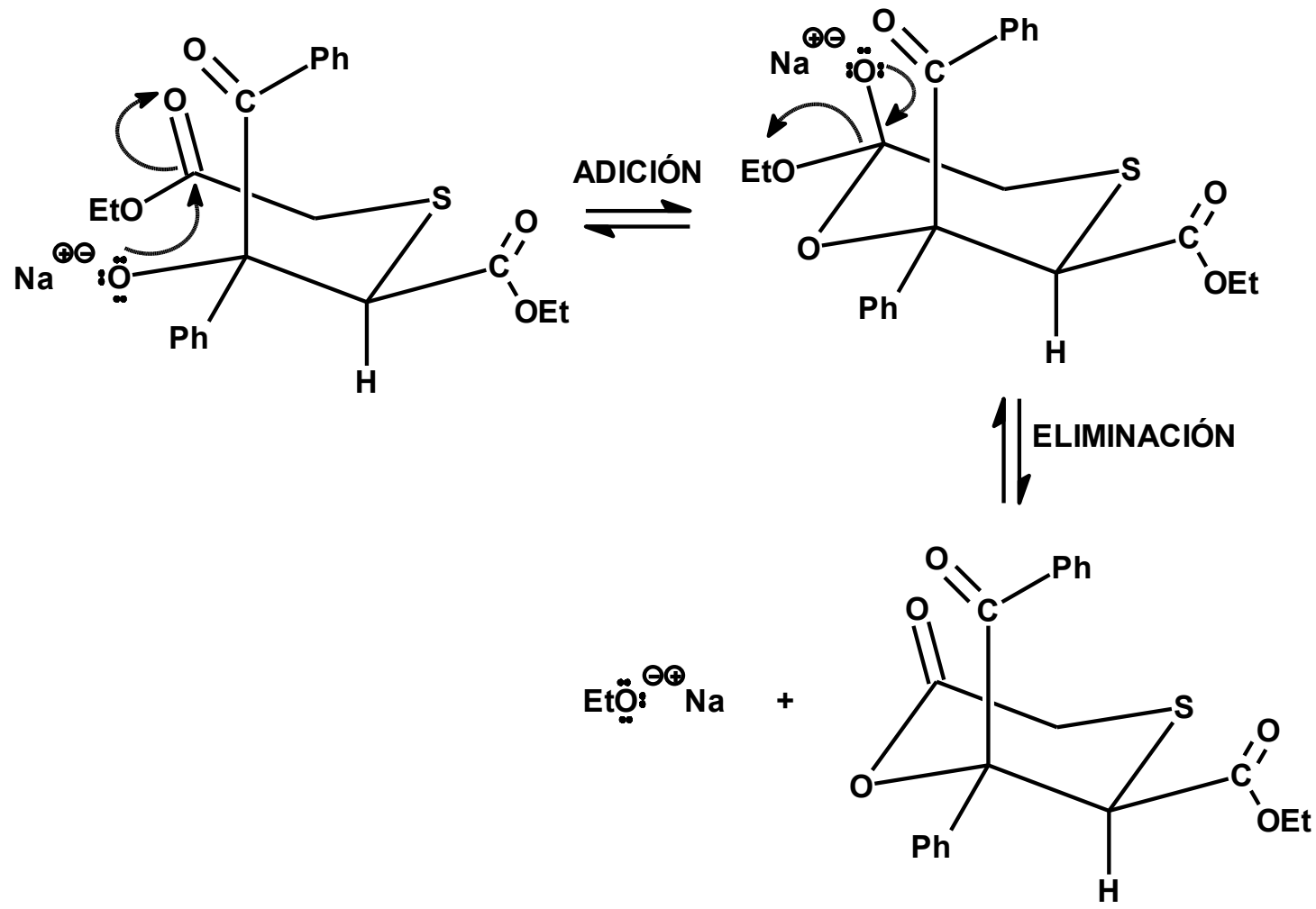
**MECANISMO HINSBERG  
REACCIÓN ÁCIDO-BASE**



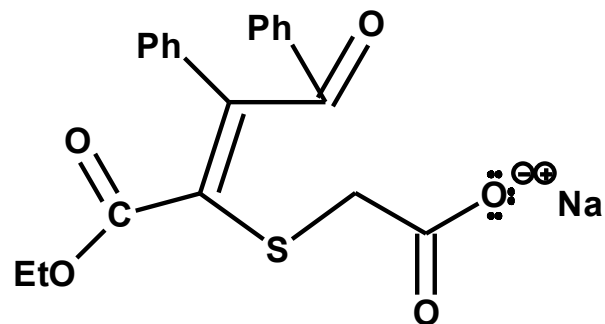
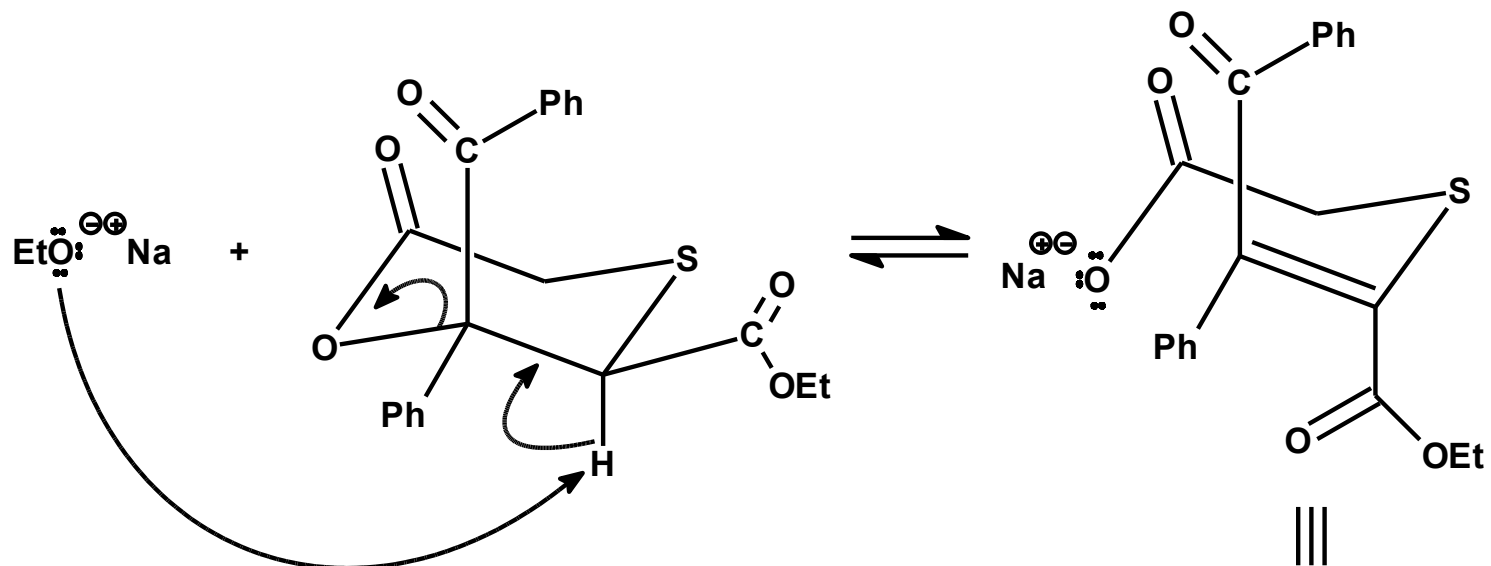
**ADICIÓN NUCLEOFÍLICA AL GRUPO CARBONILO**



# REACCIÓN DE TRANSESTERIFICACIÓN INTRAMOLECULAR

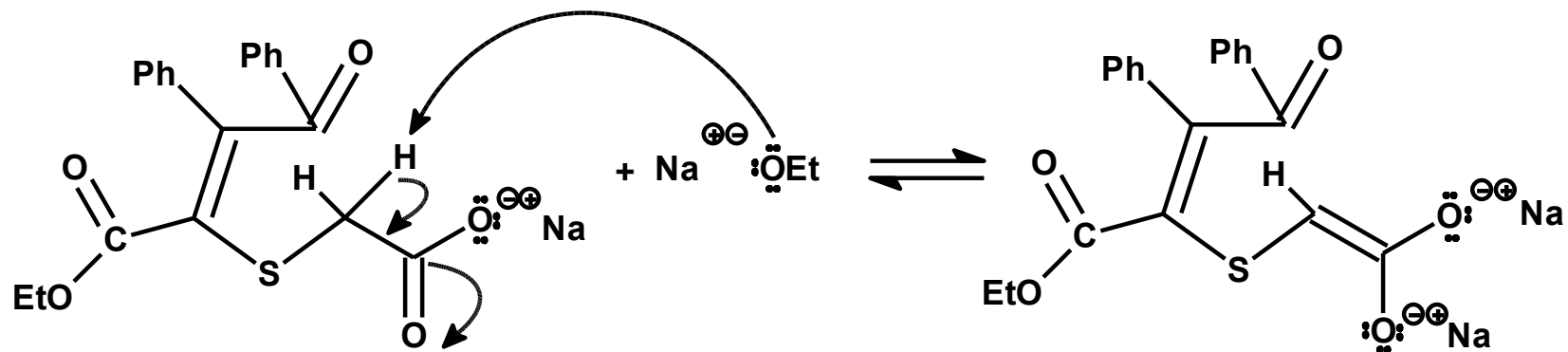


## REACCIÓN ÁCIDO-BASE

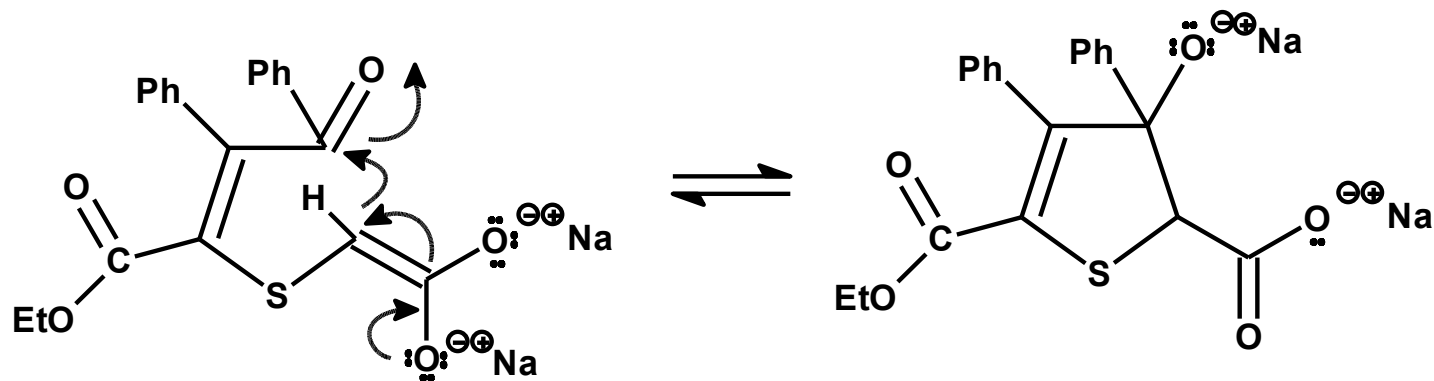


## SEGUNDA ADICIÓN NUCLEOFÍLICA AL GRUPO CARBONILO

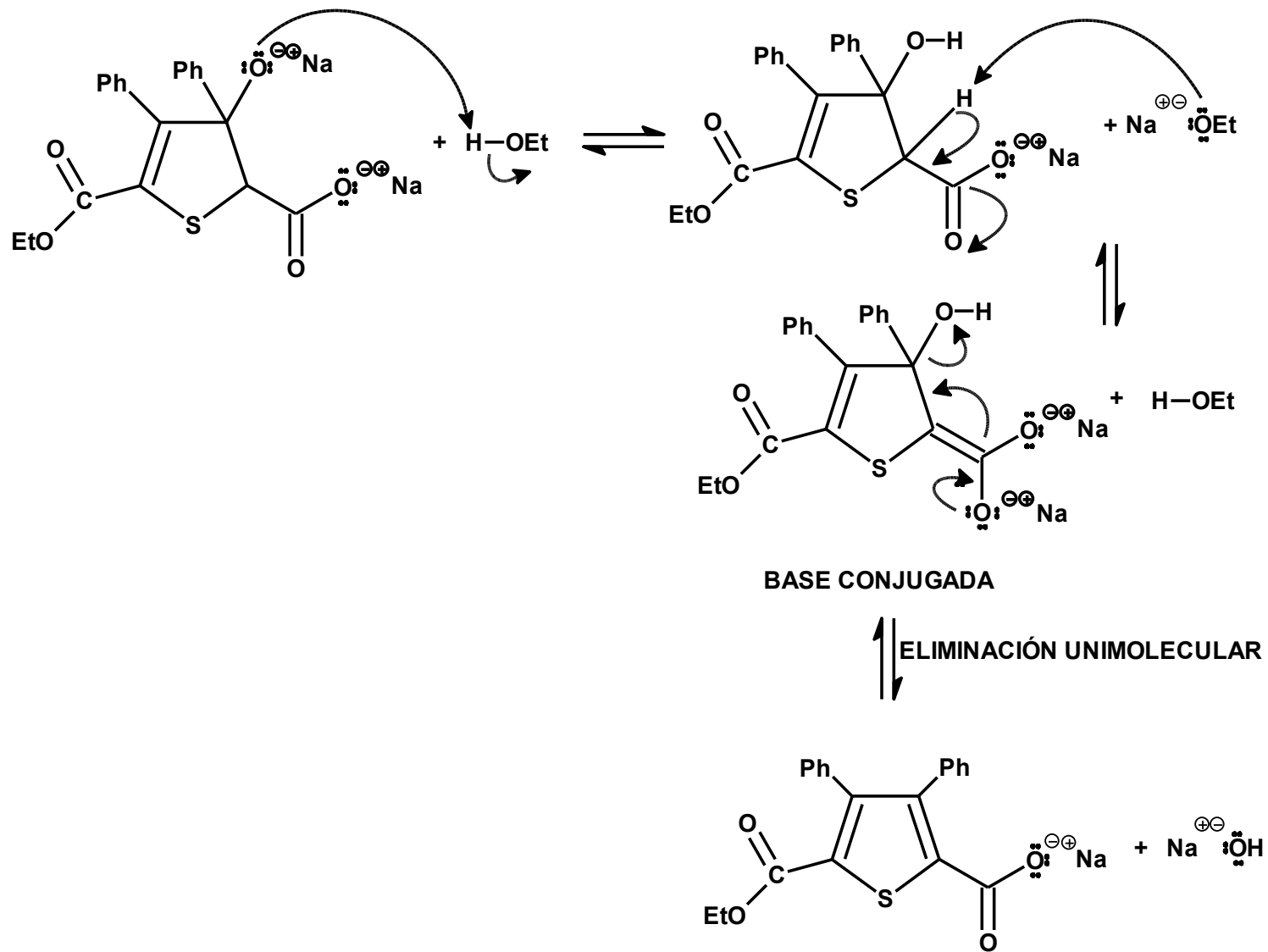
### a) REACCIÓN ÁCIDO-BASE



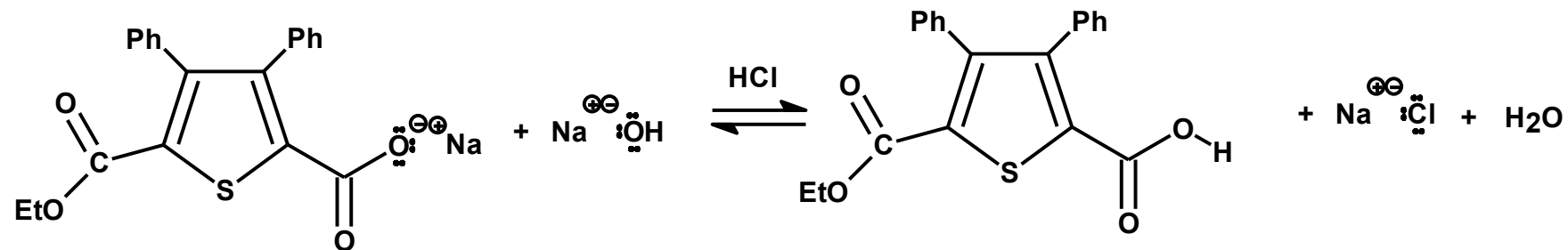
### b) ADICIÓN AL GRUPO CARBONILO

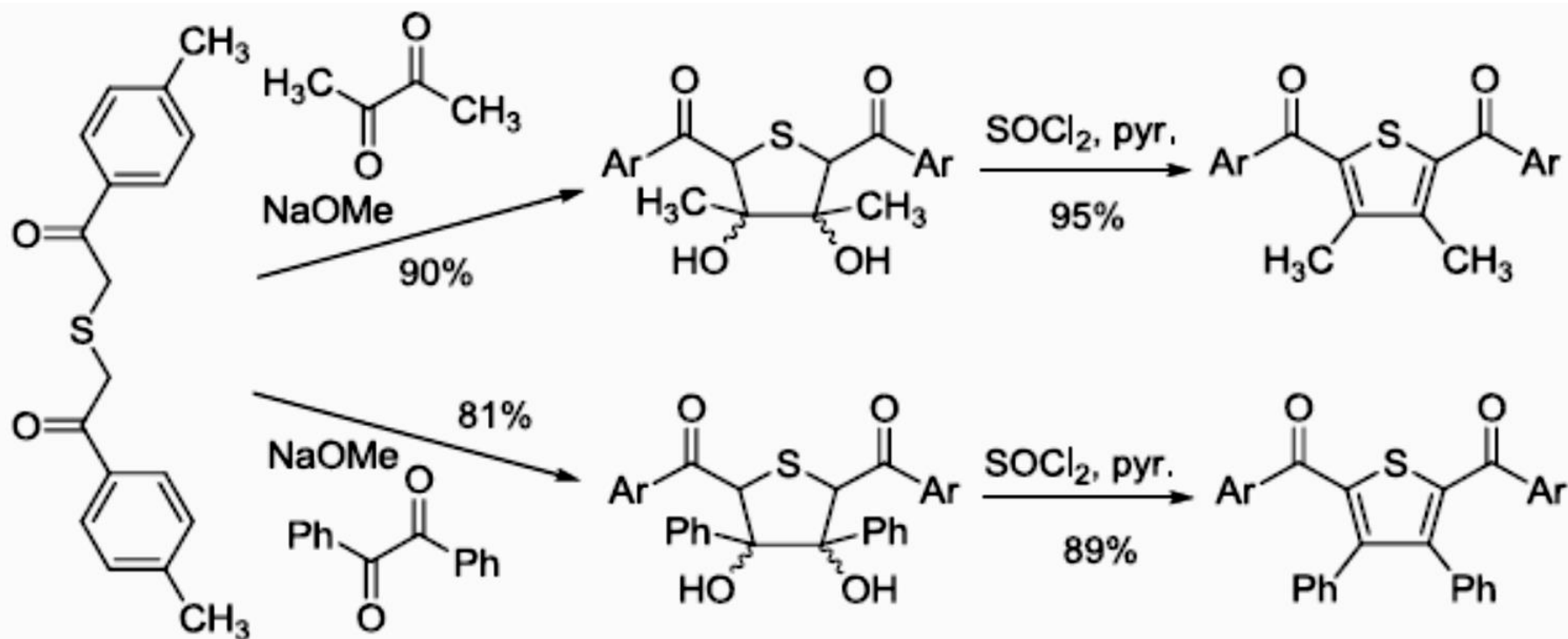


## ELIMINACIÓN E1bc:



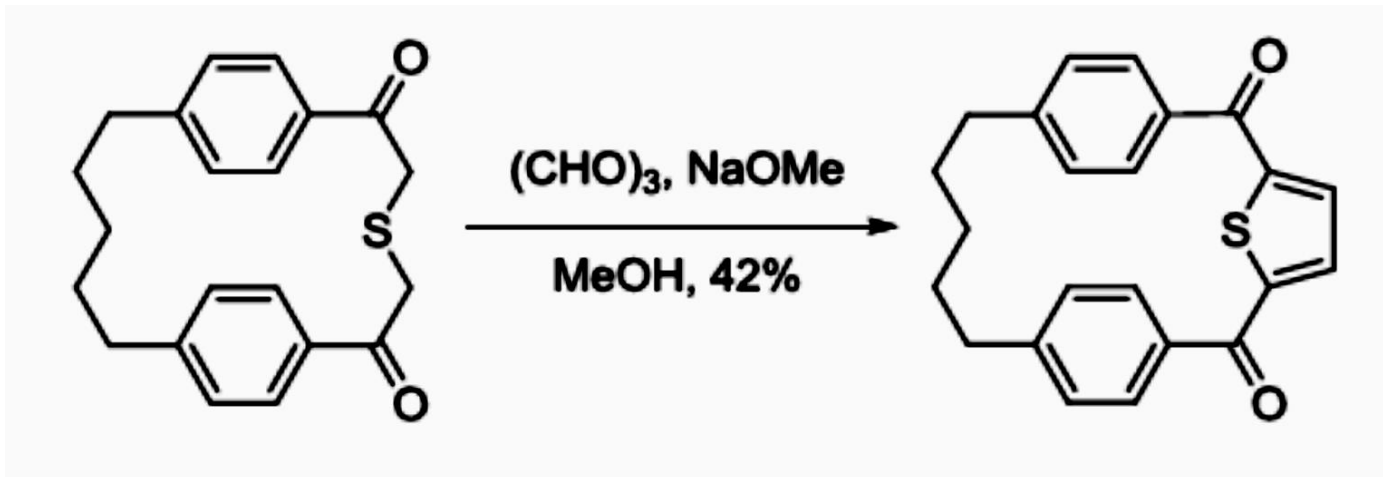
## LIBERACIÓN DE LA SAL DE CARBOXILATO:



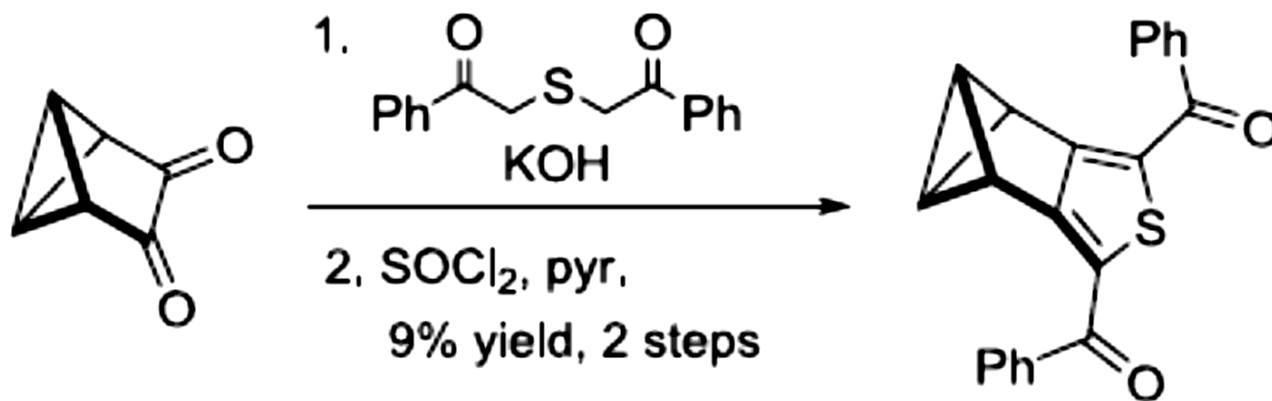


Miyahara, Y.; Inazu, T.; Yoshino, T. *Bull. Chem. Soc. Jpn.* 1980, 53, 1187–1188.



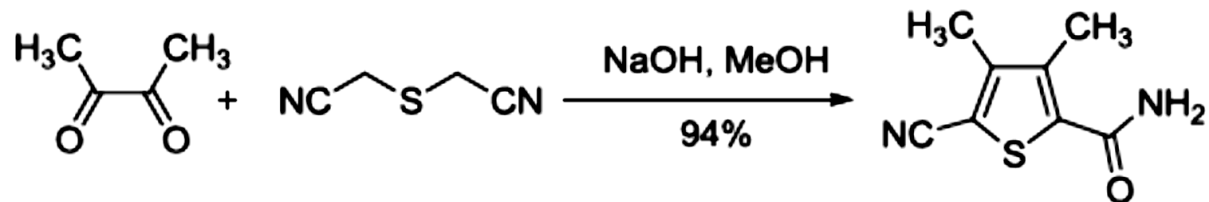


Miyahara, Y.; Inazu, T.; Yoshino, T. *J. Org. Chem.* 1984, 49, 1177–1182.

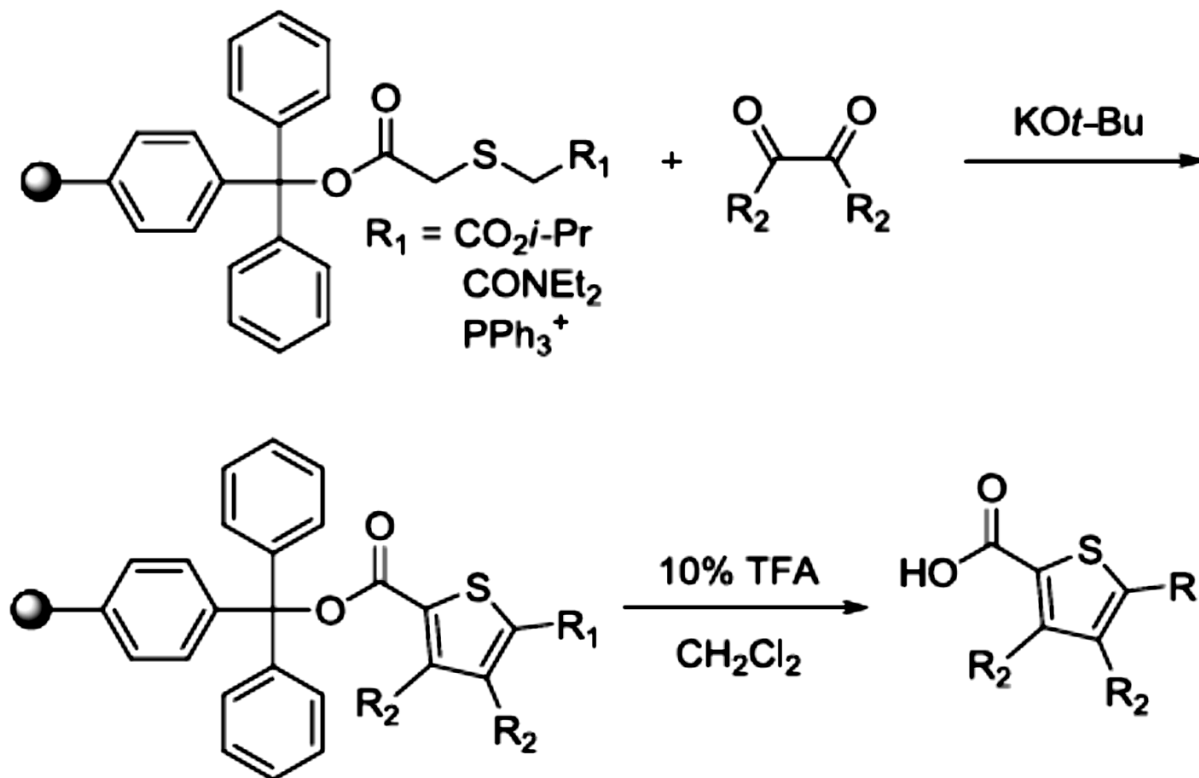


Christl, M.; Krimm, S.; Kraft, A. *Angew. Chem. Int. Ed.* 1990, 29, 675–677.



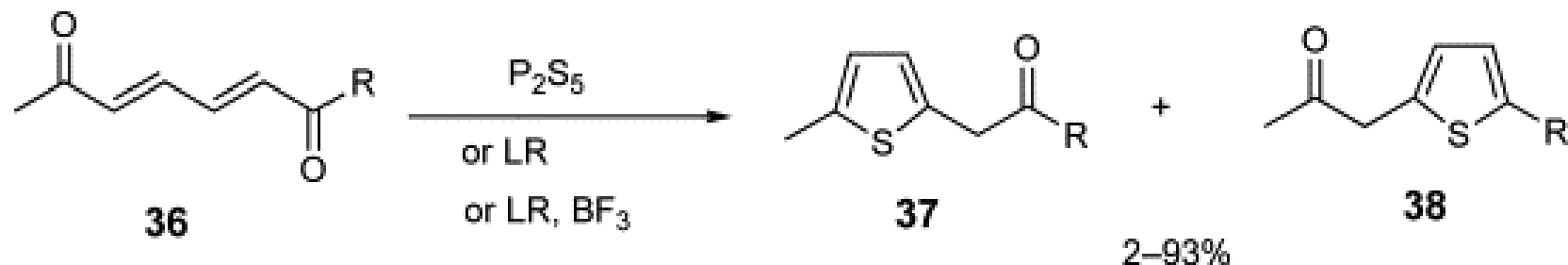
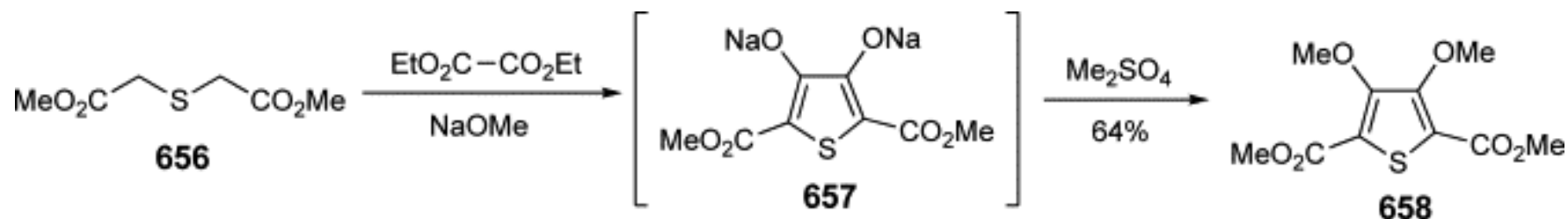


Beye, N.; Cava, M. P. *J. Org. Chem.* 1994, 59, 2223–2226.



Traversone, A.; Brill, W. K.-D. *Tetrahedron Lett.* 2007, 48, 3535–3538.





R = Ph, OEt, C<sub>6</sub>H<sub>4</sub>-4-CO<sub>2</sub>Me, C<sub>6</sub>H<sub>4</sub>-4-OMe

**37:38** = 0:1–1:27

Comprehensive Heterocyclic Chemistry III Volume 3

, 2008, Pages 843-930

3.11 - Thiophenes and their Benzo Derivatives: Synthesis

O. Sato and J. Nakayama



Tsutsui, Hironori, Narasaka, Koichi

Synthesis of Pyrrole Derivatives by the Heck-Type Cyclization of  $\gamma,\delta$ -Unsaturated Ketone O-Pentafluorobenzoyloximes,

Volume 28, Issue 1, January 1999, Pages, Chemistry Letters, 1999, 28, 45–46

<https://doi.org/10.1246/cl.1999.45>

Substituted pyrroles are synthesized from  $\gamma,\delta$ -unsaturated ketone O-pentafluorobenzoyloximes by the intramolecular Heck-type amination of the olefinic moiety catalyzed by  $\text{Pd}(\text{PPh}_3)_4$ .



Anita Kongor, Manthan Panchal, Viren Mehta, Keyur Bhatt, Dehin Bhagat, Devayani Tipre, Vinod K. Jain,

Basketing nanopalladium into calix[4]pyrrole as an efficient catalyst for Mizoroki-Heck reaction, Arabian Journal of Chemistry, 2017, 10, 1125-1135, <https://doi.org/10.1016/j.arabjc.2016.06.019>.

**Abstract:** An approach to synthesize calix[4]pyrrole protected palladium nanoparticles (PdNPs) employed for catalytic Mizoroki-Heck C-C coupling reaction is reported. The nanoparticles are synthesized in water using novel calix[4]pyrrole tetrahydrazide (CPTH) as a reducing as well as stabilizing agent which is a proficient “one-pot” synthesis discouraging the need of an external stabilizer. CPTH-PdNPs have been characterized and studied by UV–Vis spectroscopy, Fourier transform infrared, transmission electron microscopy, energy-dispersive X-ray and powder X-ray diffraction. The synthesized palladium nanoparticles with a size range of 5–9nm show an efficient catalytic activity for Heck cross-coupling reactions giving good yields within short reaction time in comparison with conventional palladium catalyst. Also, a good degree of recyclability is shown by the nanocatalyst with five consecutive catalytic cycles. CPTH-PdNPs also exhibit a potential antimicrobial activity against gram-negative bacteria which shows the biological applicability of the synthesized CPTH-PdNPs.



L. Lavenot, C. Gozzi, K. Ilg, I. Orlova, V. Penalva, M. Lemaire,  
Extension of the Heck reaction to the arylation of activated thiophenes,  
Journal of Organometallic Chemistry, 1998, 567, 49-55,  
[https://doi.org/10.1016/S0022-328X\(98\)00667-6](https://doi.org/10.1016/S0022-328X(98)00667-6).

The direct arylation of activated thiophenes was accomplished in moderate to good yields using a Heck-type reaction with the mixture of Pd(OAc)<sub>2</sub> and n-Bu<sub>4</sub>NBr as a catalytic system. This new arylation method is applied to different derivatives and has proved to be compatible with sensitive functional groups. Furthermore, the substituent nature and position on the thiophene moiety influence the cross coupling. In particular the substitution is regiospecific when the heterocycle is substituted at position 2 with an electron withdrawing group.  
Keywords: Heck reaction; Activated thiophenes; Arylation

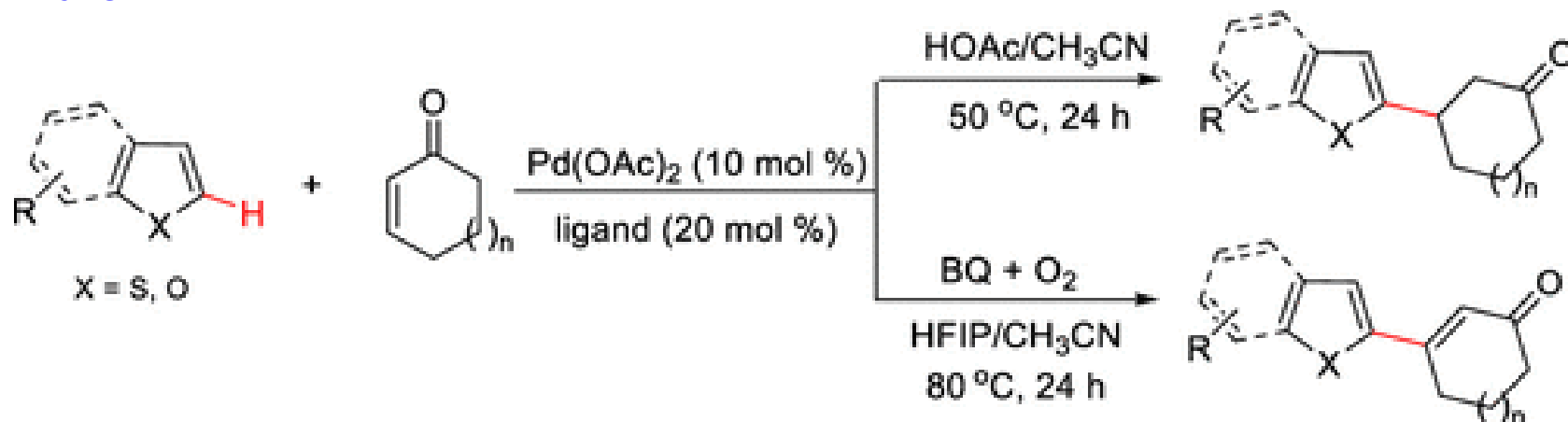


# Palladium-Catalyzed Controllable Reductive/Oxidative Heck Coupling between Cyclic Enones and Thiophenes via C–H Activation

Organic Letters 2019, 21, 23, 9545-9549

DOI: 10.1021/acs.orglett.9b03721

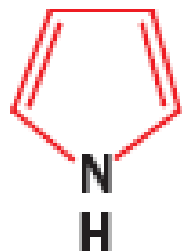
Herein, we report a straightforward, environmentally friendly, and controllable palladium/ligand catalytic system to enable reductive/oxidative Heck reactions of cyclic enones with thiophene or furan derivatives via C–H activation. The key to this tunable reaction is the appropriate intercepting thienyl-Pd(II)-enolate during the enolization process. Such a controllable and economic protocol would not only provide efficient methods to construct various value-added  $\beta$ -heteroarylated cyclic ketones/enones but also shed light on developing other conjugate addition reactions via C–H activation.



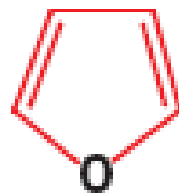
# REACCIONES DE FURANO, PIRROL Y TIOFENO

## COMPUESTOS $\pi$ EXCESIVOS

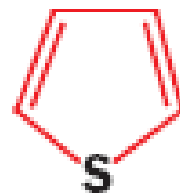




pirrol



furano



tiofeno

ENERGÍAS DE  
RESONANCIA  
(Kcal / mol):

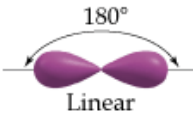

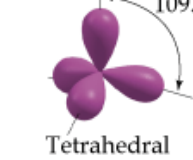
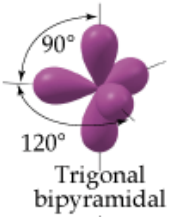
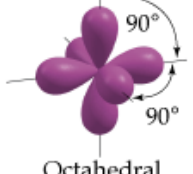
21

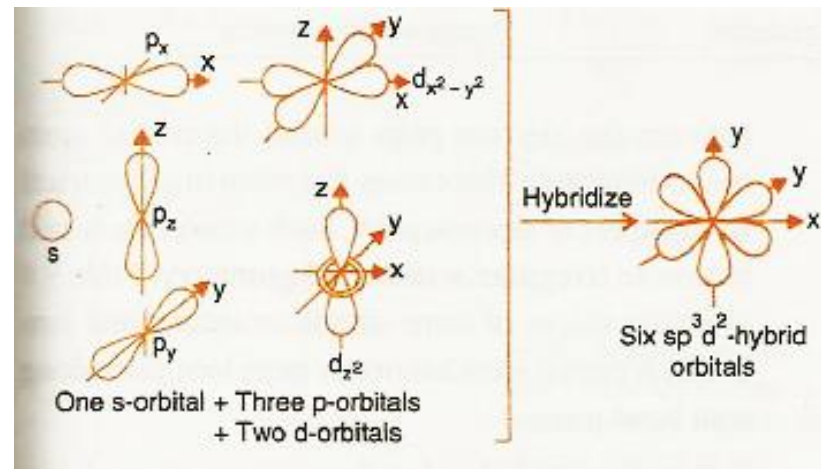
16

28



$sp^3d^2$

TABLE 9.4 Geometrical Arrangements Characteristic of Hybrid Orbital Sets			
Atomic Orbital Set	Hybrid Orbital Set	Geometry	Examples
$s, p$	Two $sp$	 Linear	$\text{BeF}_2, \text{HgCl}_2$
$s, p, p$	Three $sp^2$	 Trigonal planar	$\text{BF}_3, \text{SO}_3$
$s, p, p, p$	Four $sp^3$	 Tetrahedral	$\text{CH}_4, \text{NH}_3, \text{H}_2\text{O}, \text{NH}_4^+$
$s, p, p, p, d$	Five $sp^3d$	 Trigonal bipyramidal	$\text{PF}_5, \text{SF}_4, \text{BrF}_3$
$s, p, p, p, d, d$	Six $sp^3d^2$	 Octahedral	$\text{SF}_6, \text{ClF}_5, \text{XeF}_4, \text{PF}_6^-$



<https://www.quora.com/In-FeF6-3-how-can-Fe-have-five-unpaired-electrons-while-simultaneously-contributing-two-3D-orbitals-to-form-hybrid-orbitals>

## Enlace covalente coordinado

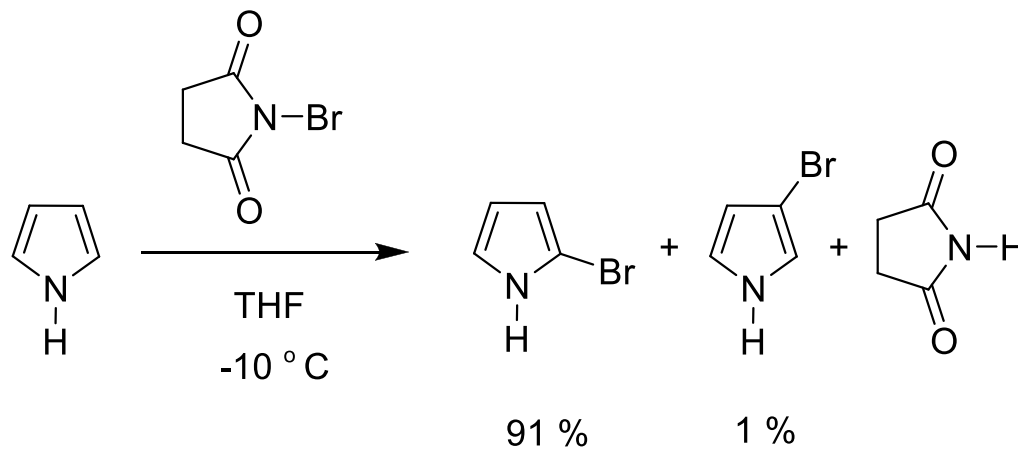
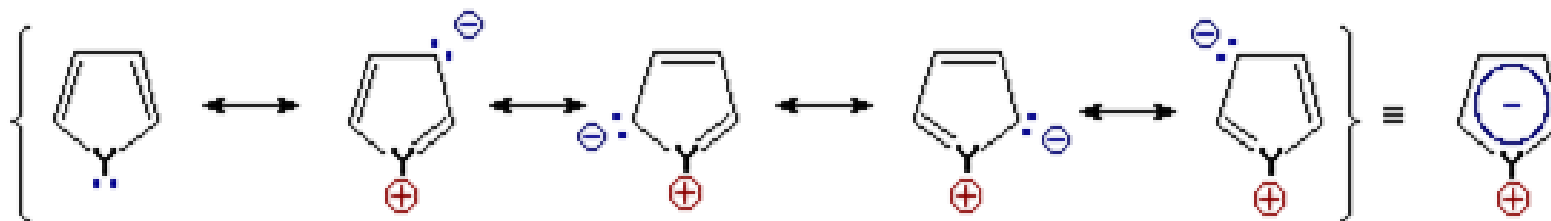


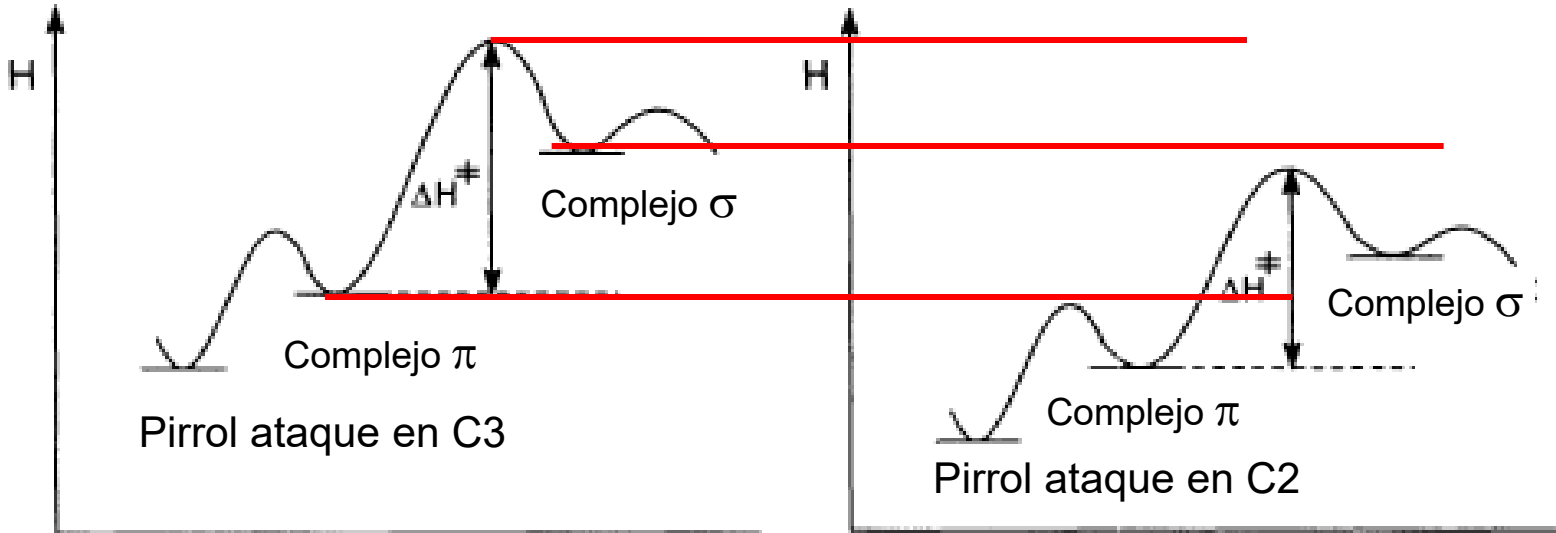
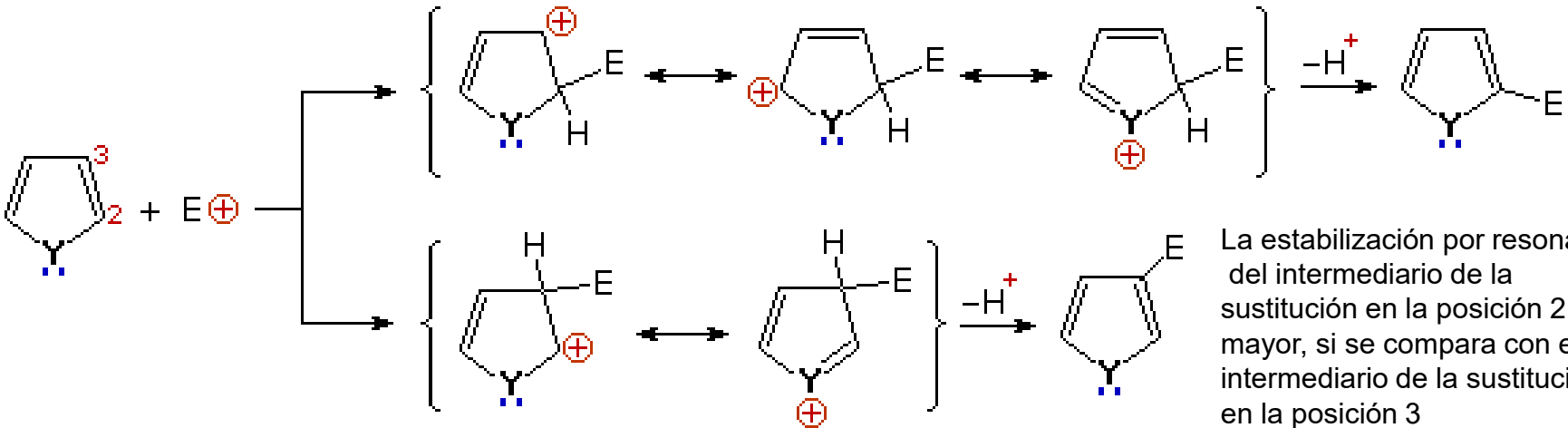
Nevil Vincent Sidgwick  
Químico inglés  
(1873 - 1952)

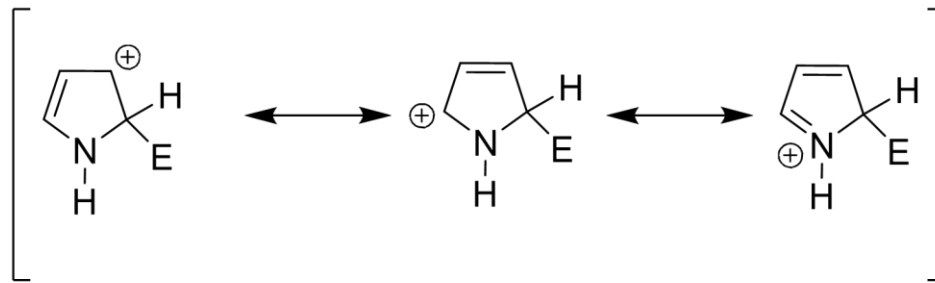
[http://www.oneonta.edu/faculty/viningwj/Chem111/Chapters\\_9%20and\\_11\\_study\\_guide%20.htm](http://www.oneonta.edu/faculty/viningwj/Chem111/Chapters_9%20and_11_study_guide%20.htm)



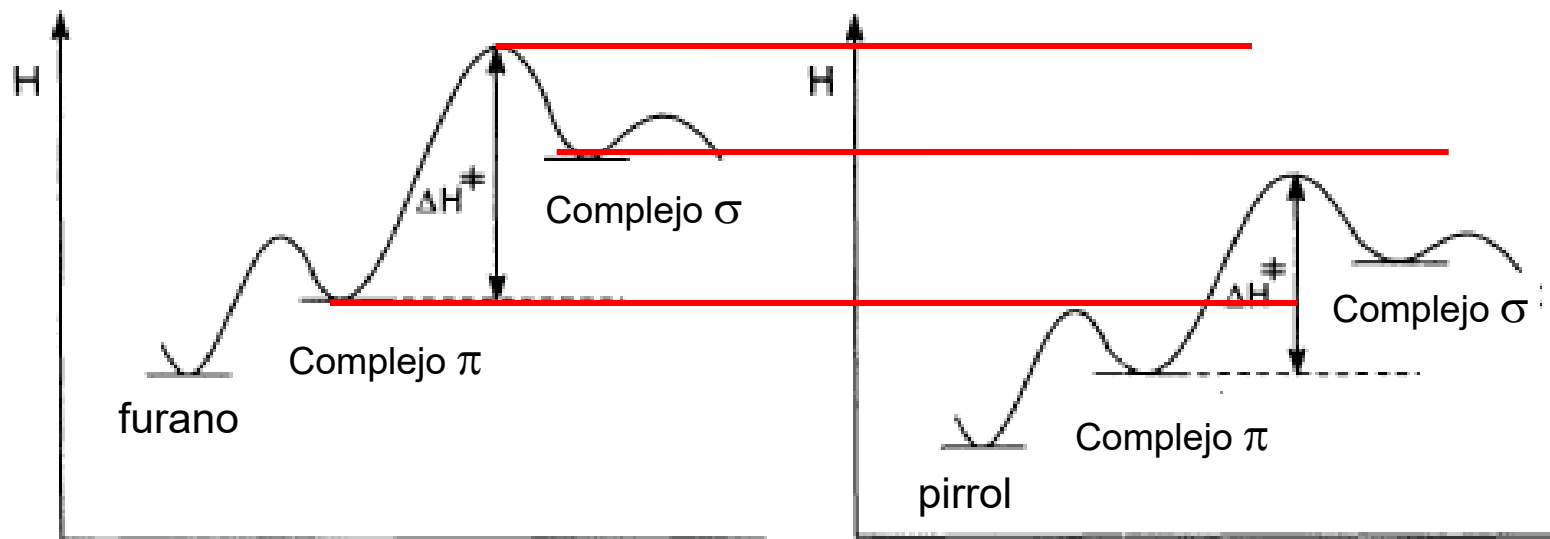
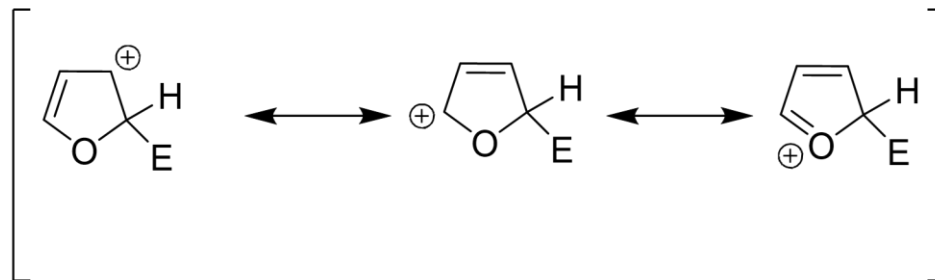
# COMPUESTOS $\pi$ -EXCESIVOS: FORMAS RESONANTES CON CARGA

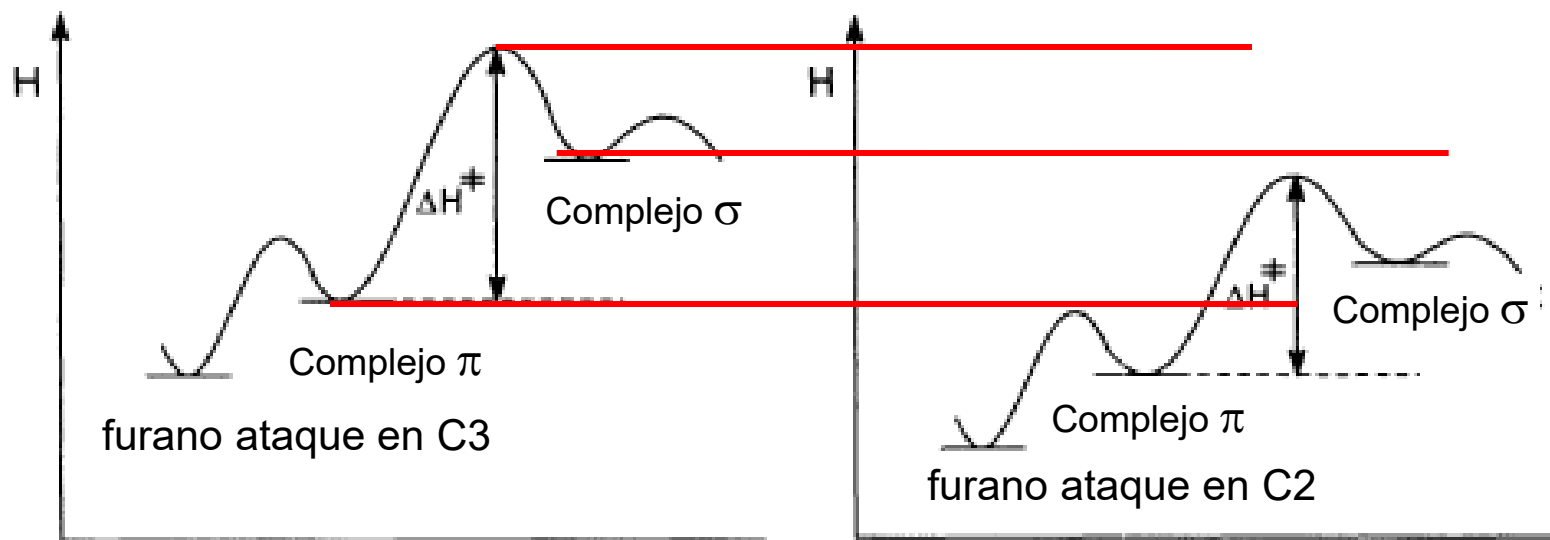
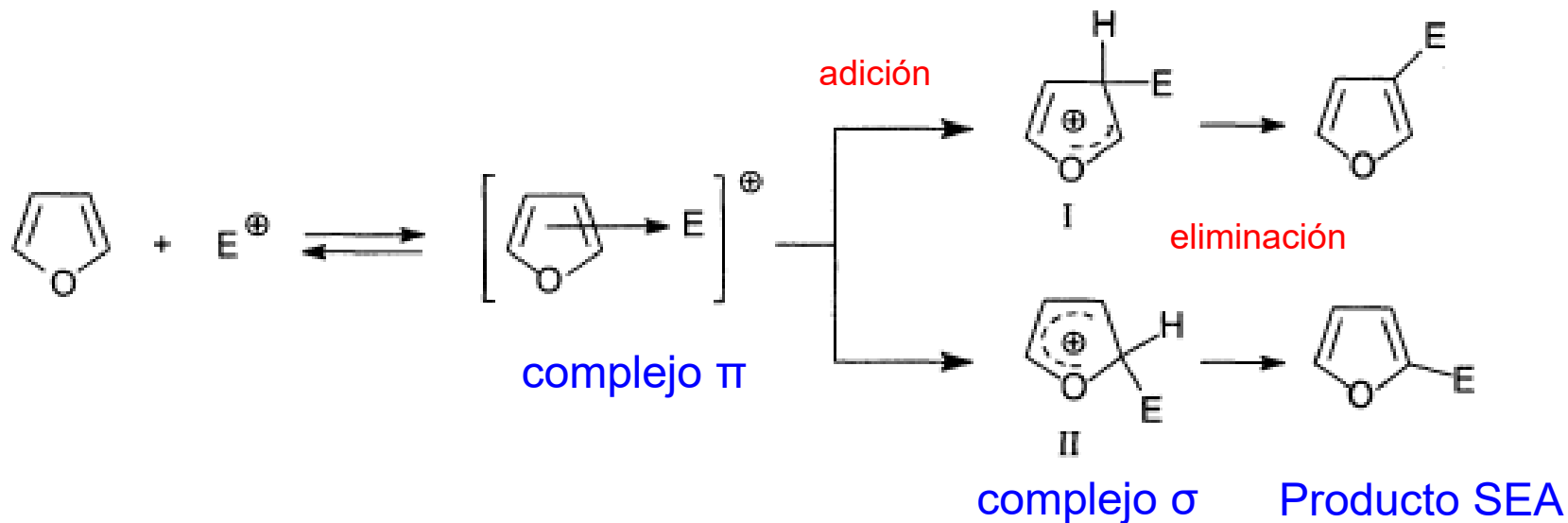




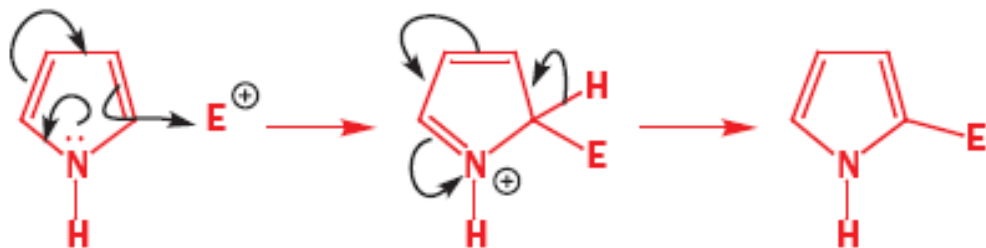


Sistema más estable

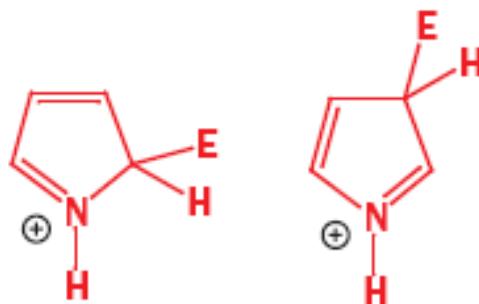
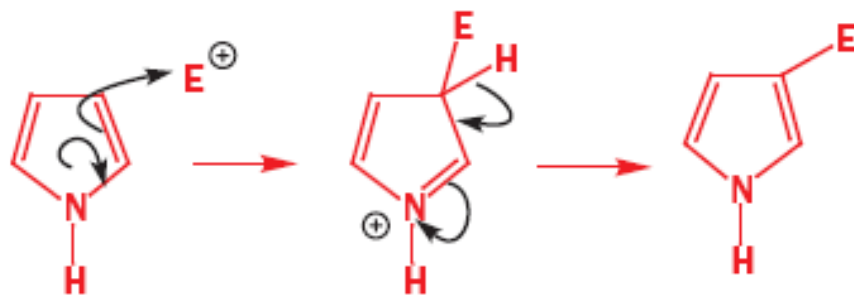




## Reacción con electrófilo en la posición 2

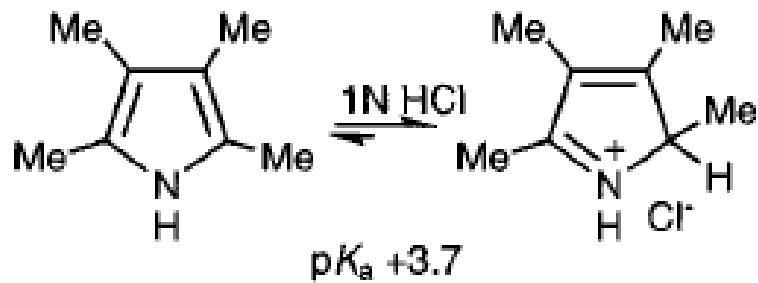
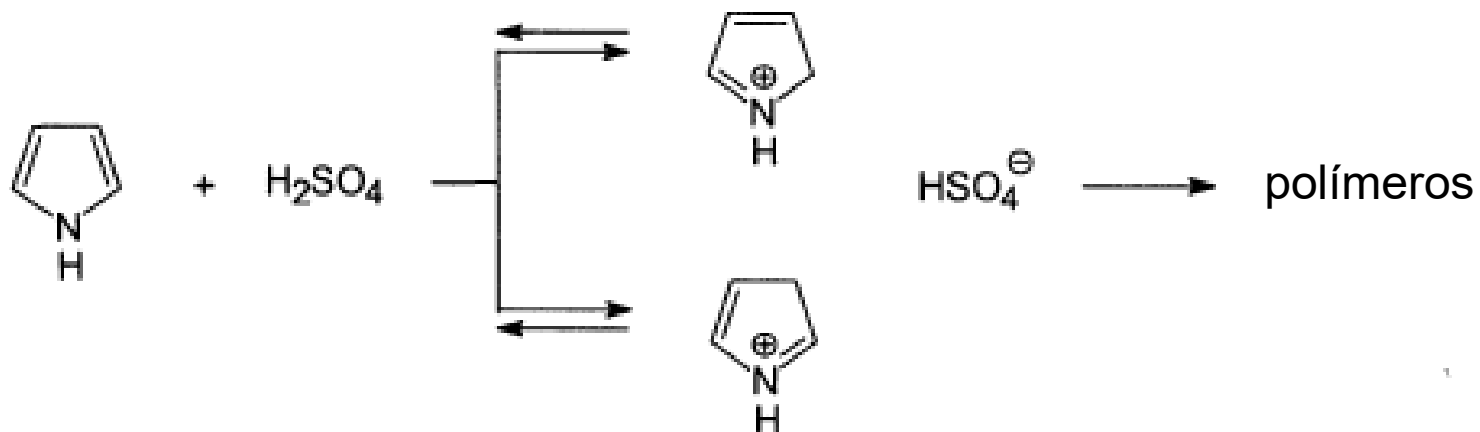


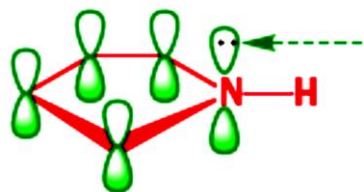
## Reacción con electrófilo en la posición 3



Más estable      Menos estable

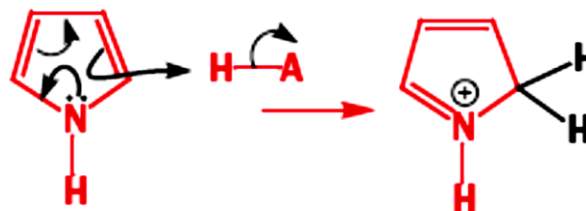
# POLIMERIZACIÓN





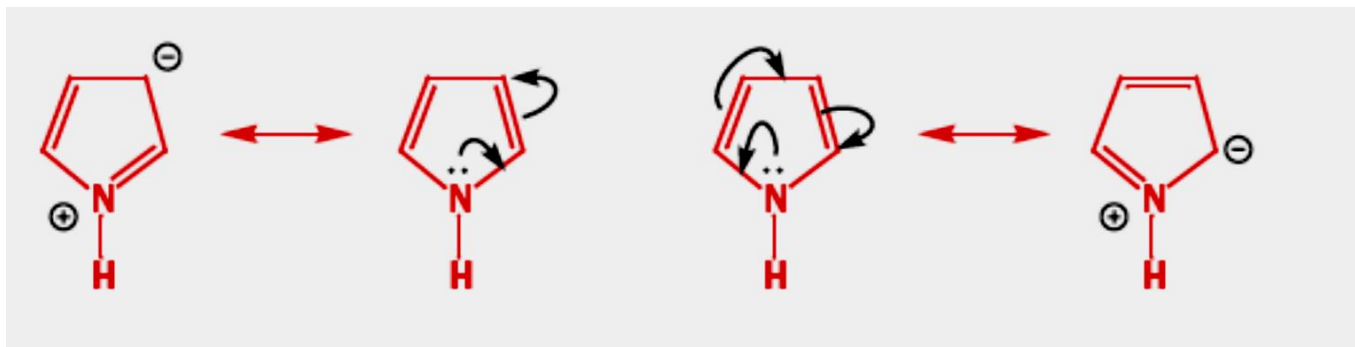
El par de electrones del N permite que el pirrol complete la capa de orbitales moleculares de enlace

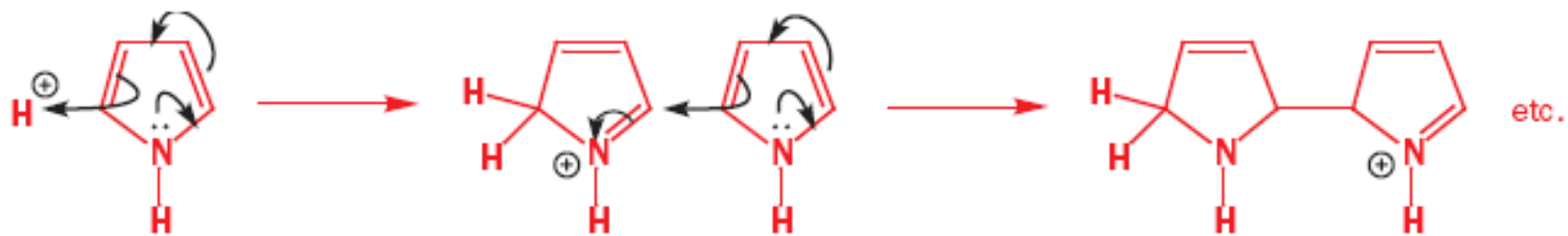
pKa del pirrol  $\cong$  4



pirrol aromático

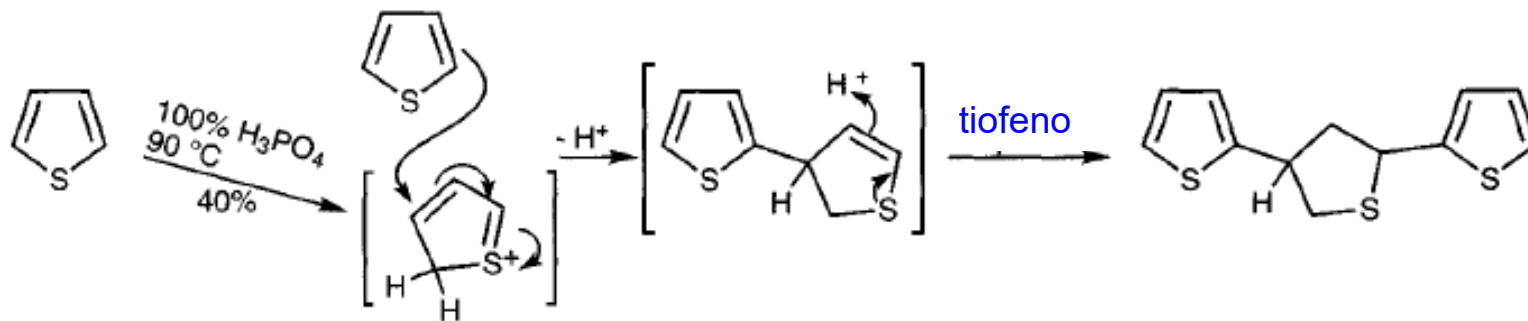
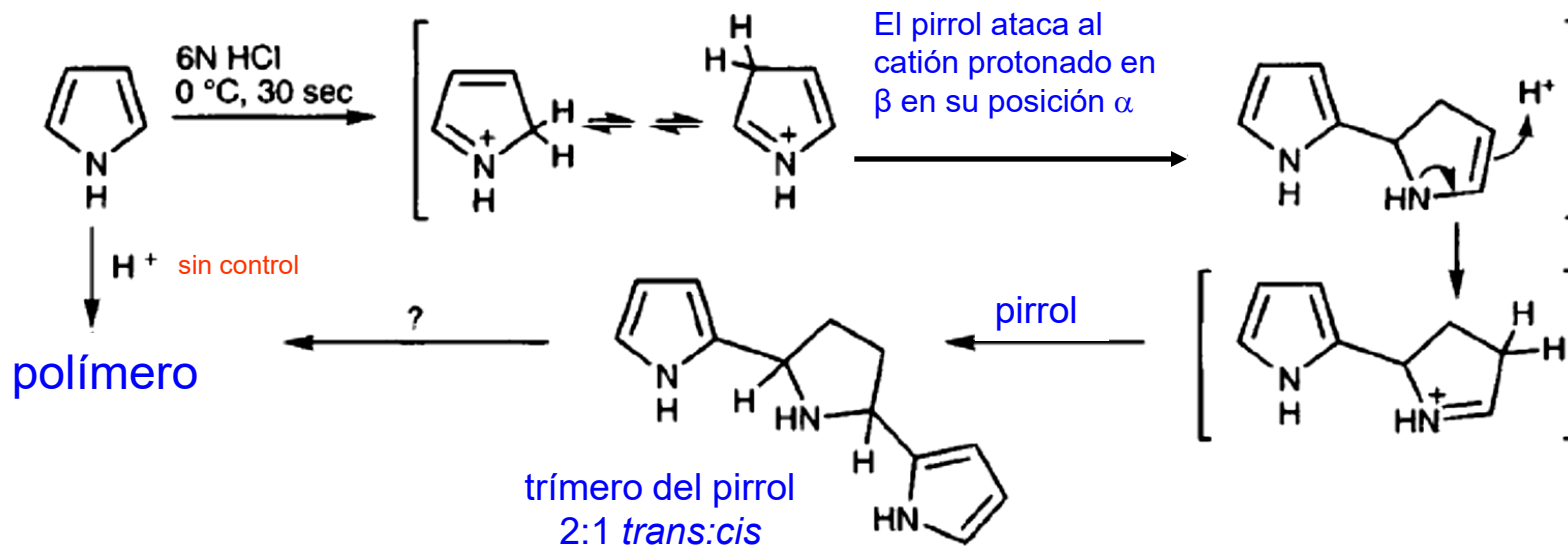
Catión del pirrol  
No aromático



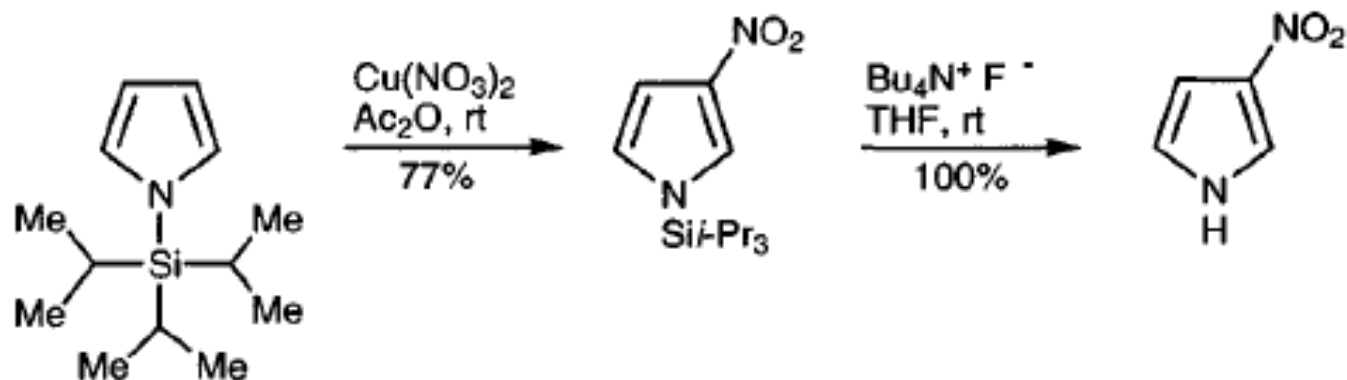
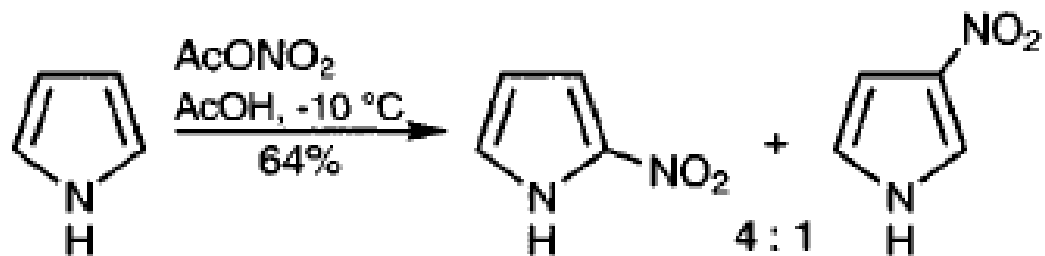
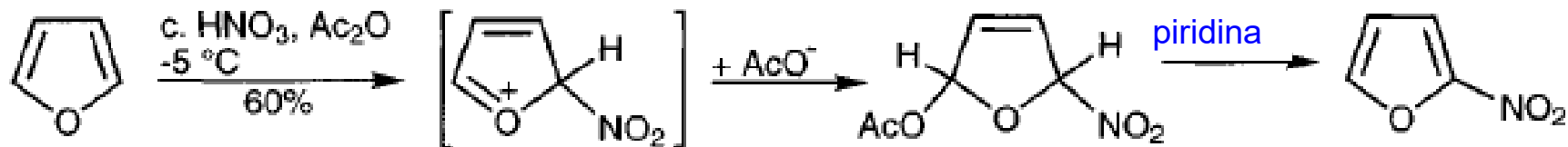


La reacción continúa para dar el polímero

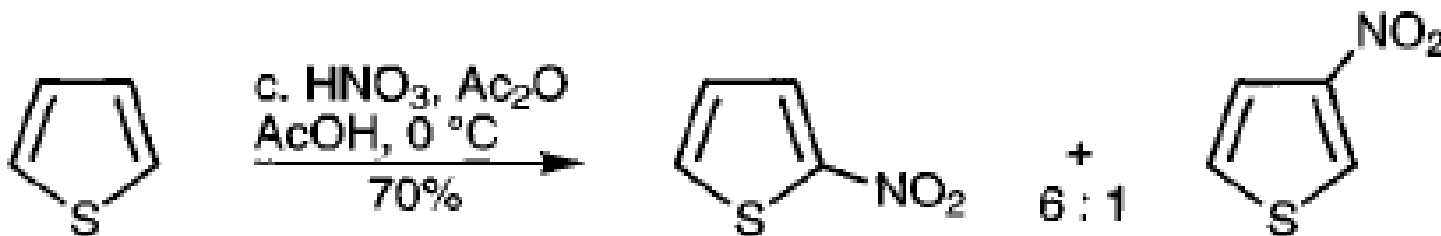




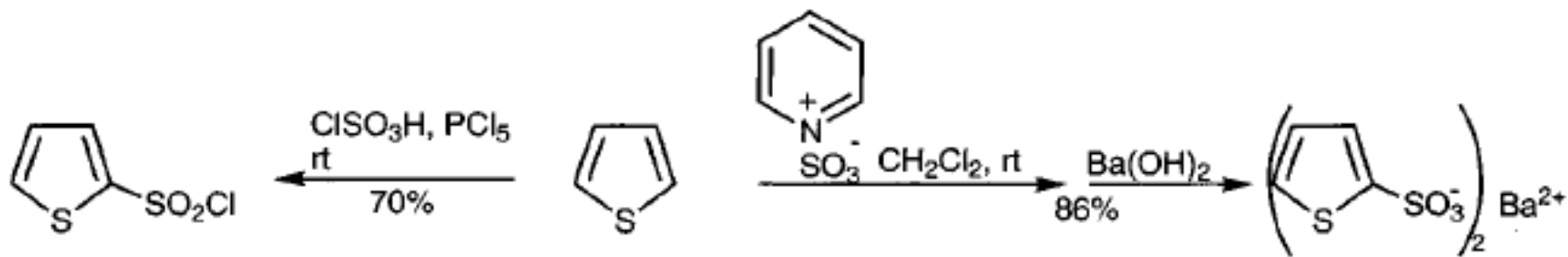
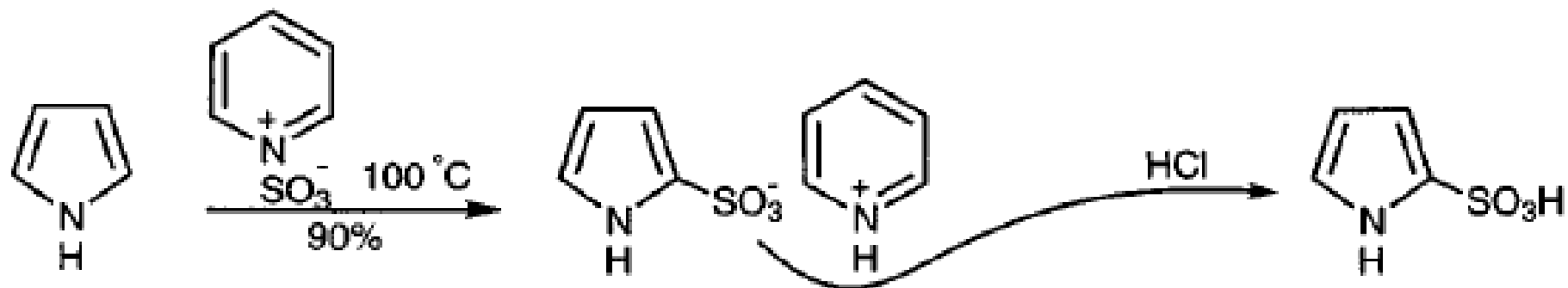
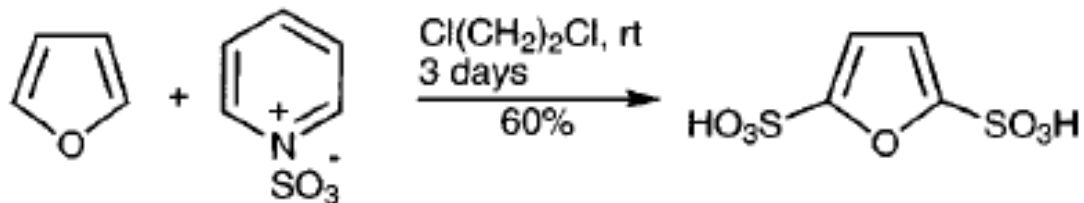
# NITRACIÓN



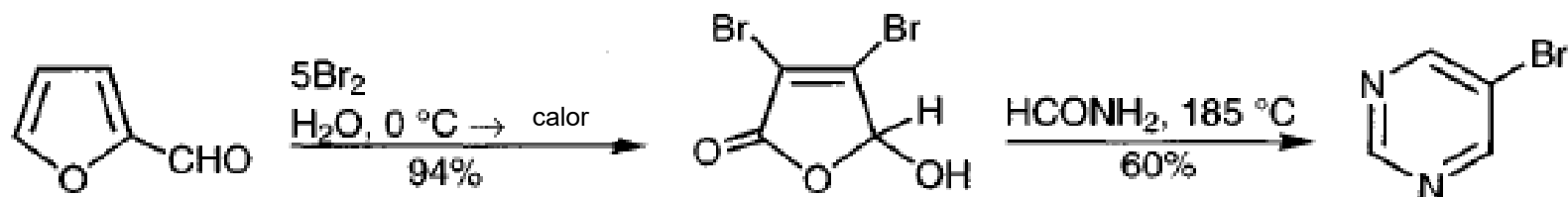
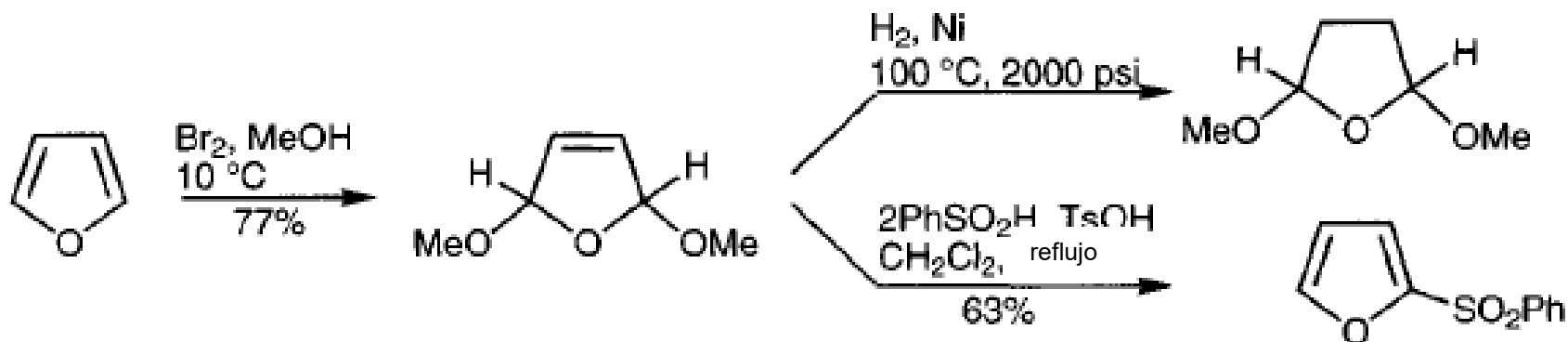
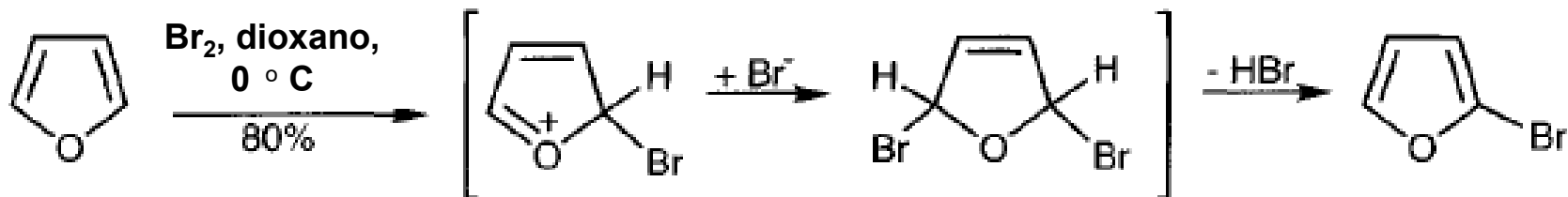
## Nitración tiofeno



# SULFONACIÓN



# HALOGENACIÓN



Ácido mucobromico



# Guillermo de Ockham

- Filósofo Inglés
- Principal exponente de la Baja Escolástica
- Excomulgado de la iglesia



Navaja De Ockham → Separación entre fe y razón

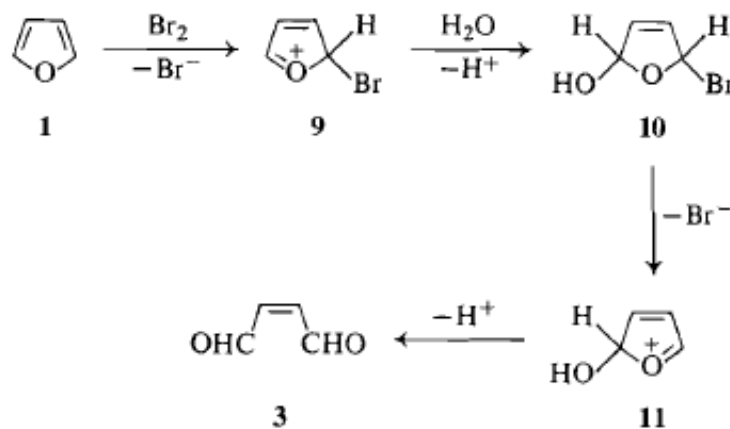
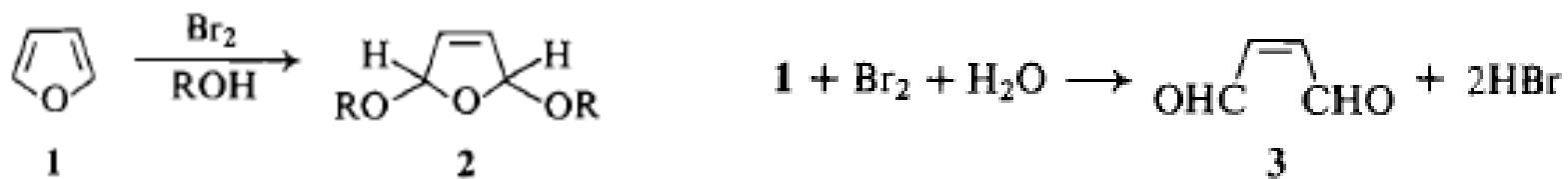
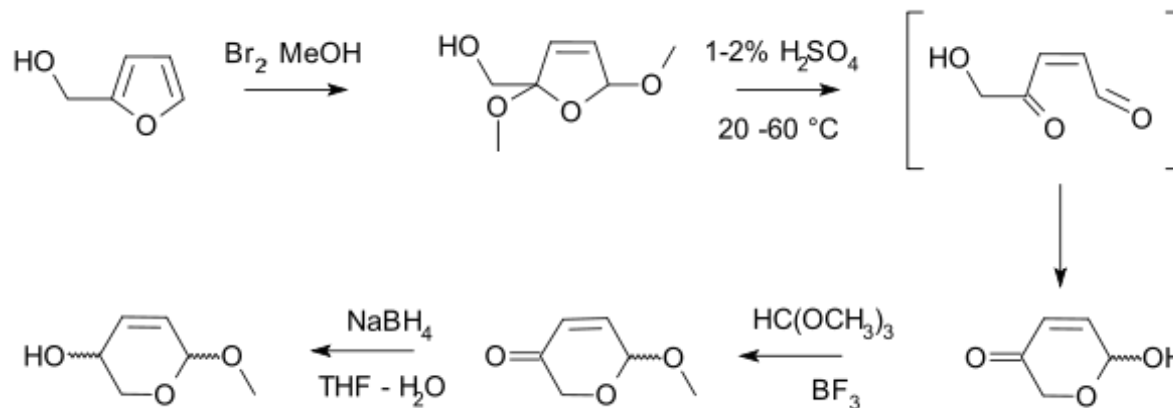
**Navaja:** *'Entia non sunt multiplicanda sine necessitate'* o 'Los entes no deben ser multiplicados sin necesidad'

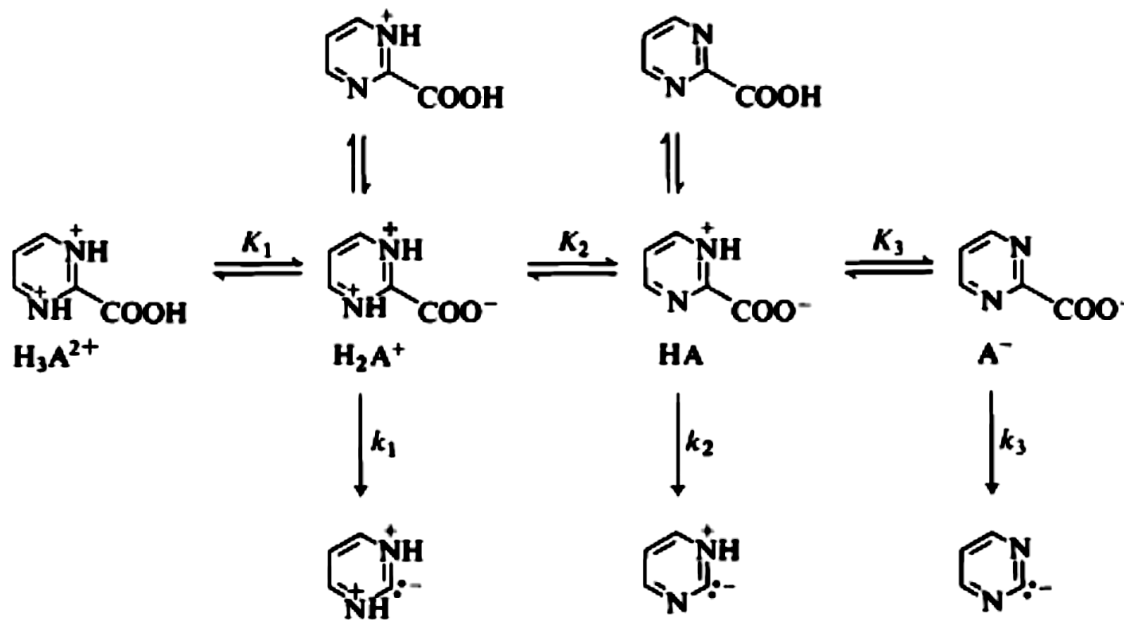
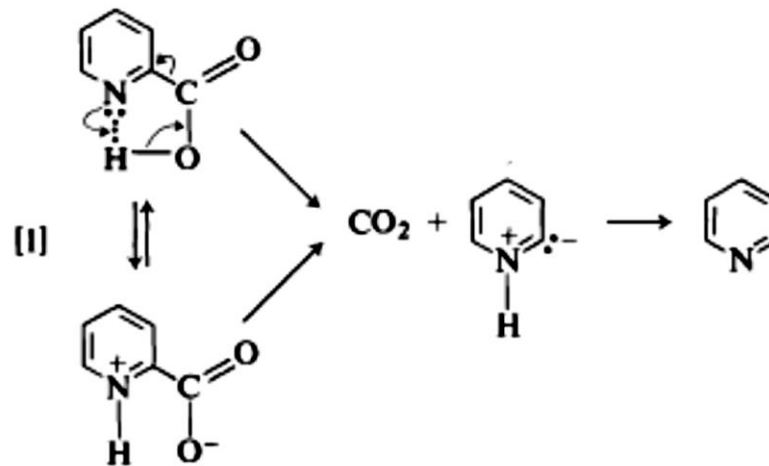
La opción más sencilla, es probablemente la correcta

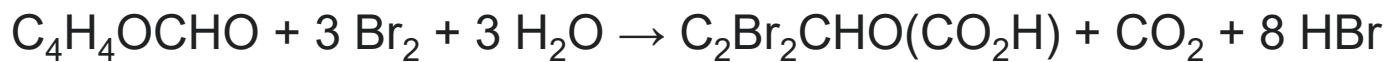
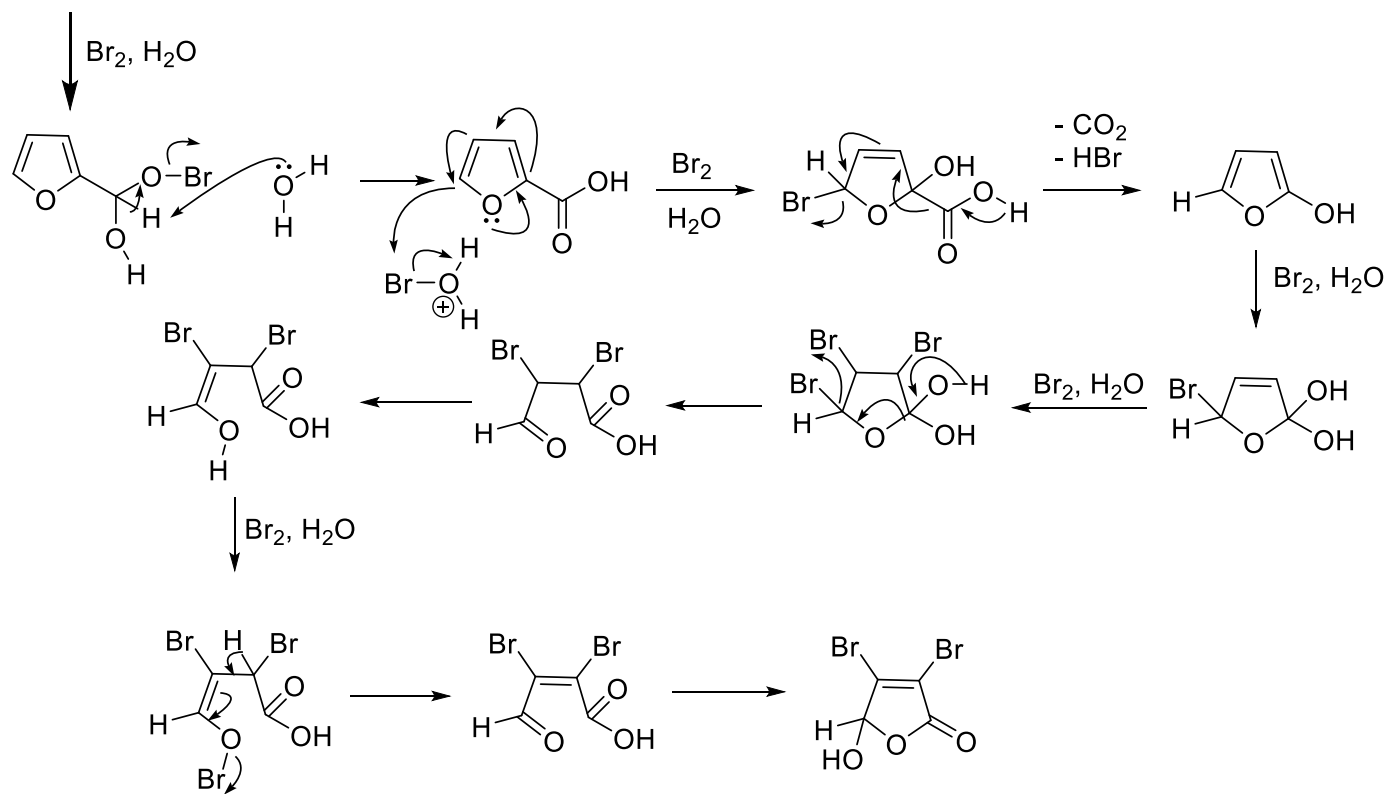
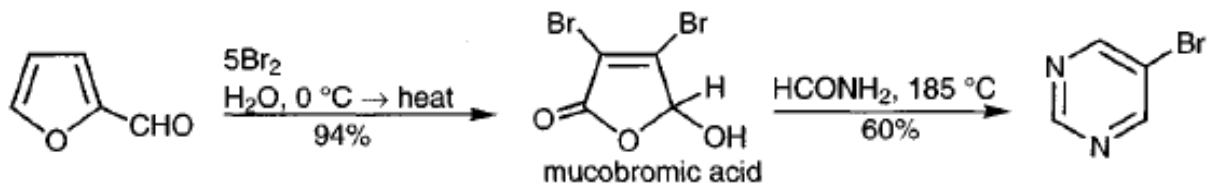
<http://triflenew.blogspot.com/2015/09/navaja-de-ockham.html>

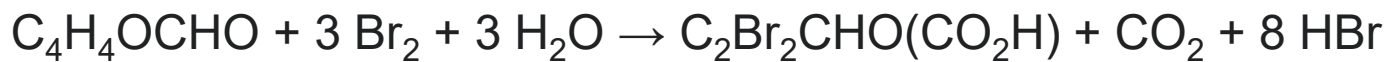
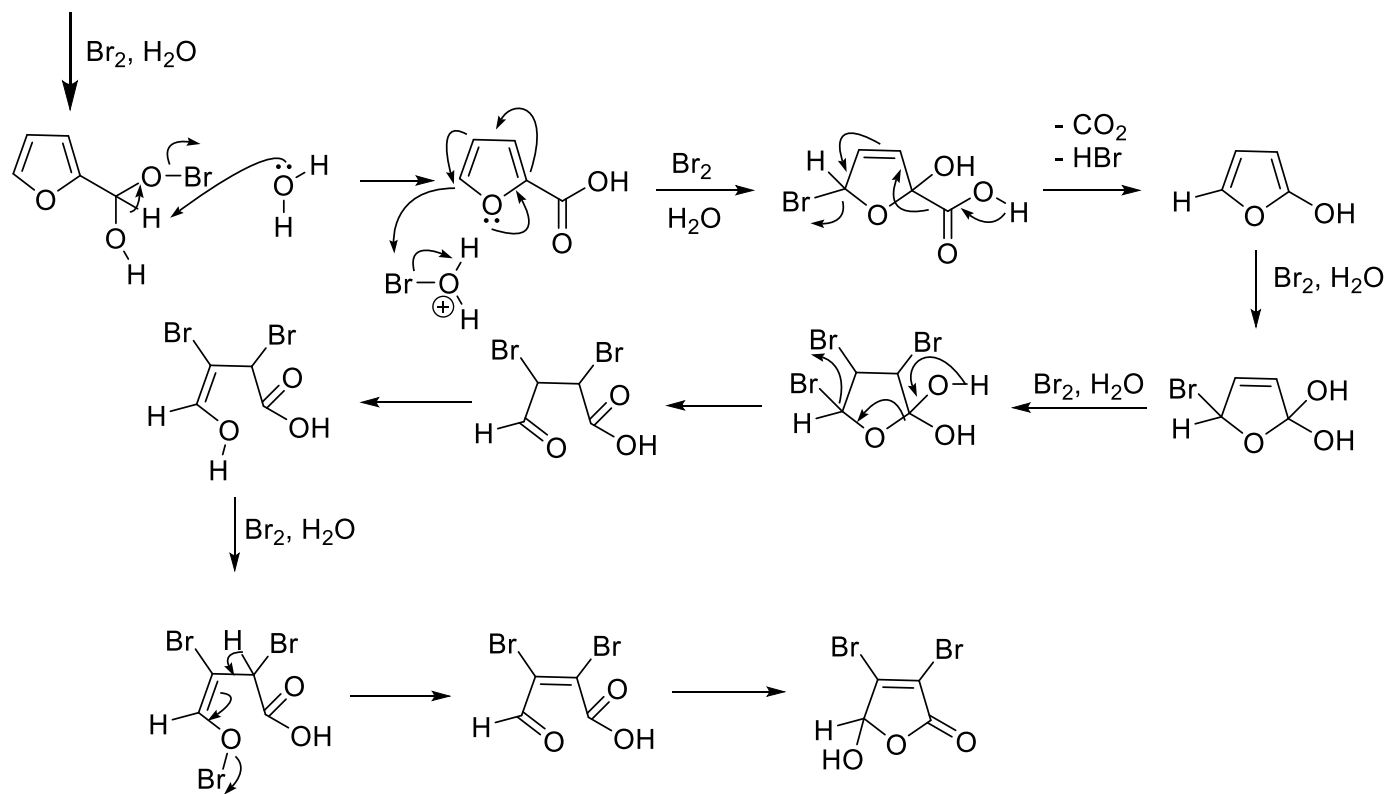
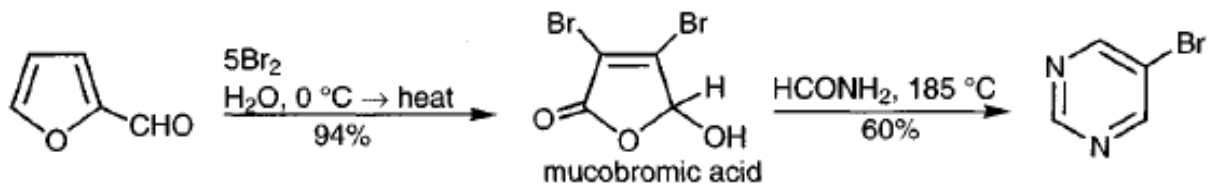
En su forma más simple, el principio de Ockham indica que las explicaciones nunca deben multiplicar las causas sin necesidad. Cuando dos o más explicaciones se ofrecen para un fenómeno, la explicación completa más simple es preferible; es decir, no deben multiplicarse las entidades sin necesidad.

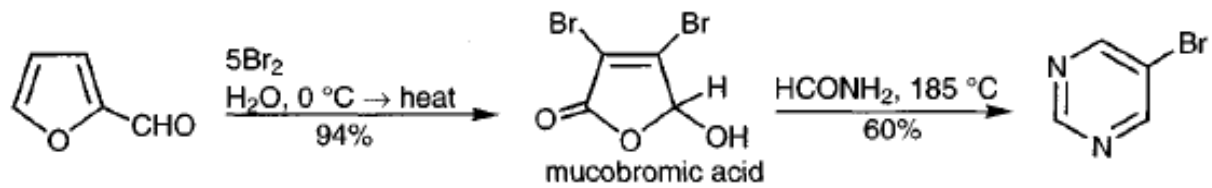


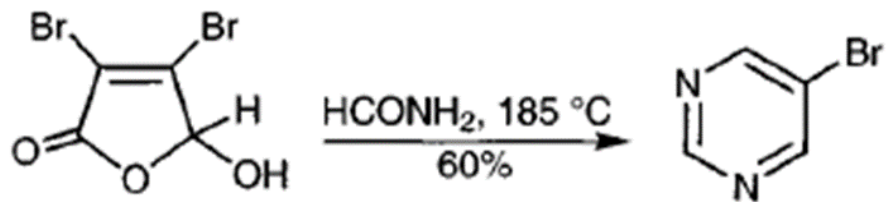




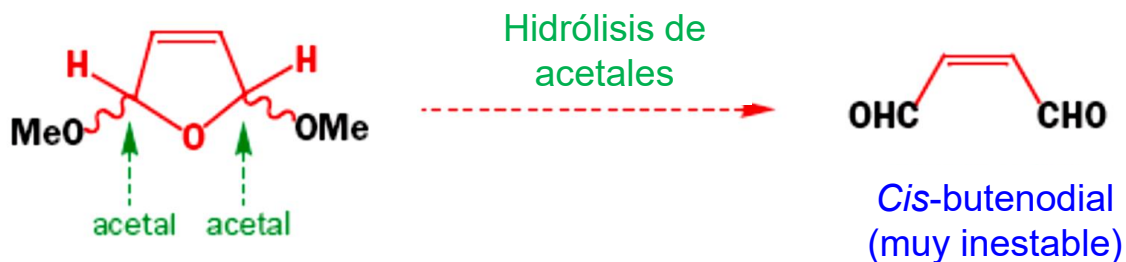
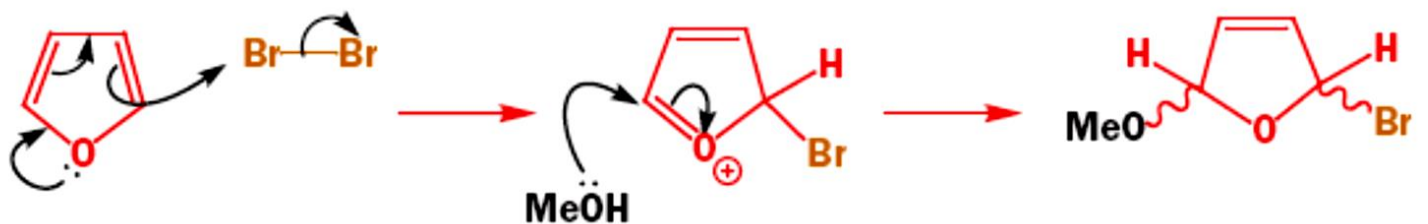
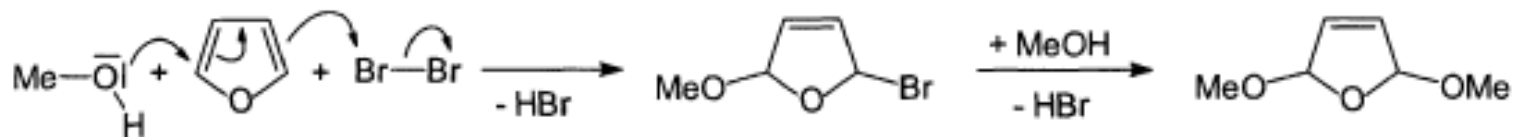




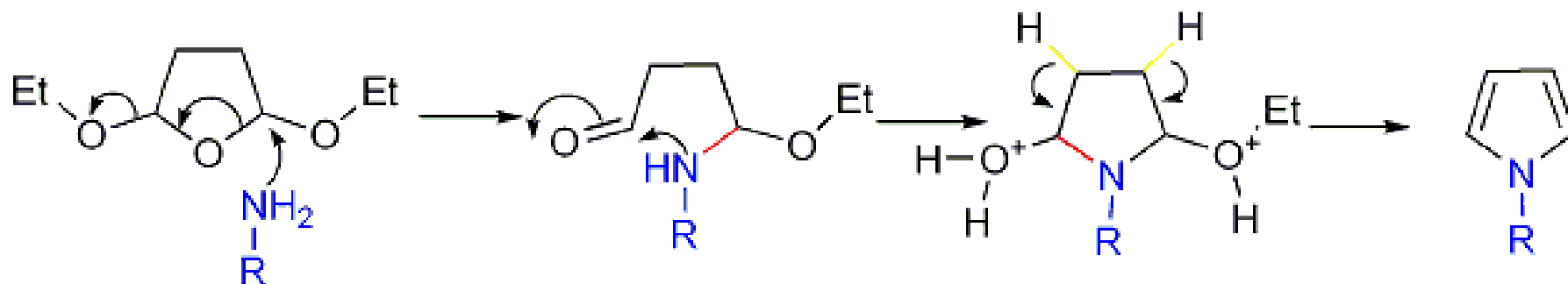
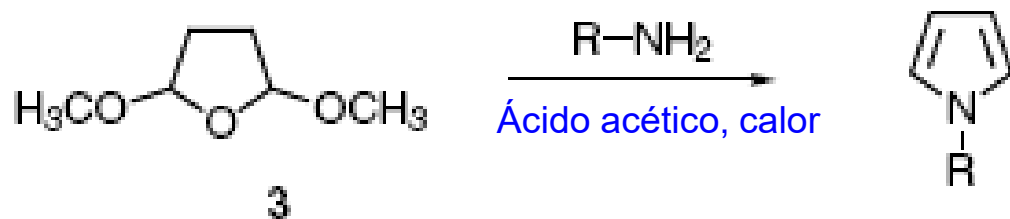




# HALOGENACIÓN. REACCIONES DE ADICIÓN



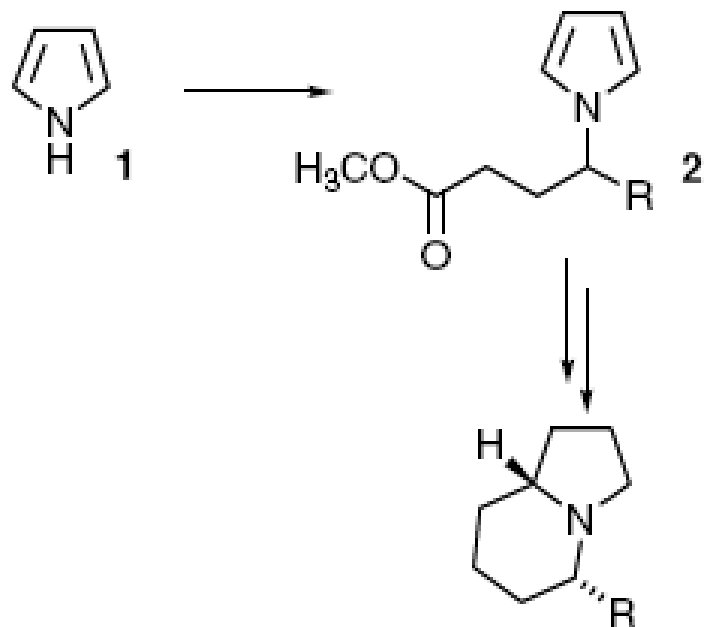
## Reacción de Clauson-Kaas



# A new and high yielding synthesis of unstable pyrroles via a modified Clauson-Kaas reaction

Brendon S. Gourlay,<sup>a</sup> Peter P. Molesworth,<sup>a</sup> John H. Ryan<sup>b</sup> and Jason A. Smith<sup>a,\*</sup>

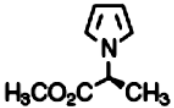
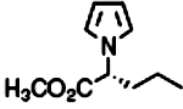
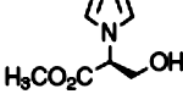
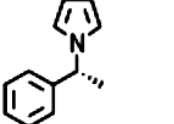
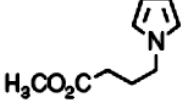
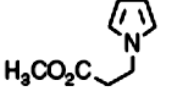
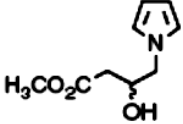
Tetrahedron Letters 47 (2006) 799–801



R = *n*-C<sub>8</sub>H<sub>17</sub> (±)-indolizidine 209D

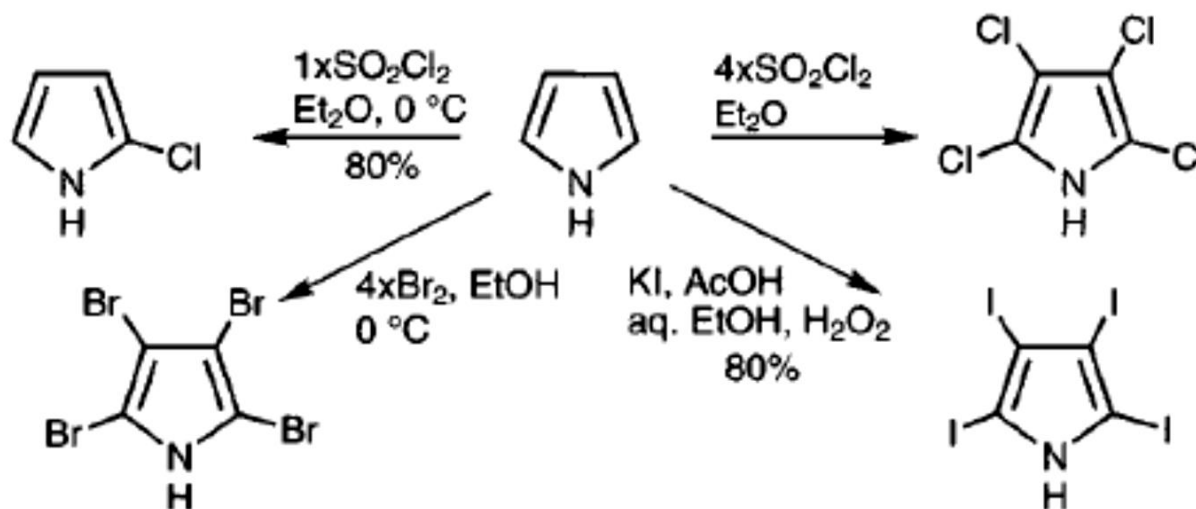
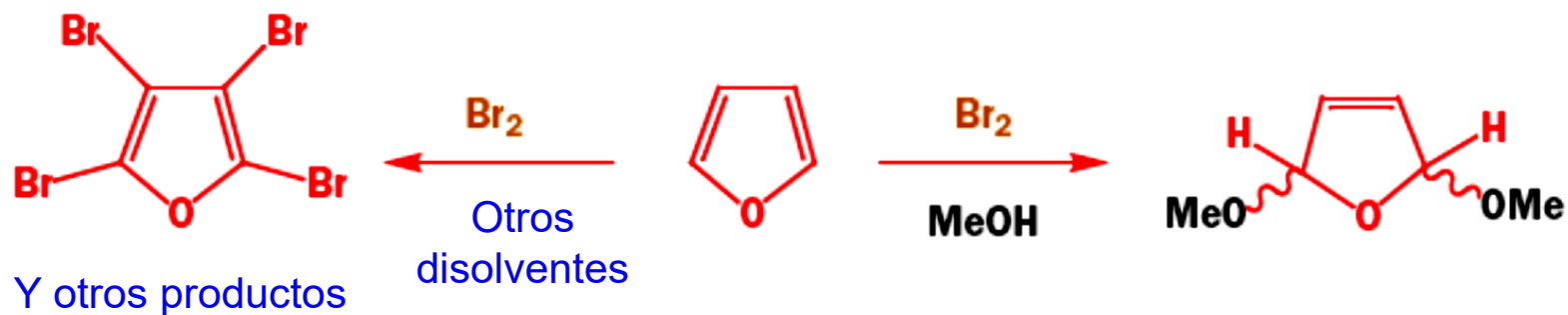


**Table 1.** Yields and ee's of pyrroles from the modified Clauson-Kaas reaction

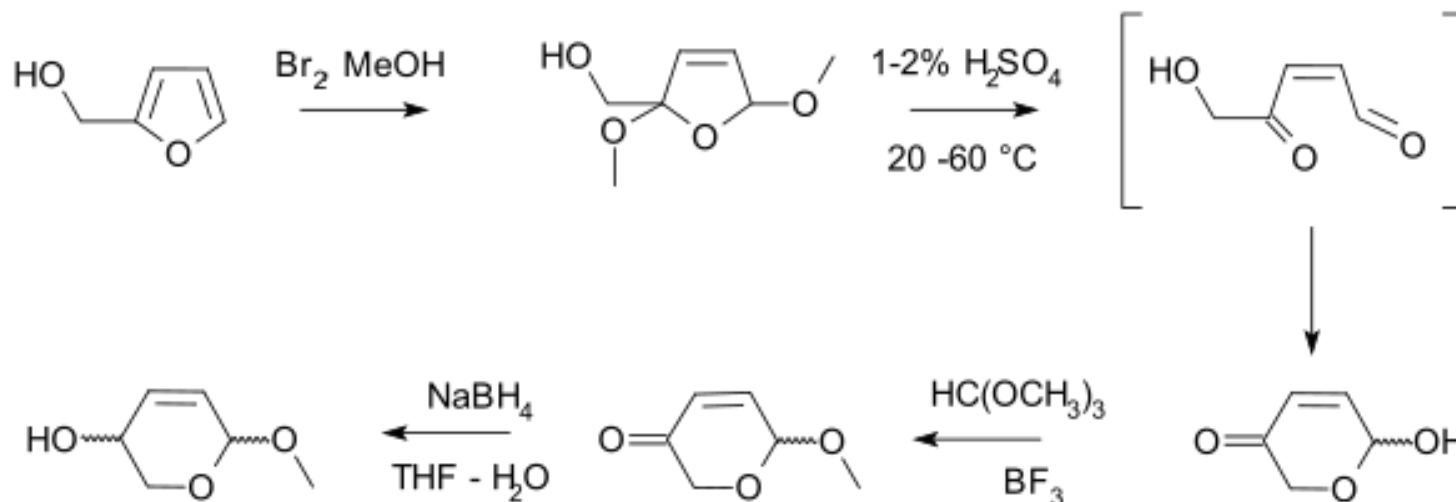
Entry	Amine	Product	Yield/% <sup>a</sup> (ee/%) <sup>b</sup>
1	L-Alanine methyl ester hydrochloride		93 (99)
2	D-Norvaline methyl ester hydrochloride		94 (99)
3	L-Serine methyl ester hydrochloride		89 (99)
4	R-(−)-Phenylethylamine		91 (99)
5	γ-Aminobutyric acid methyl ester hydrochloride		91
6	β-Alanine methyl ester hydrochloride		90
7	(±)-4-Amino-3-hydroxybutyric acid methyl ester hydrochloride		93

<sup>a</sup> Yields quoted are isolated yields.<sup>b</sup> ee's Determined by chiral GC on an Agilent Technologies Cyclosil B capillary (30 m, 0.25 mm, 0.25 μm) featuring a 30% heptakis (2,3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin in DB-1701 stationary phase.

# HALOGENACIÓN



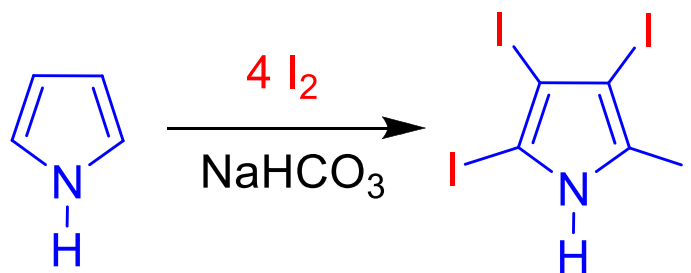
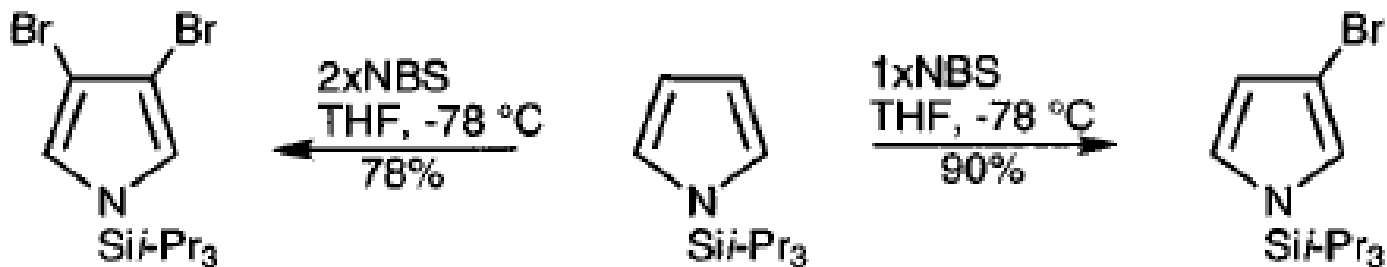
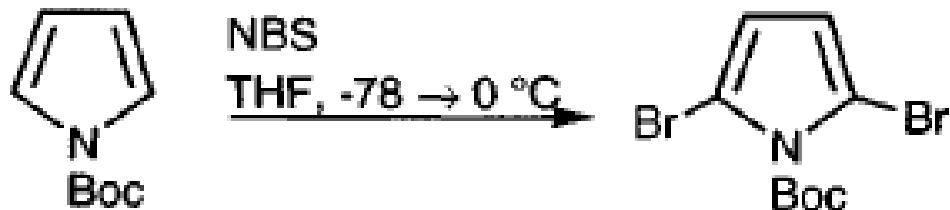
## Rearreglo de Achmatowicz



Achmatowicz, O.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. (-01-01). "Synthesis of methyl 2,3-dideoxy-DL-alk-2-enopyranosides from furan compounds: A general approach to the total synthesis of monosaccharides". *Tetrahedron*. **1971**, 27 (10): 1973–1996. [doi:10.1016/S0040-4020\(01\)98229-8](https://doi.org/10.1016/S0040-4020(01)98229-8). ISSN 0040-4020

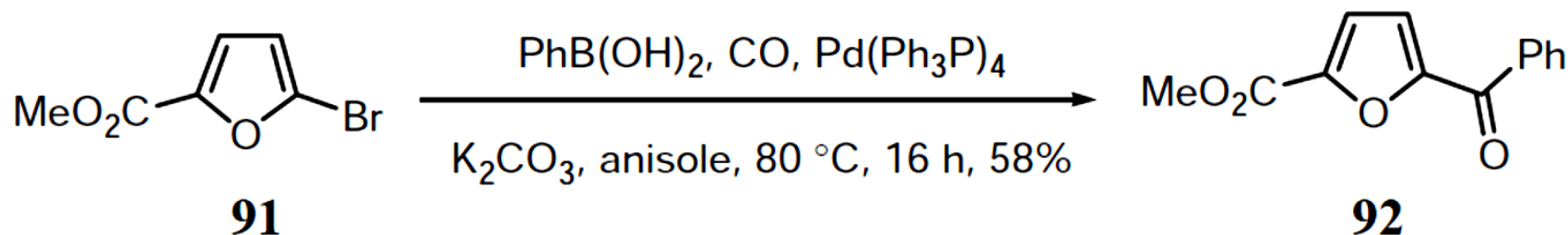


# HALOGENACIÓN



# Acoplamiento Suzuki-Miyaura

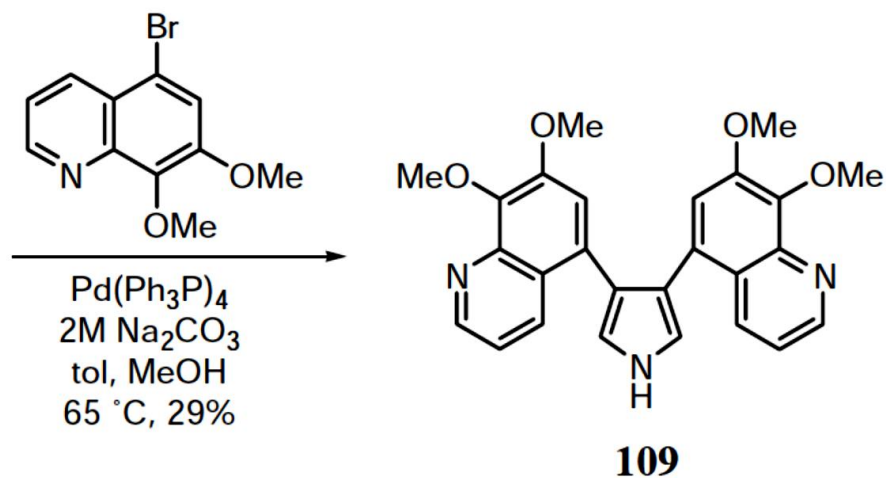
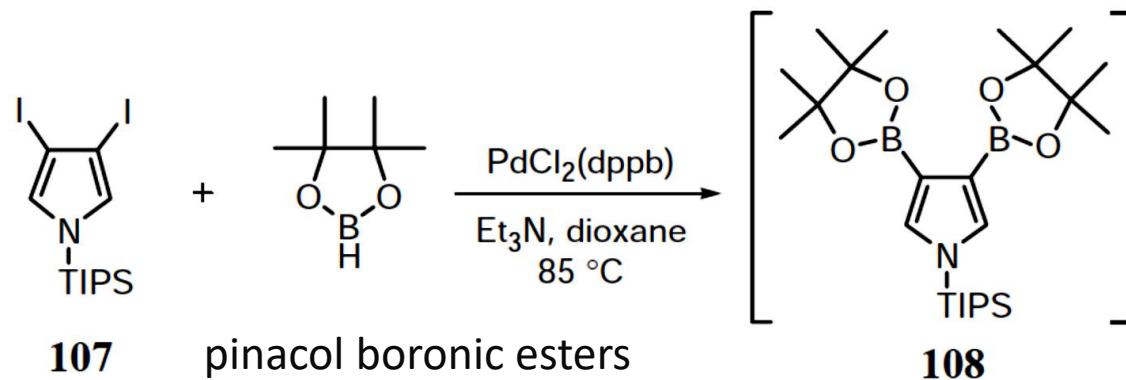
La reacción de acoplamiento cruzado de tres componentes catalizada por Pd entre reactivos de aril metal, monóxido de carbono y aril electrófilos es una ruta sencilla y conveniente para el síntesis de biaril cetonas asimétricas. La reacción de electrófilos deficientes en electrones, generalmente sufre de una reacción secundaria que da el producto de acoplamiento directo sin inserción de monóxido. Miyaura desarrolló un eficiente carbonilativo catalizado por Pd reacción de acoplamiento cruzado de tres componentes de un ácido arilborónico con aril electrófilos incluyendo un sustrato de bromofurano. Usando Pd (Ph<sub>3</sub>P)<sub>4</sub> como catalizador, el asimétrico biaril cetona 92 se sintetiza a partir de 2-bromofurano 91. Es notable que el PdCl<sub>2</sub> (dppf), el catalizador de elección para otros haluros de arilo, proporciona un producto de acoplamiento directo exclusivo sin inserción de CO.



Ishiyama, T.; Kizaki, H.; Hayashi, T.; Suzuki, A.; Miyaura, N. *J. Org. Chem.* **1998**, *63*, 4726–31

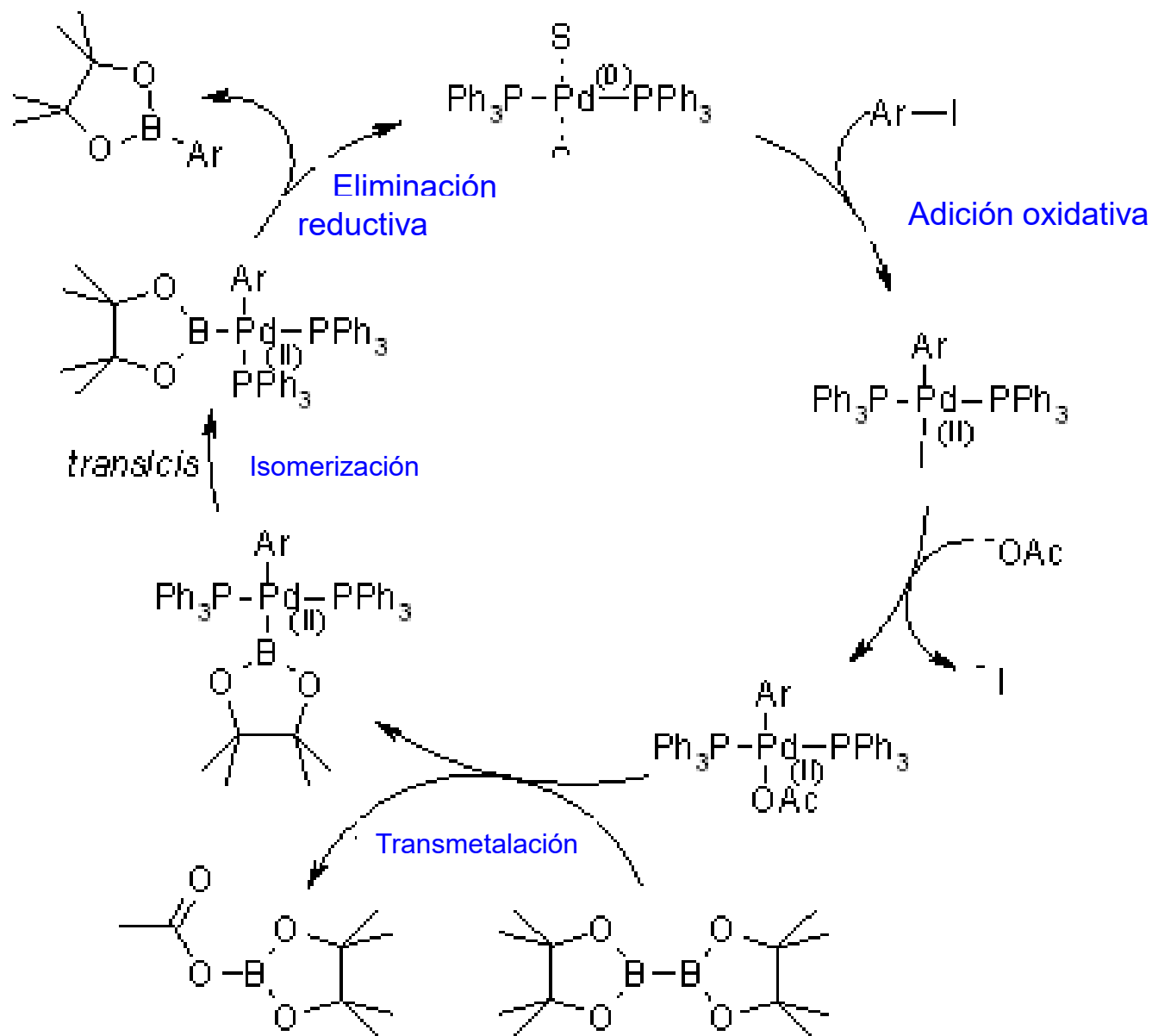


Banwell y sus colaboradores han convertido diiodopirrol 107 en bis-boronato 108, el cual sin purificación se acopló con éxito para producir la bis-quinolina pirrol 109

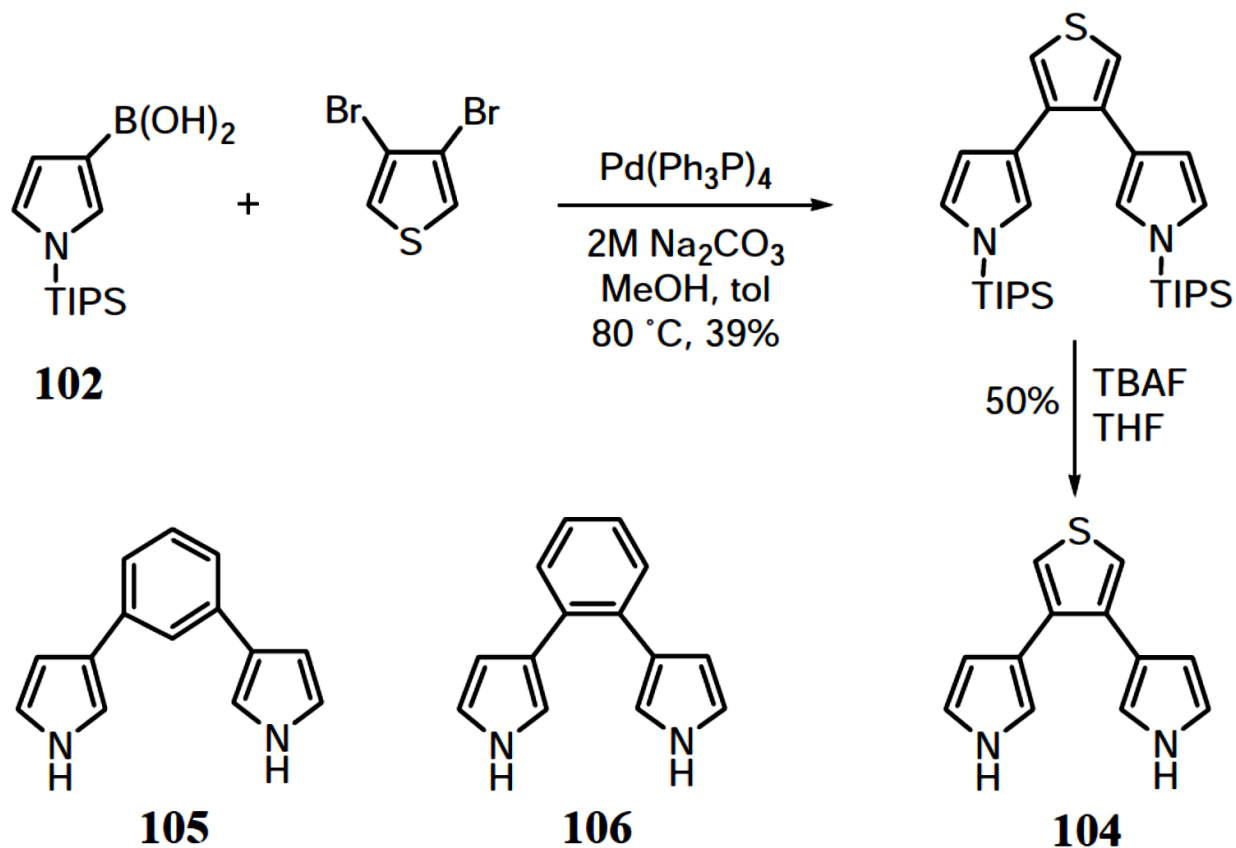


Banwell, M. G.; Bray, A. M.; Edwards, A. J.; Wong, D. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1340–3.



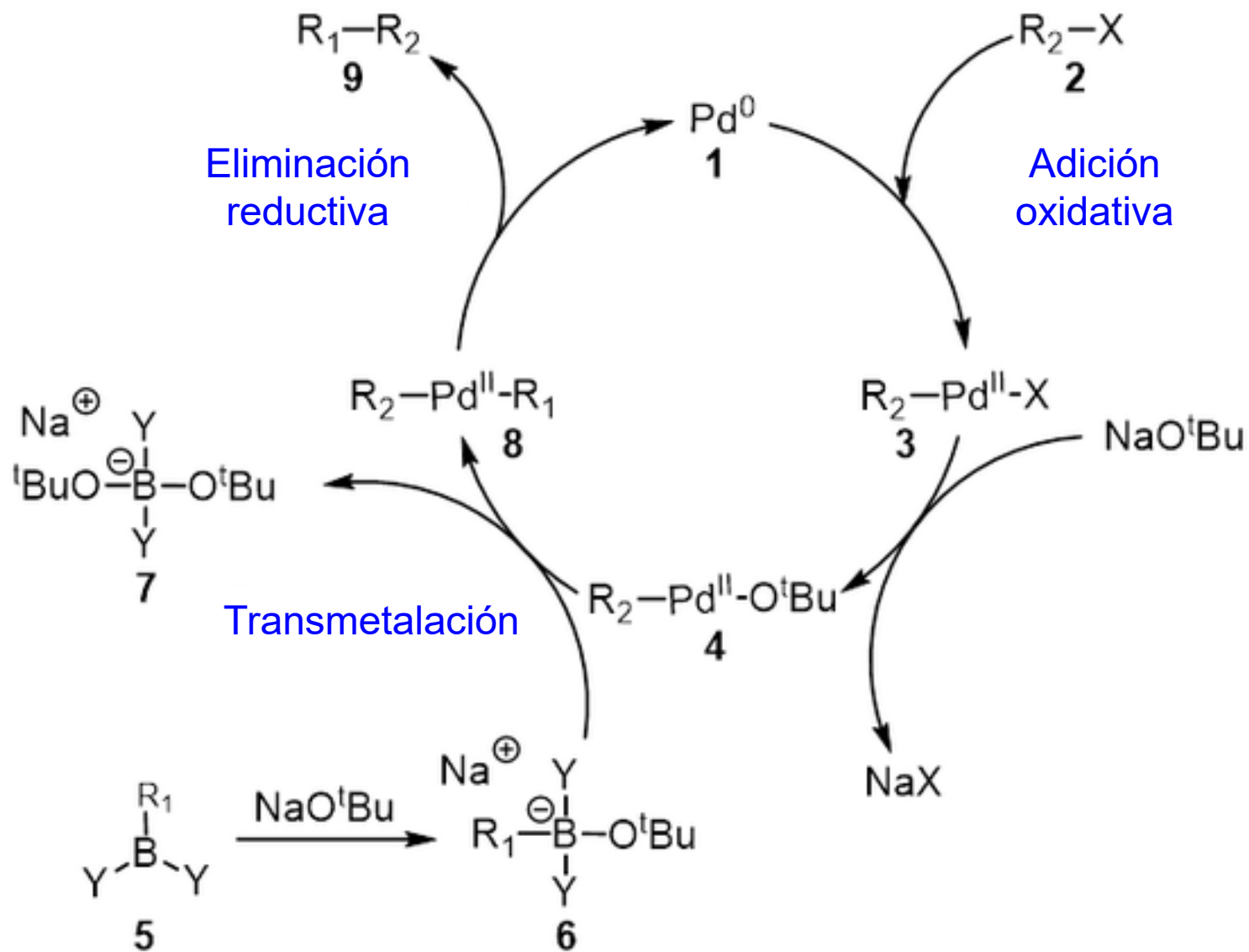


Swager ha utilizado ácido pirrol-3-borónico 102, que fue preparado a partir de 6 por NBS bromación (88%), litiación (BuLi) y boronación (B(OMe)<sub>3</sub>; aq MeOH) (50% en total), en las reacciones de Suzuki para sintetizar bis-pirroles 104-106, en una ruta sintética para obtener polímeros electrocrómicos



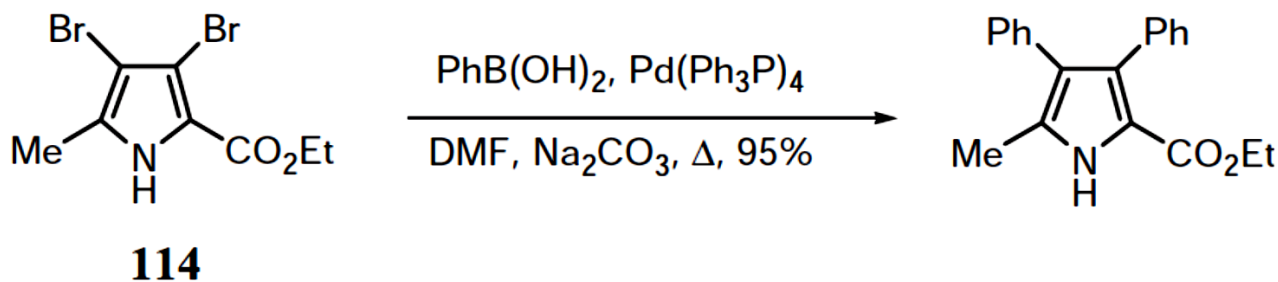
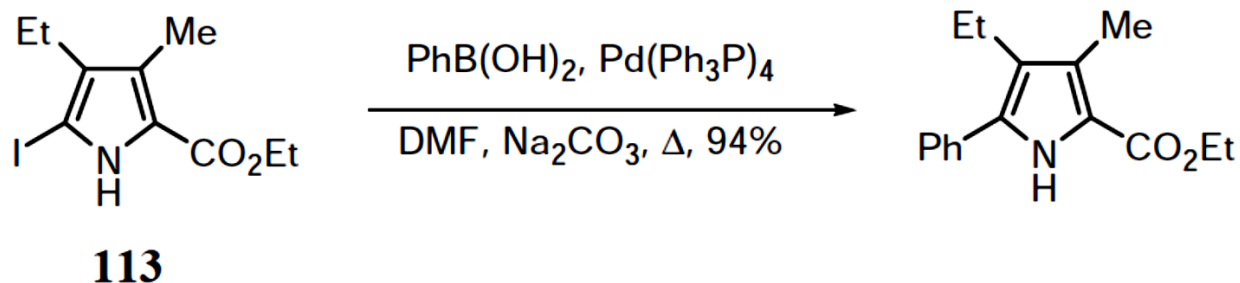
Nadeau, J. M.; Swager, T. M. *Tetrahedron* **2004**, *60*, 7141–6.



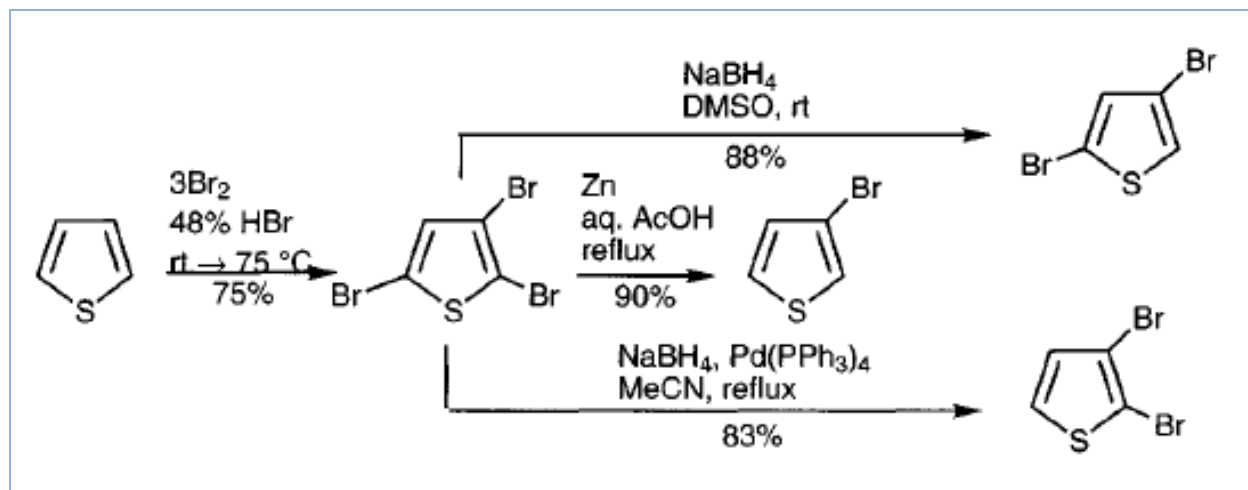
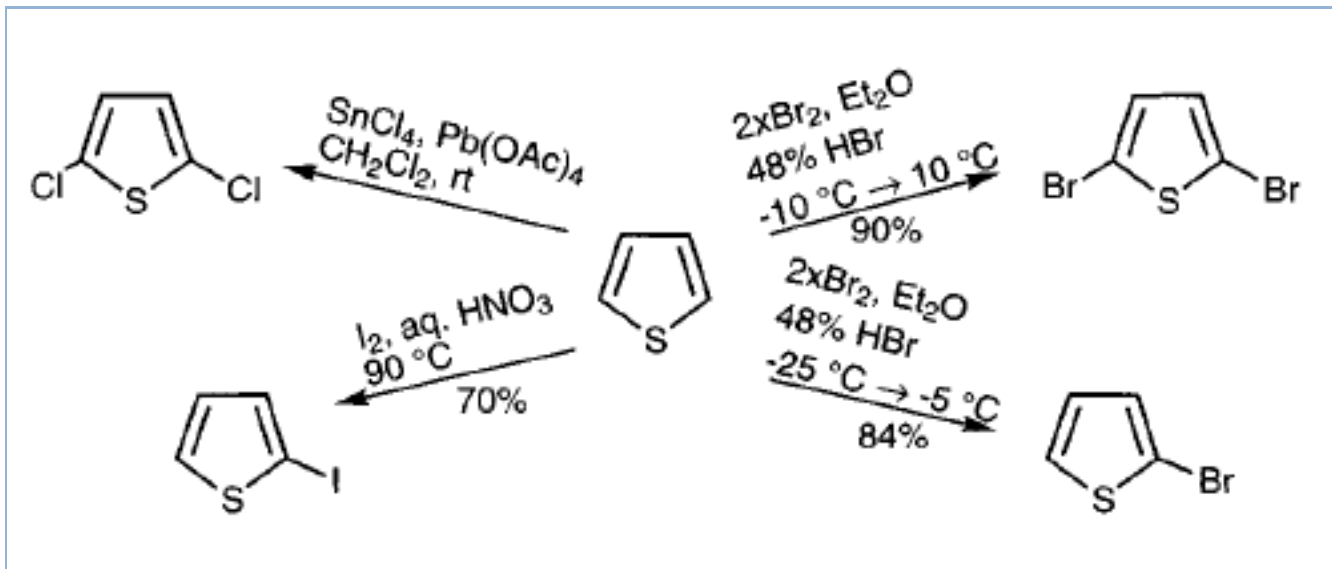


El componente pirrol también se puede emplear como haluro de arilo en el acoplamiento de Suzuki con ácidos aril borónicos. Chang ha efectuado varias de estas reacciones utilizando ácido fenilborónico y halopirrol como 113 y 114.

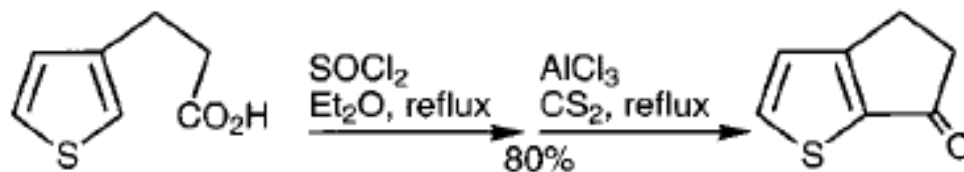
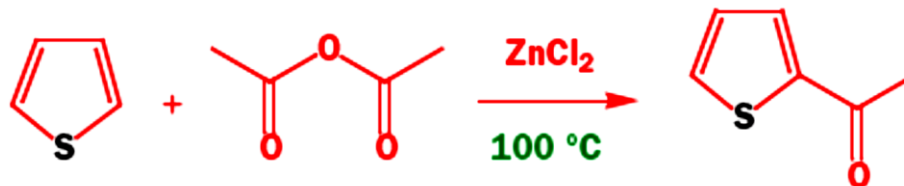
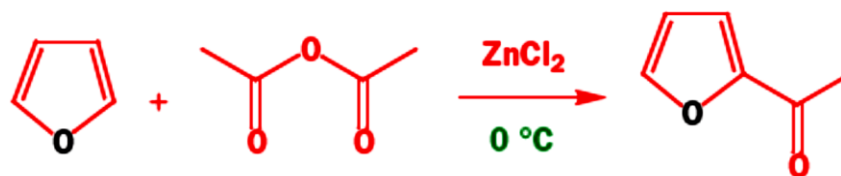
## SUZUKI CON ÁCIDOS ARIL BORÓNICOS



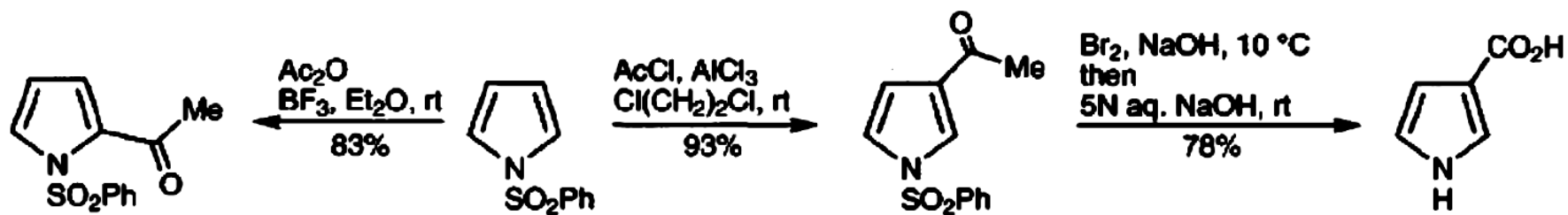
# HALOGENACIÓN



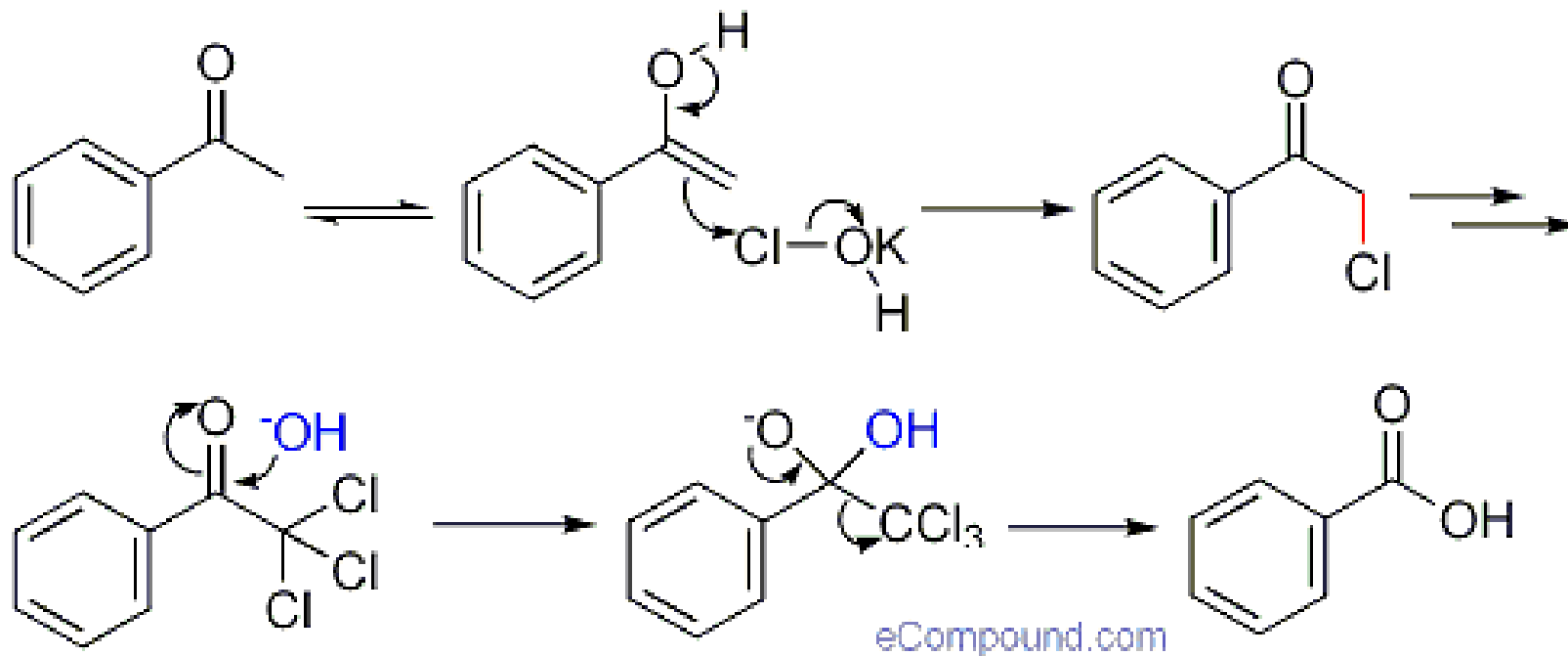
# ACILACIÓN



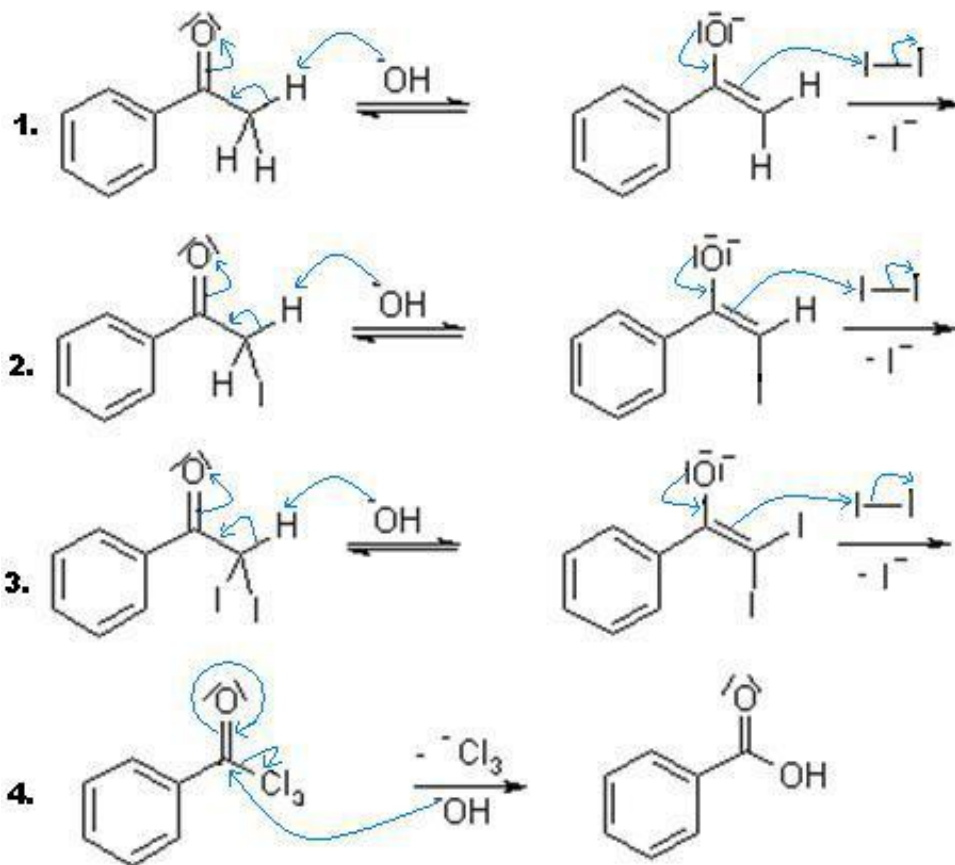
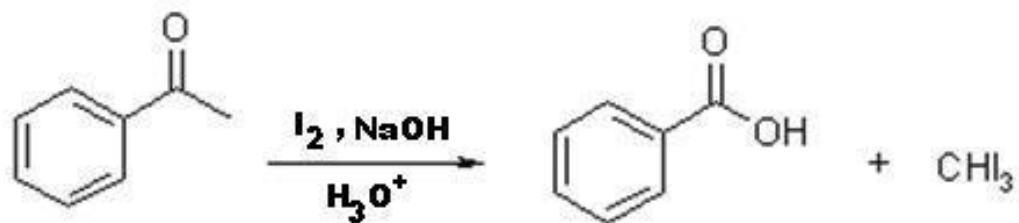
# ACILACIÓN



## REACCIÓN DEL CLOROFORMO

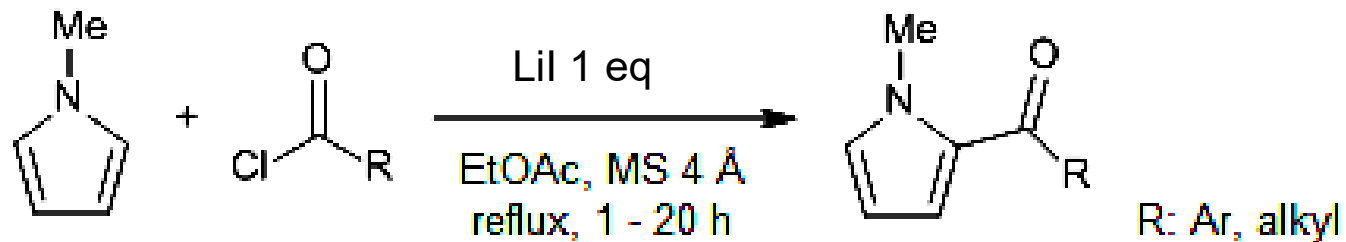


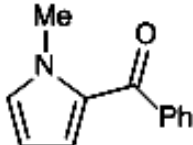
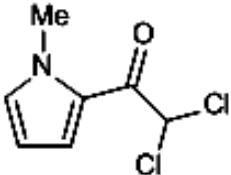
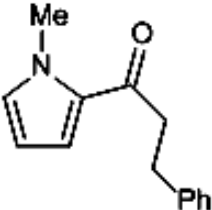
# REACCIÓN DEL YODOFORMO



## Iodide as an Activating Agent for Acid Chlorides in Acylation Reactions

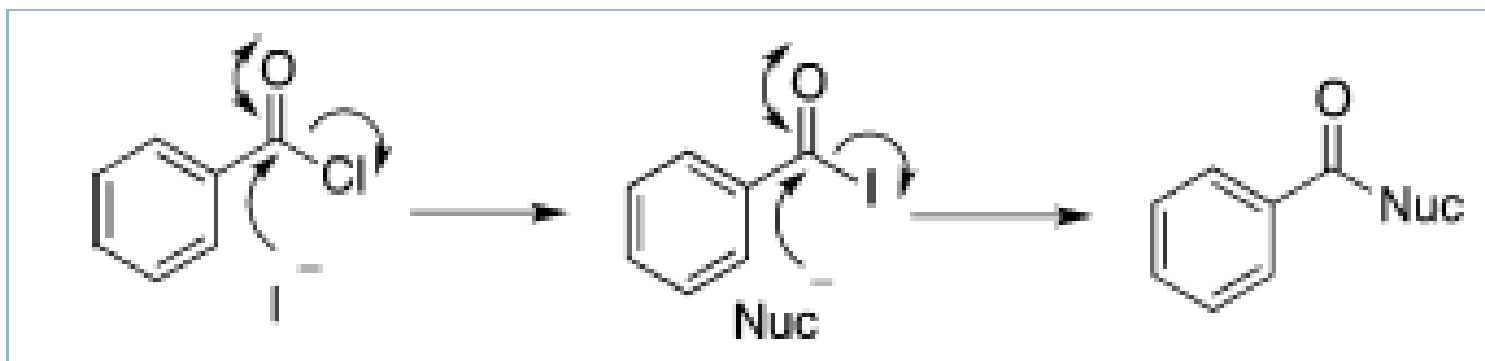
1.3 eq.



product	t (h)	yield (% isol.)
	1	68
	1	63
	4	50



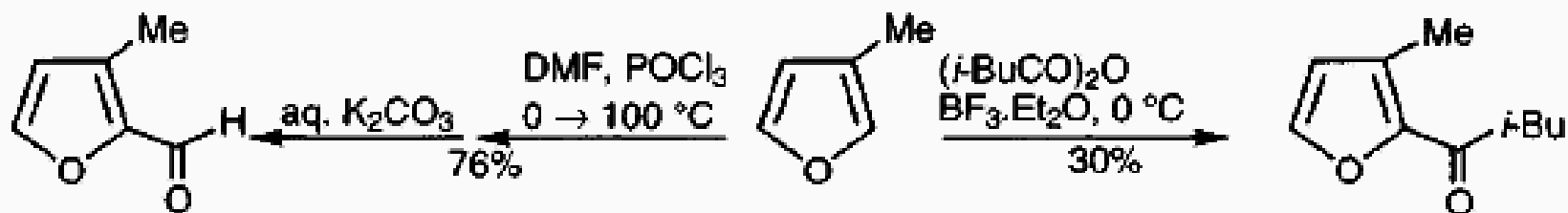
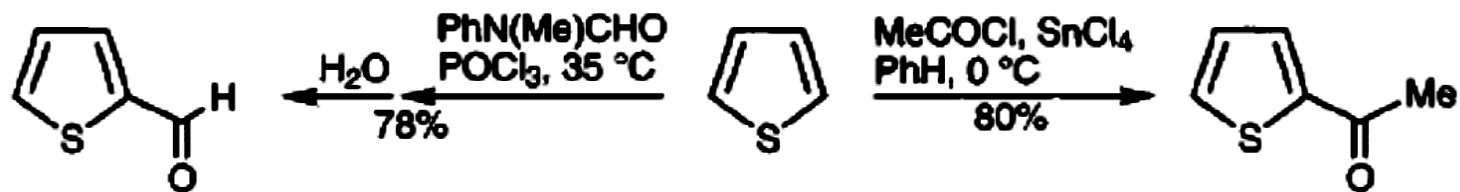
La activación ocurre por la formación del yoduro de acilo correspondiente



Yoduro de acilo



# ACILACIÓN



# REACCIÓN DE FORMILACIÓN DE VILSMEIER-HAACK

## ACILACIÓN



Anton Vilsmeier descubrió la reacción de Vilsmeier-Haack junto con Albrecht Haack



Anton Vilsmeier  
(1894 – 1962)  
Químico alemán



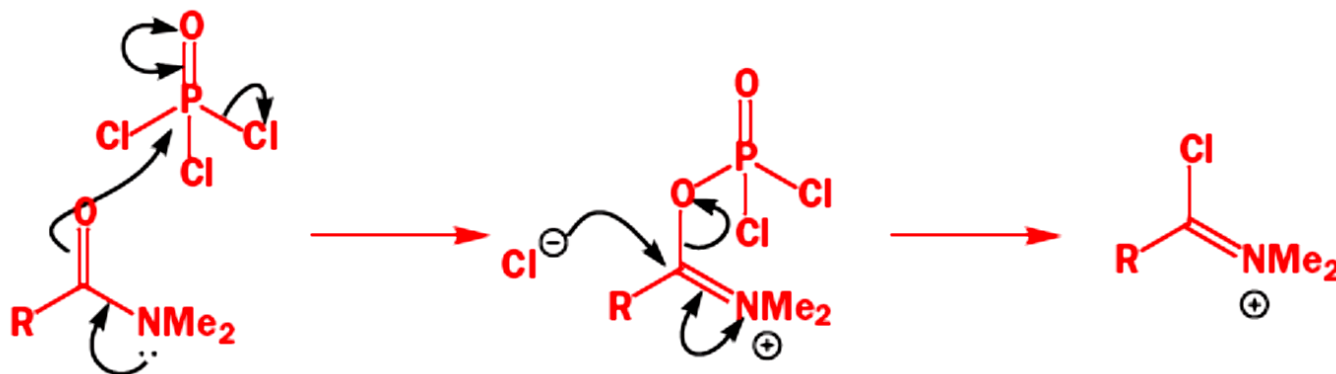
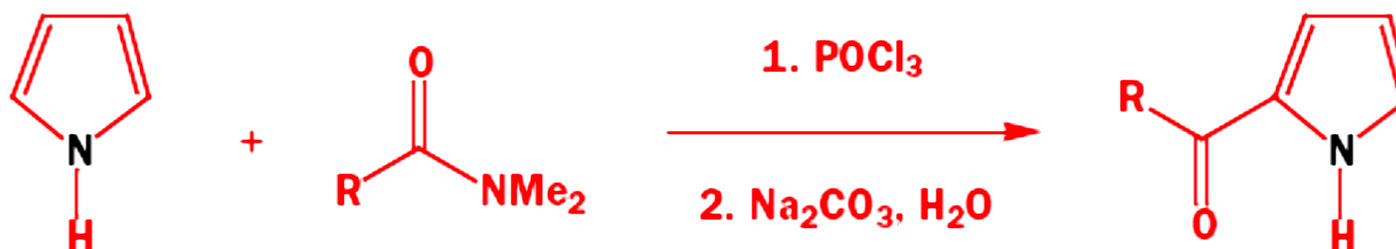
Albrecht Haack  
(1898-1976)  
Químico alemán



*Student und Assistent an der FAU:  
Dr. Anton Vilsmeier, Entdecker der  
nach ihm benannten chemischen Re-  
aktion. Foto: Archiv BASF*



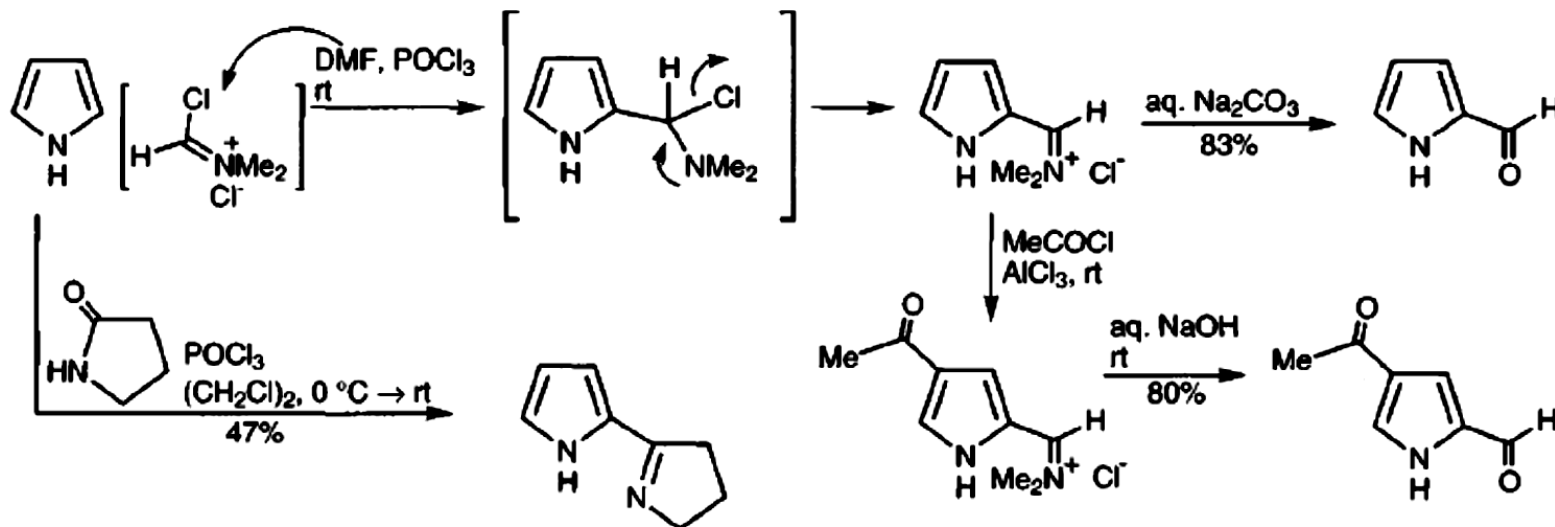
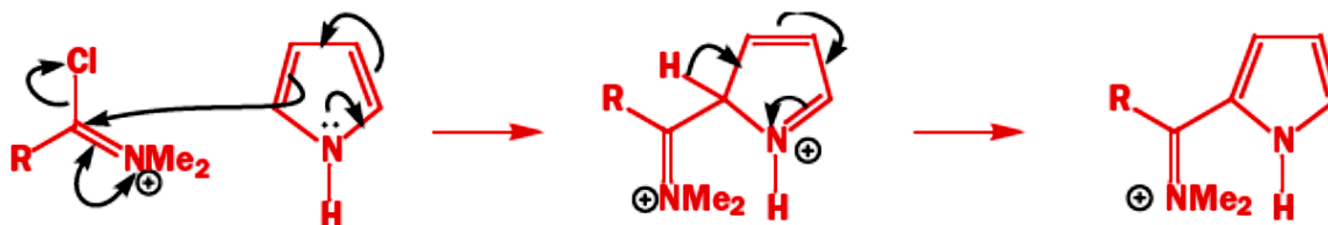
## REACCIÓN DE ACILACIÓN DE VILSMEIER-HAACK (ANTON VILSMEIER and ALBRECHT HAACK)



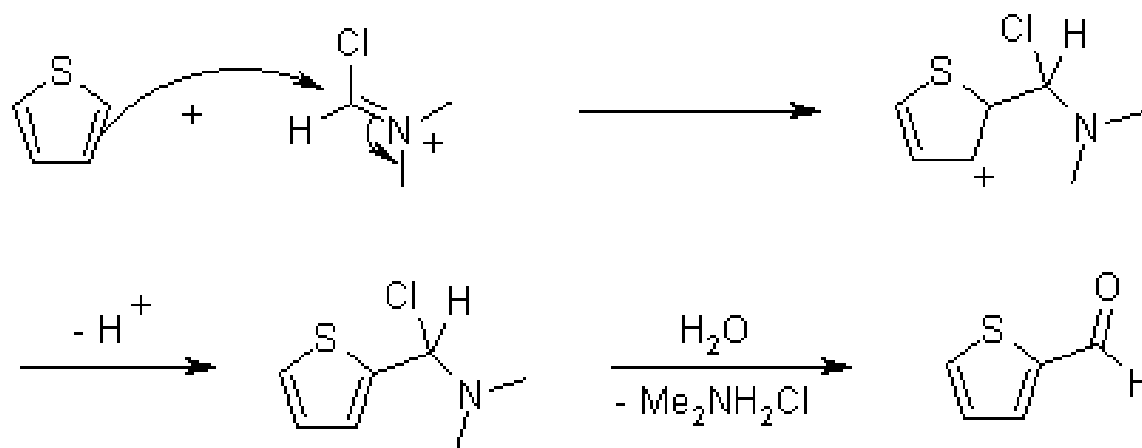
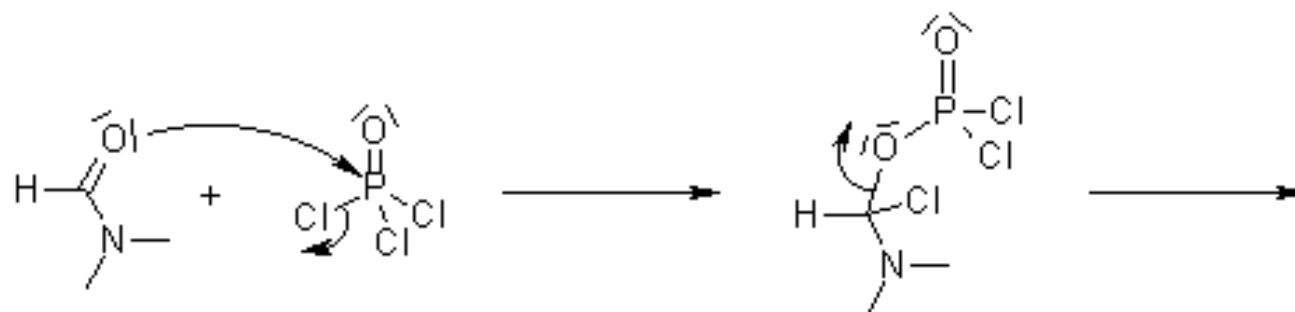
Vilsmeier, Anton; Haack, Albrecht *Berichte der Deutschen Chemischen Gesellschaft zu Berlin*. 1927,60: 119–122.  
Meth-Cohn, O.; Stanforth, S. P., *Compr. Org. Synth.* 1991,2, 777–794. [doi:10.1016/B978-0-08-052349-1.00049-4](https://doi.org/10.1016/B978-0-08-052349-1.00049-4).  
Campañe, E.; Archer, W. L. *Organic Syntheses*. 33,27. [doi:10.15227/orgsyn.033.0027](https://doi.org/10.15227/orgsyn.033.0027).; *Collective Volume*, 4, p. 331



# REACCIÓN DE ACILACIÓN DE VILSMEIER-HAACK



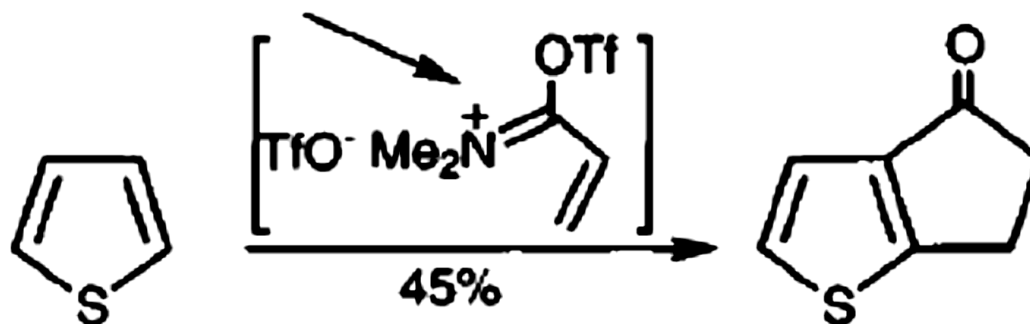
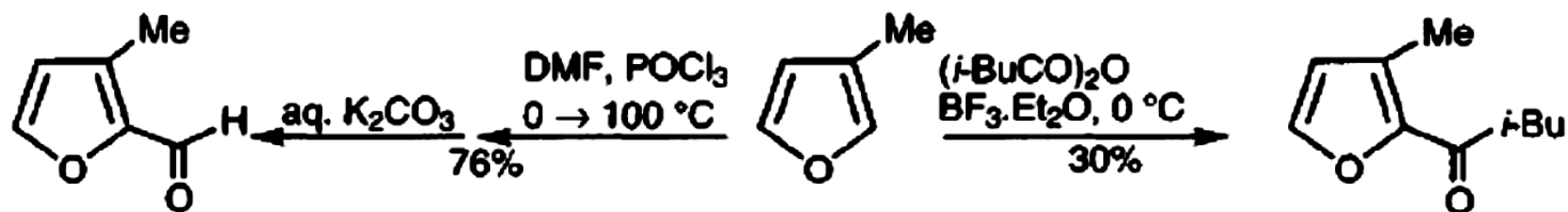
# REACCIÓN DE ACILACIÓN DE VILSMEIER-HAACK



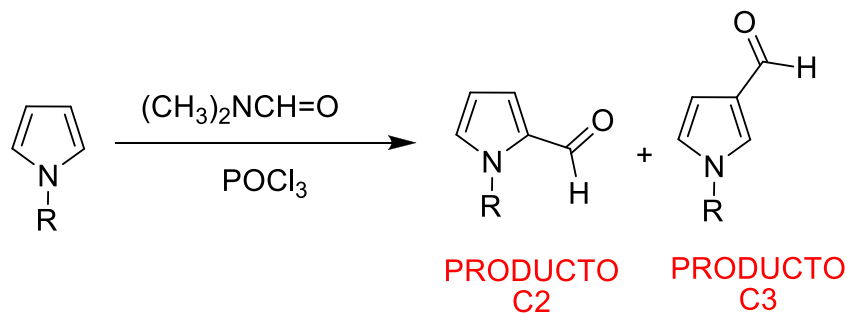
<https://www.organic-chemistry.org/namedreactions/vilsmeier-reaction.shtm>



## REACCIÓN DE ACILACIÓN DE VILSMEIER-HAACK



# INFLUENCIA DEL IMPEDIMENTO ESTÉRICO. FORMILACIÓN DE VILSMEIR-HAACK



R:      **PROPORCIÓN 2 A 3**

—CH<sub>3</sub>      **> 99 : <1**

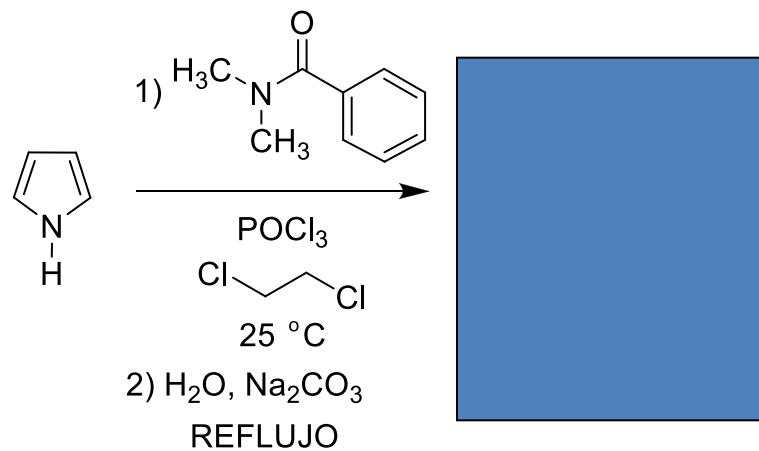
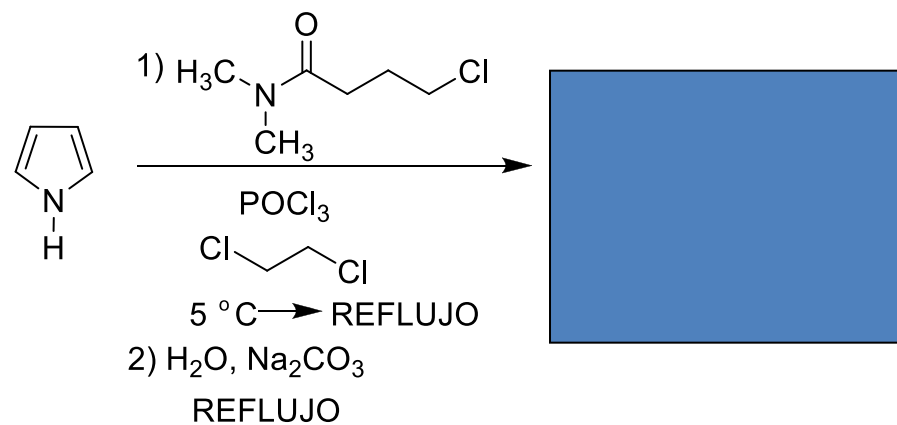
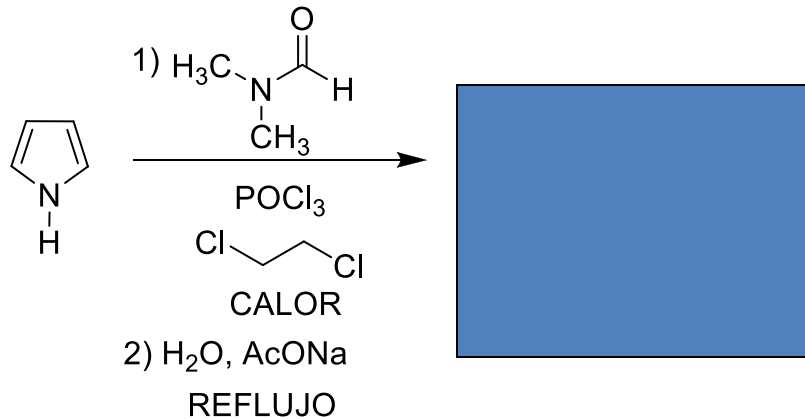
$$\begin{array}{c} \text{H} \\ | \\ \text{—C—CH}_3 \\ | \\ \text{H} \end{array}$$
      **12 : 1**

$$\begin{array}{c} \text{H} \\ | \\ \text{—C—CH}_3 \\ | \\ \text{CH}_3 \end{array}$$
      **1.9 : 1**

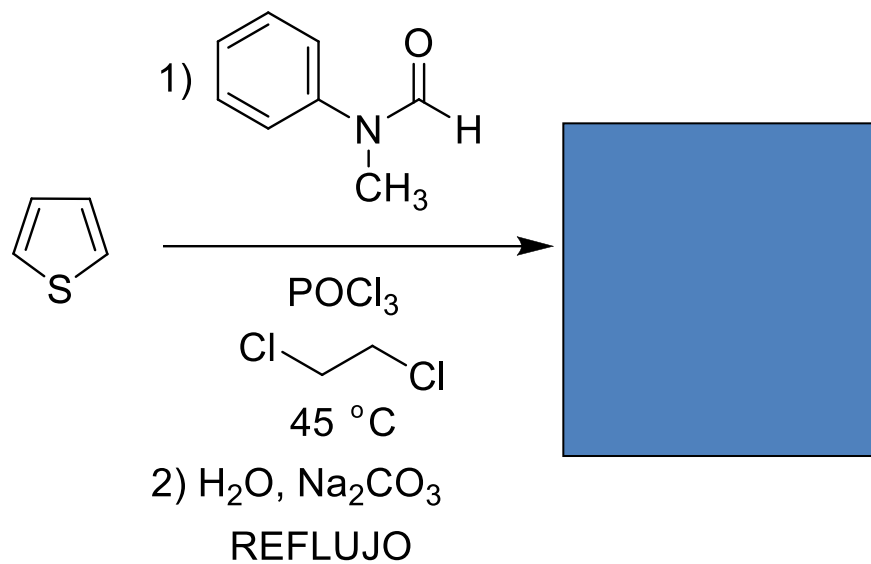
$$\begin{array}{c} \text{CH}_3 \\ | \\ \text{—C—CH}_3 \\ | \\ \text{CH}_3 \end{array}$$
      **1 : 14**

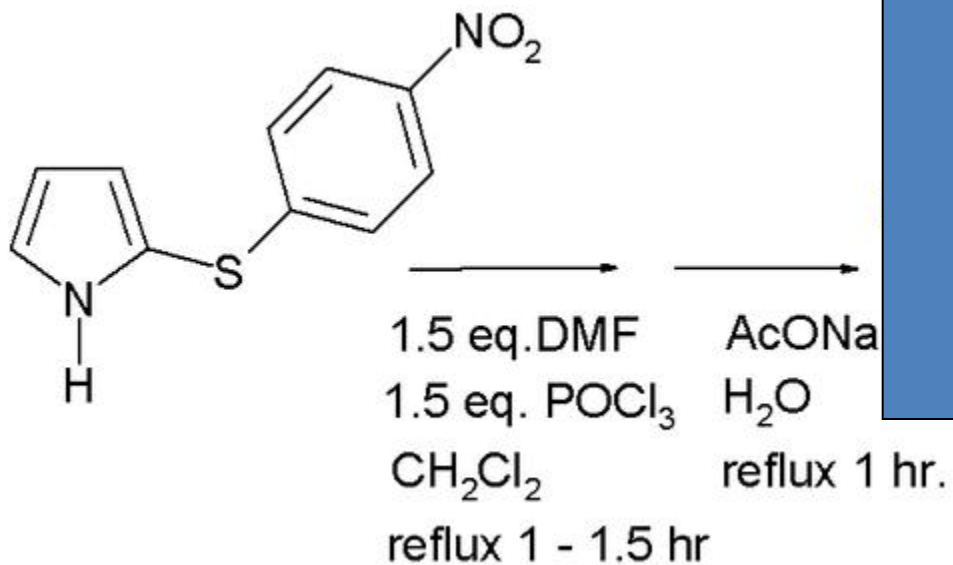


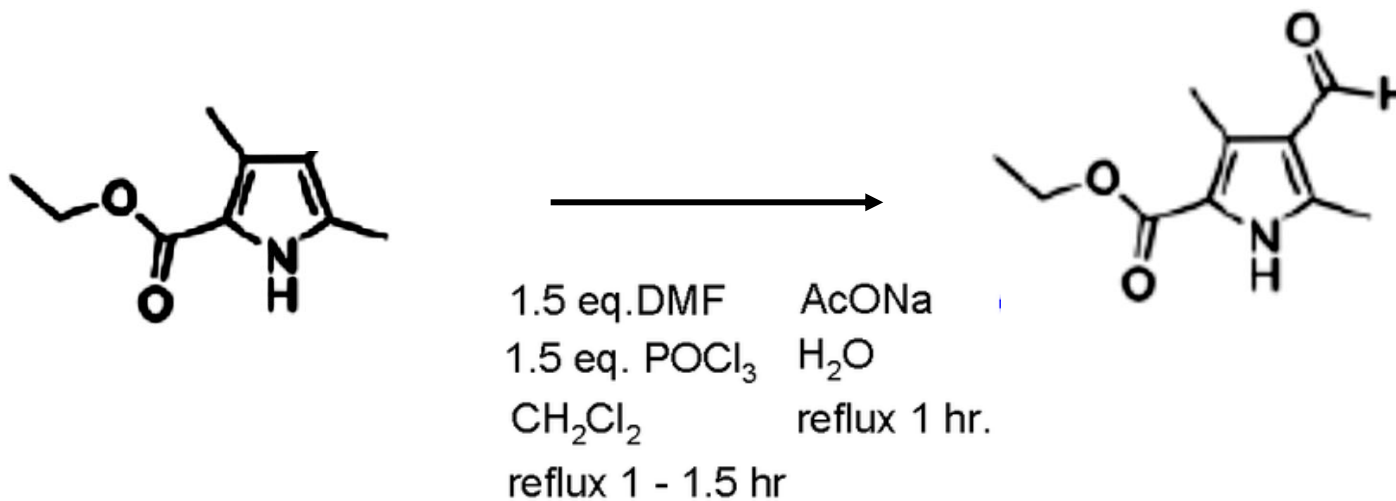
# VILSMEIR-HAACK

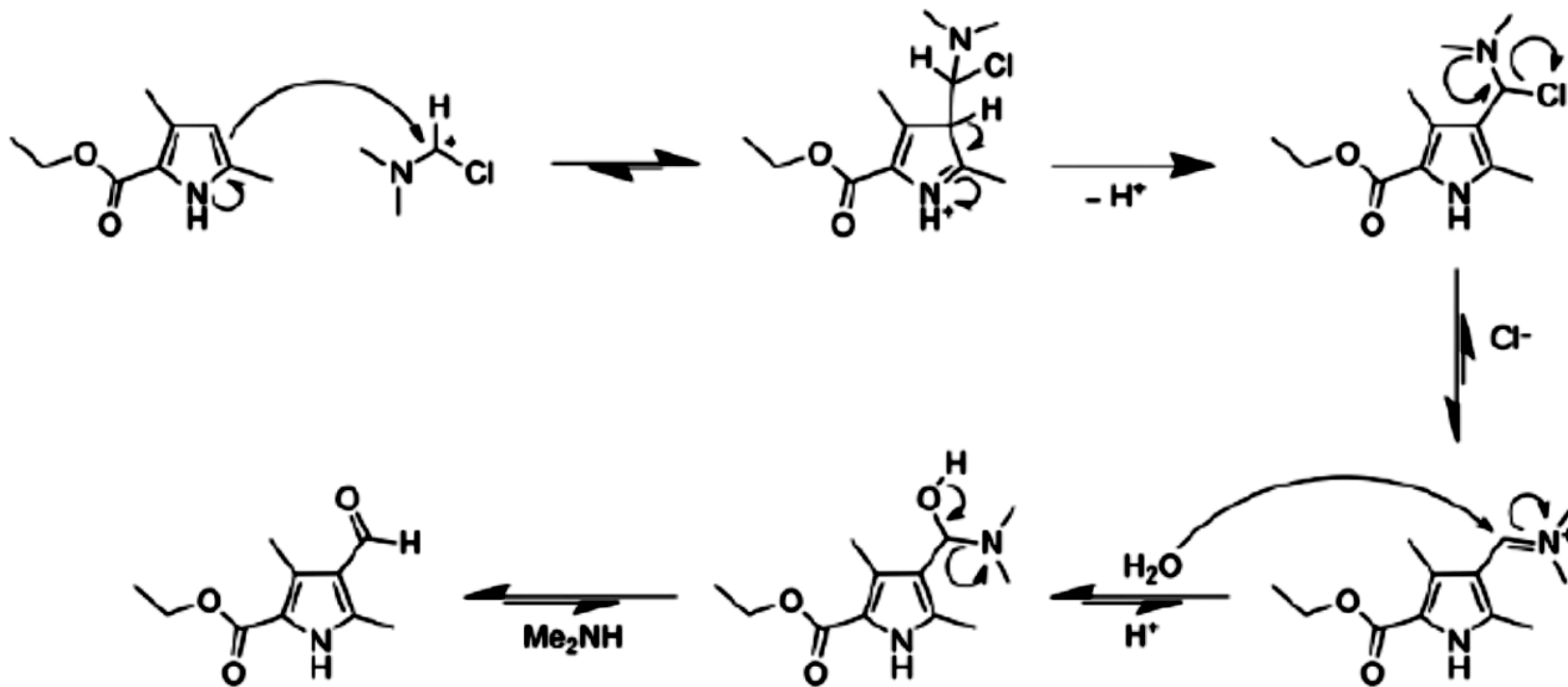
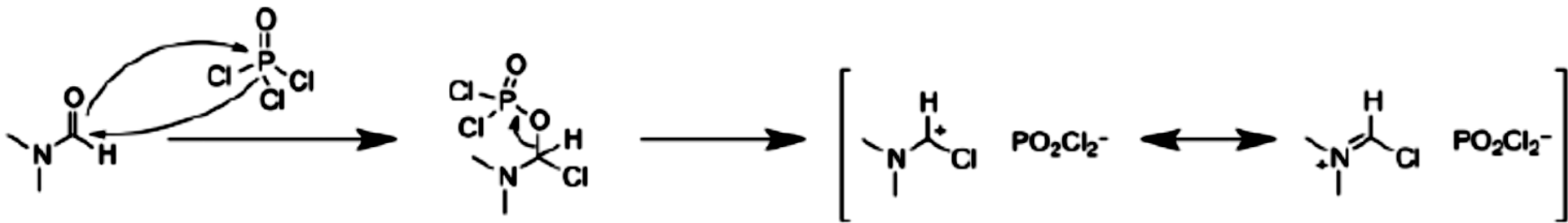


# REACCIÓN DE ACILACIÓN DE VILSMEIER-HAACK

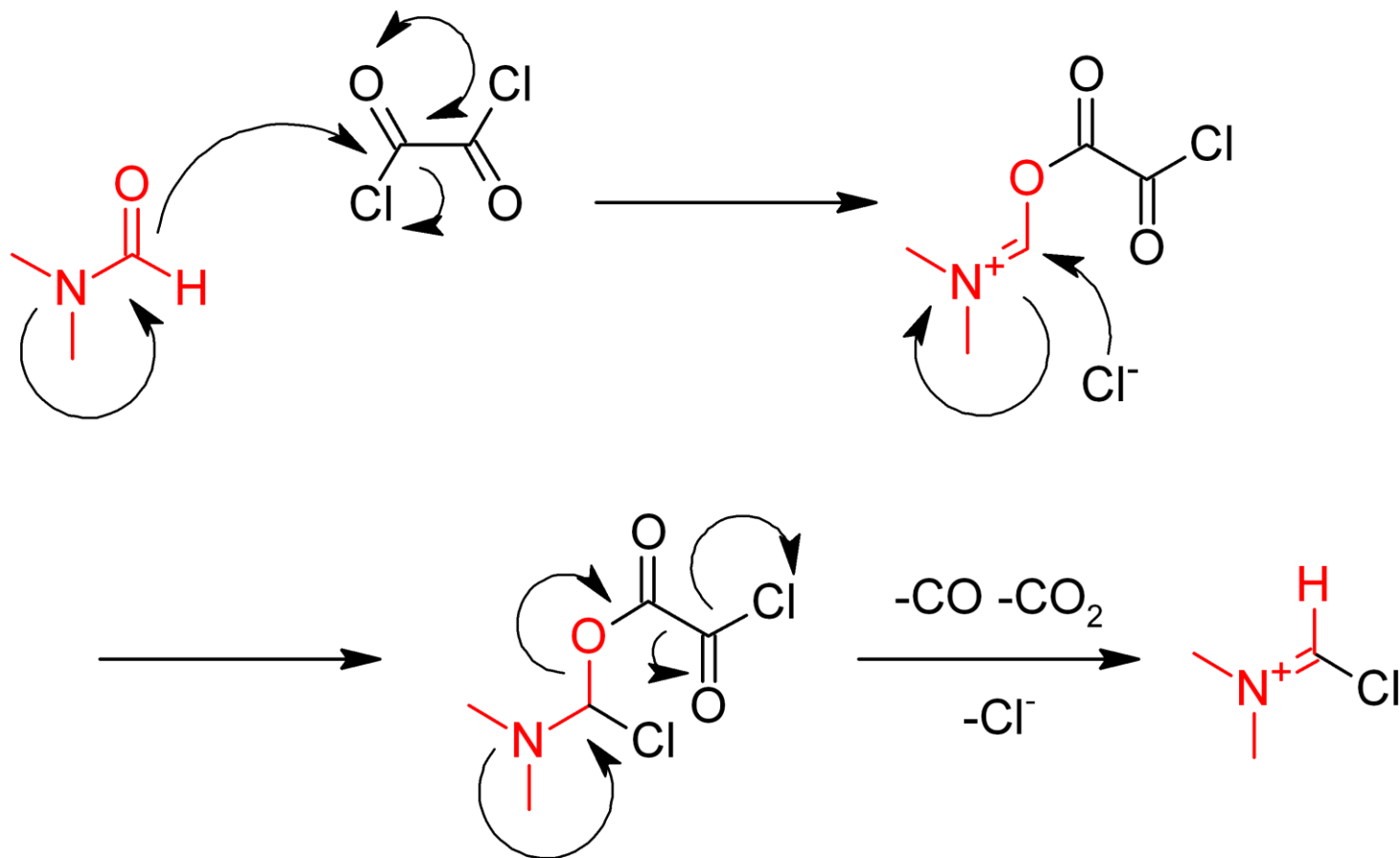








## Reaction of oxalyl chloride with DMF

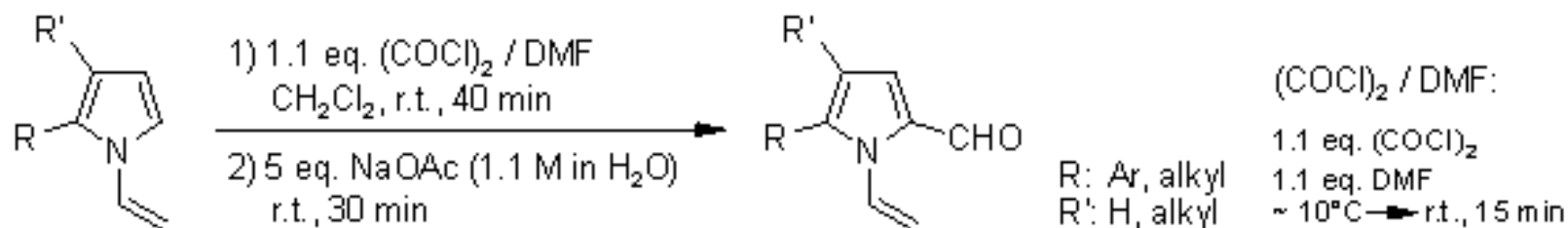


[https://nl.m.wikipedia.org/wiki/Bestand:Reaction\\_of\\_oxalyl\\_chloride\\_with\\_DMF.png](https://nl.m.wikipedia.org/wiki/Bestand:Reaction_of_oxalyl_chloride_with_DMF.png)



## An Efficient Route to 1-Vinylpyrrole-2-carbaldehydes

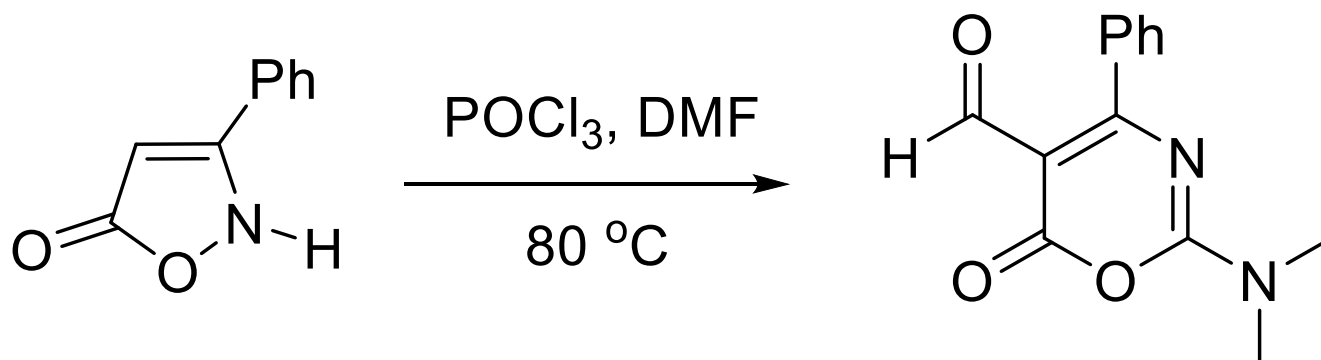
A. I. Mikhaleva, A. V. Ivanov, E. V. Skital'tseva, I. A. Ushakov, A. M. Vasil'tsov, B. A. Trofimov, *Synthesis*, 2009, 587-590.



Product	Yield (% , isol.) (COCl) <sub>2</sub> / DMF	Yield (% , isol.) POCl <sub>3</sub> / DMF <sup>1)</sup>
	48	28 <sup>2)</sup>
	93	66
	83	-
	97	88

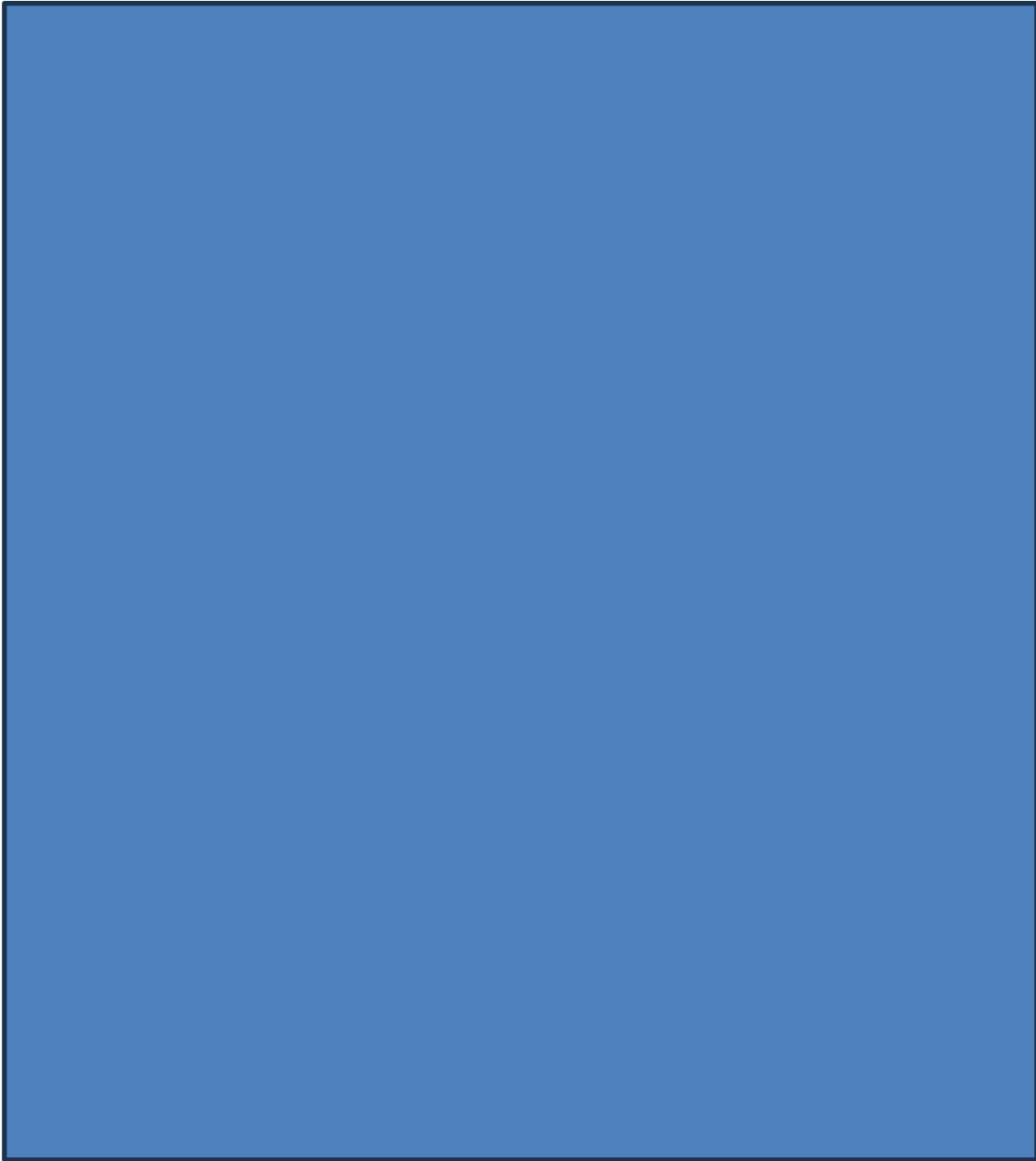


## TAREA: MECANISMO DE REACCIÓN

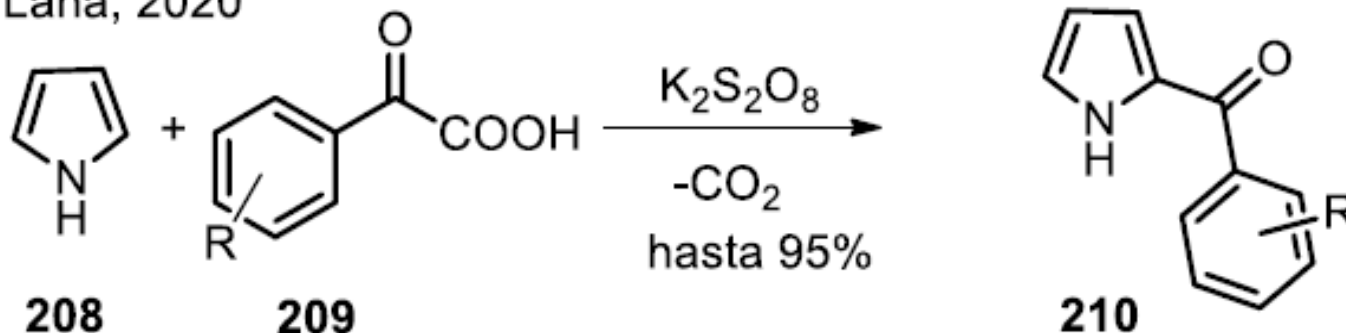


**2 EQUIVALENTES DE LOS DOS REACTIVOS  
POCl<sub>3</sub> + DMF**





C) Laha, 2020

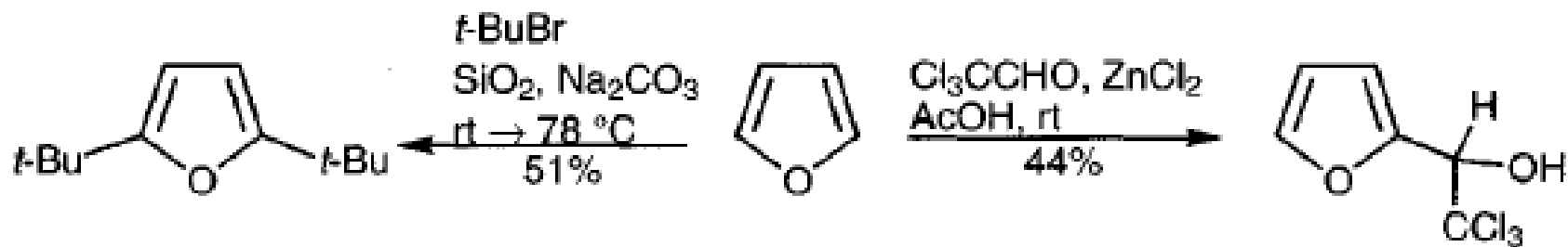


Recientemente, Laha y colaboradores describieron la monoacilación regioselectiva de tipo Minisci sobre pirroles ricos electrónicamente **208** a partir de ácidos acil-glioxálicos **209** bajo condiciones libres de Ag. Experimentos de control confirmaron la formación de un radical acilo, aunque el mecanismo de reacción requiere de estudios complementarios (C).

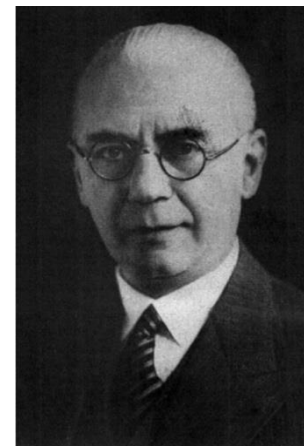
Laha, J. K.; Hunjan, M. K.; Hedge, S.; Gupta, A. *Org. Lett.* **2020**, 22, 1442-1447



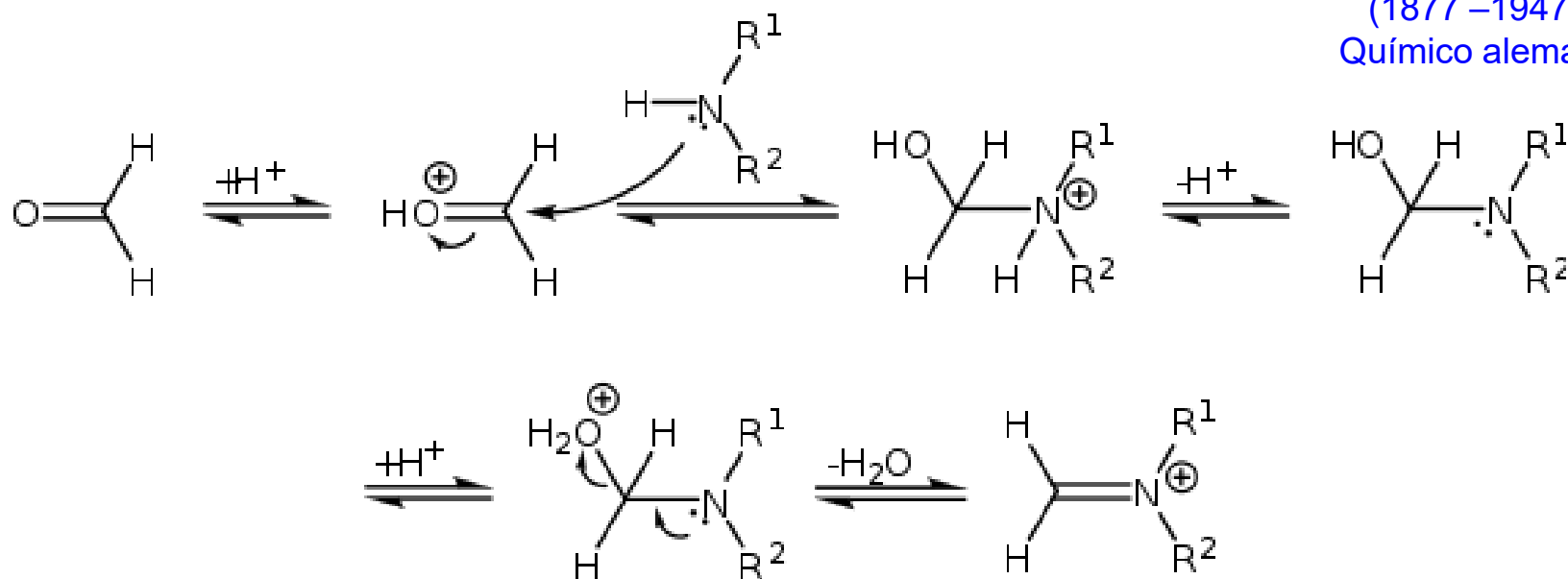
# ALQUILACIÓN



## REACCIÓN DE MANNICH (Carl Ulrich Franz Mannich )



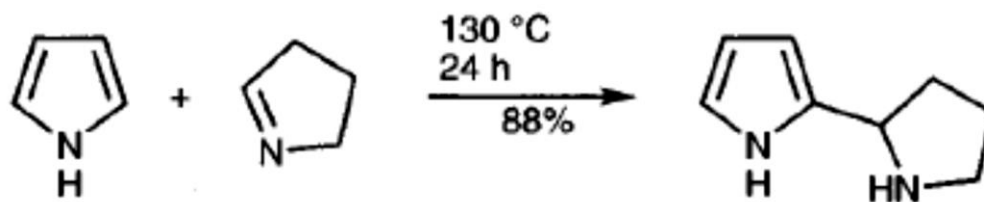
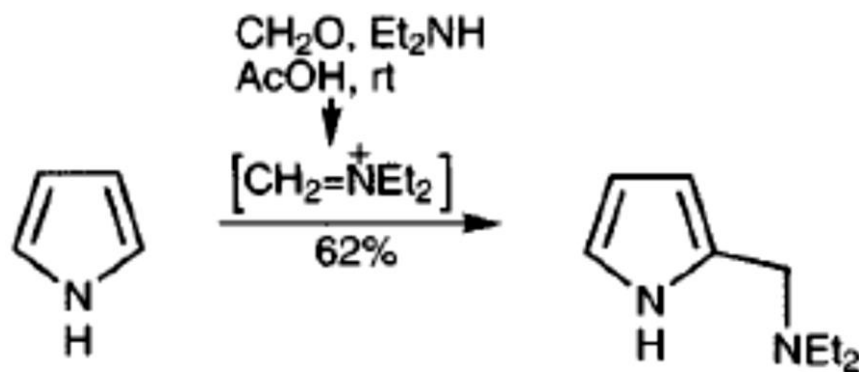
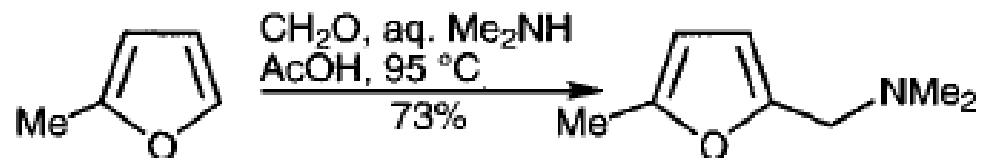
Carl Ulrich Franz Mannich  
(1877 –1947)  
Químico alemán



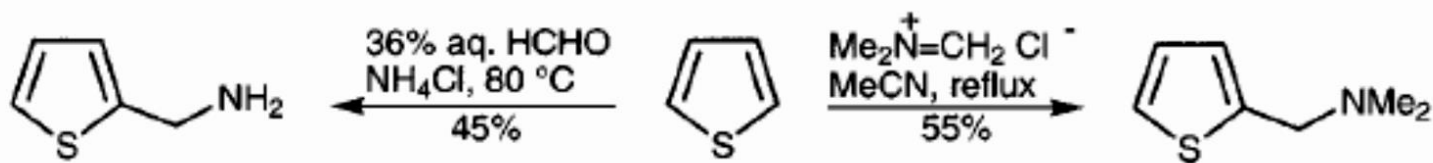
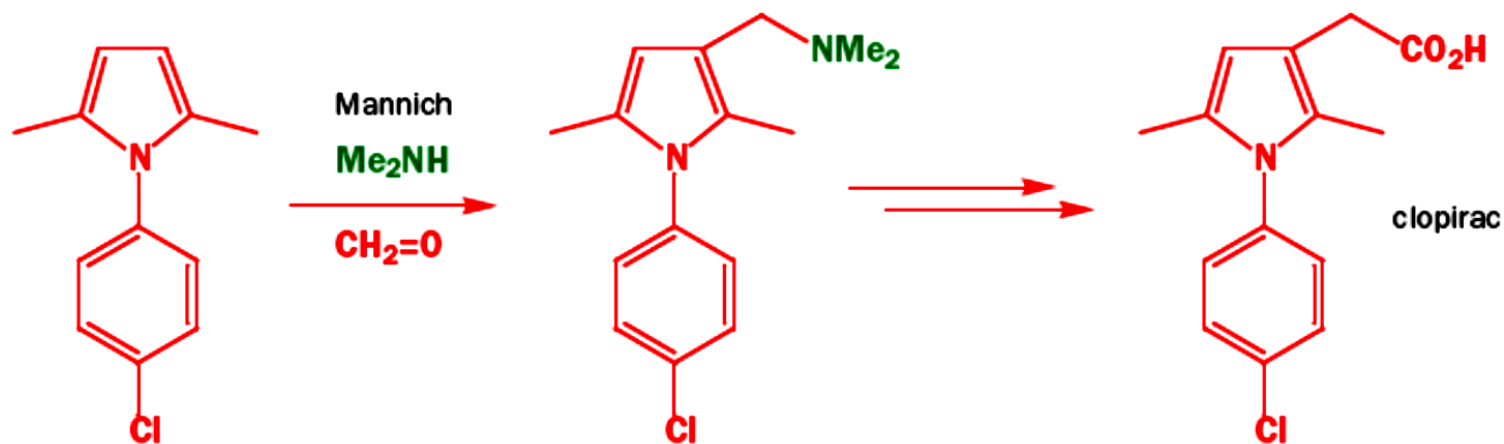
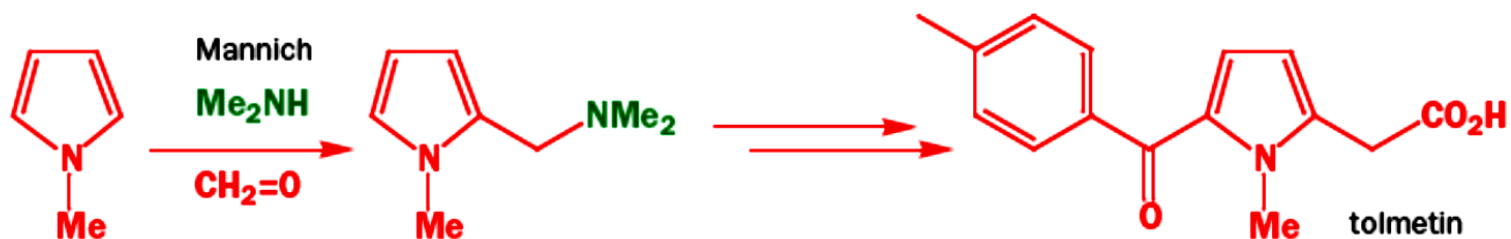
<http://www.liveinternet.ru/users/kakula/post316185121/>



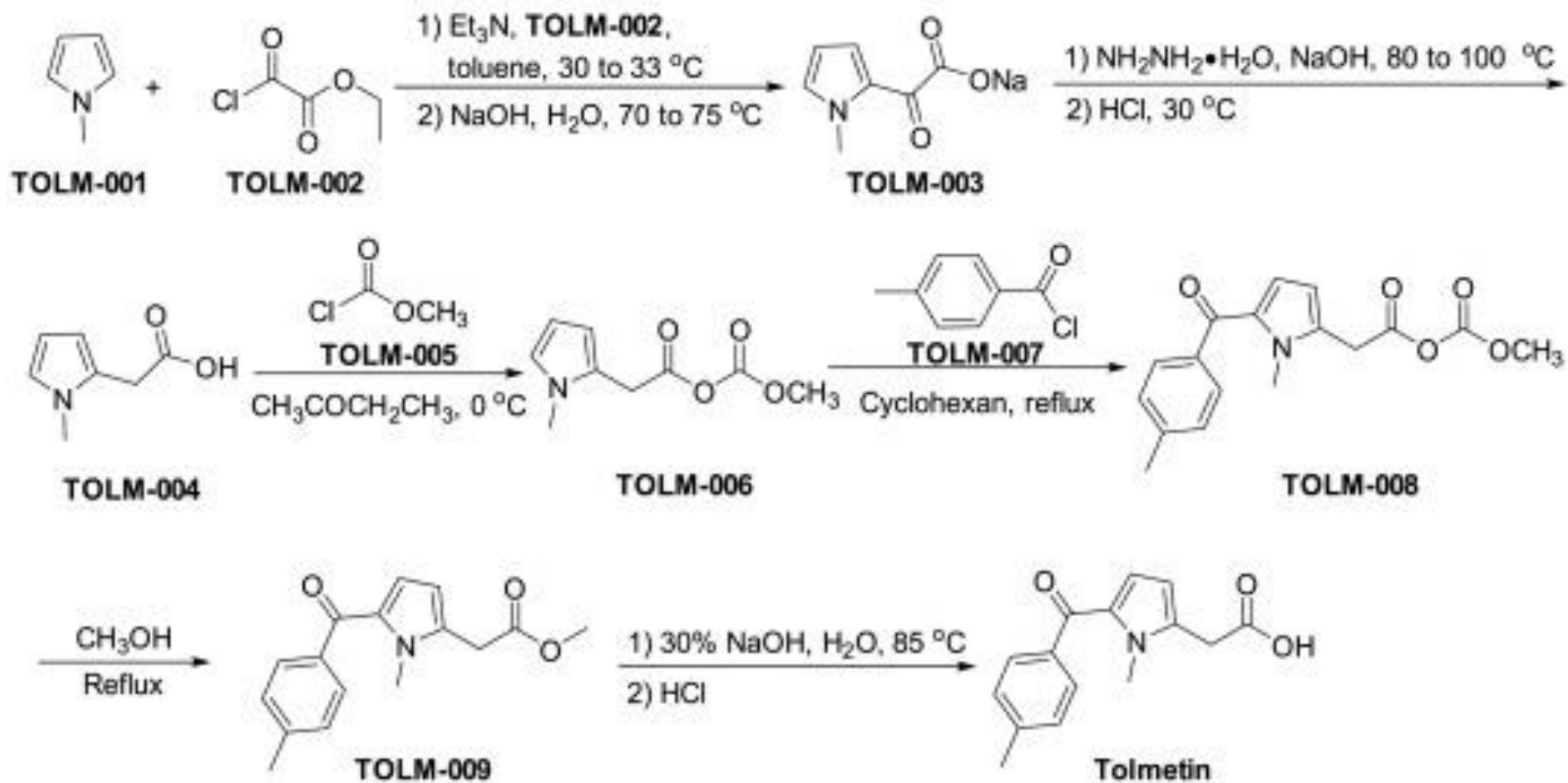
## REACCIÓN DE MANNICH



# REACCIÓN DE MANNICH



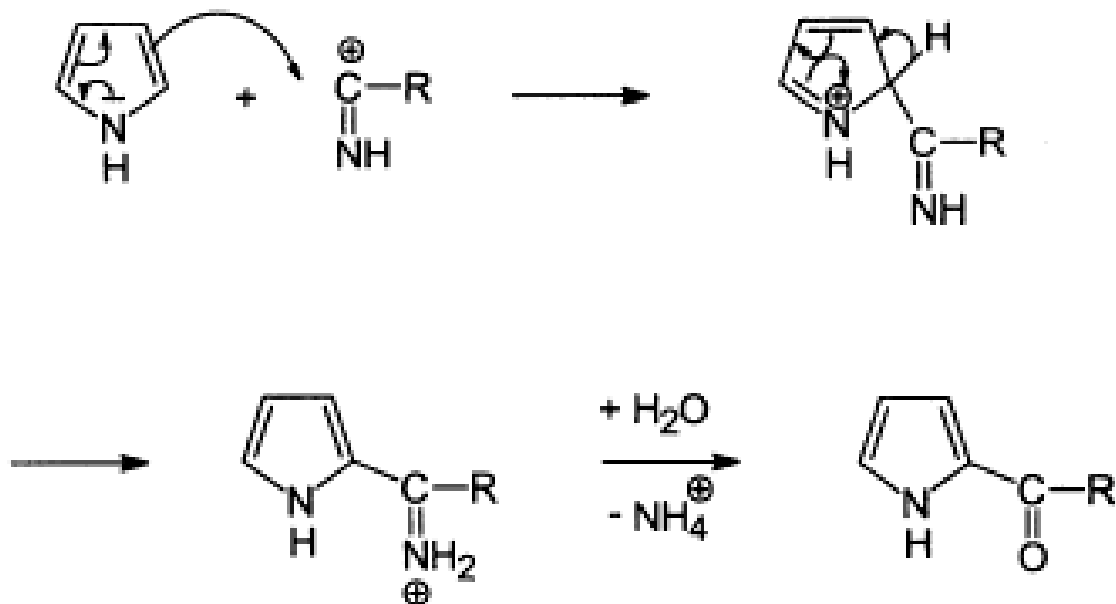




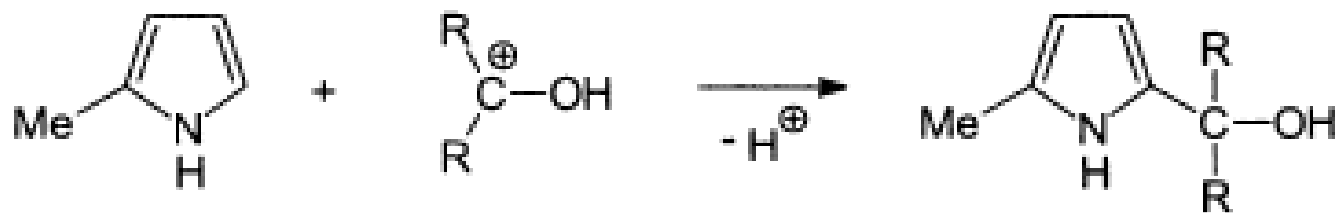
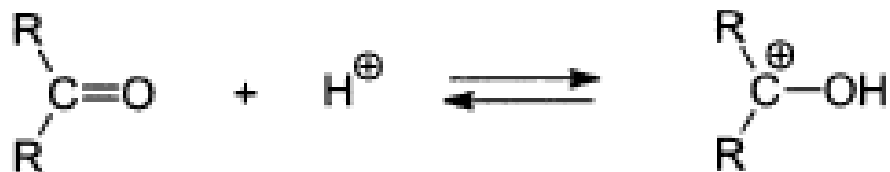
Eliza Robertson, xPharm: The Comprehensive Pharmacology Reference Reference Work • 2008



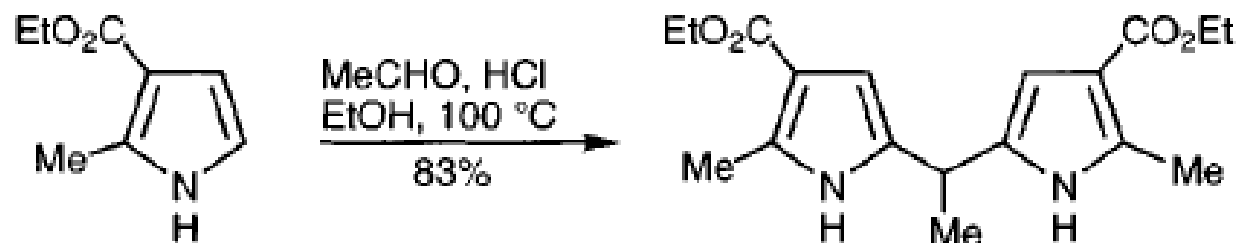
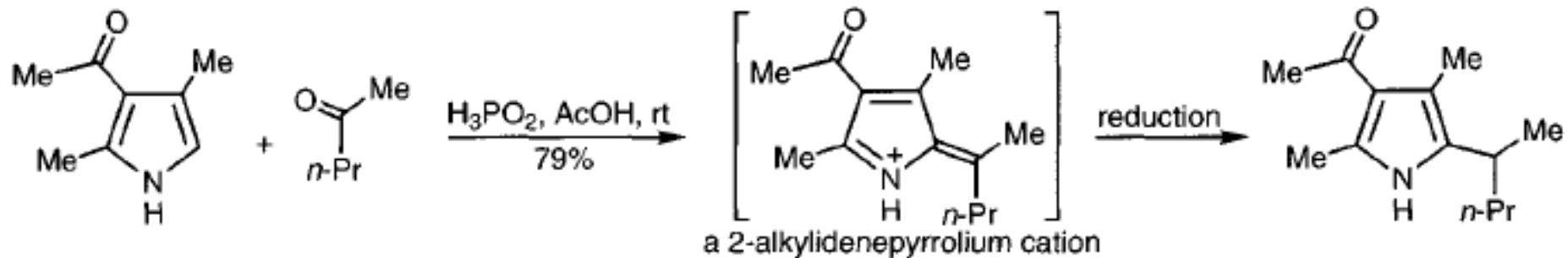
## REACCIÓN DE ACILACIÓN DE HOUBEN-HOESCH



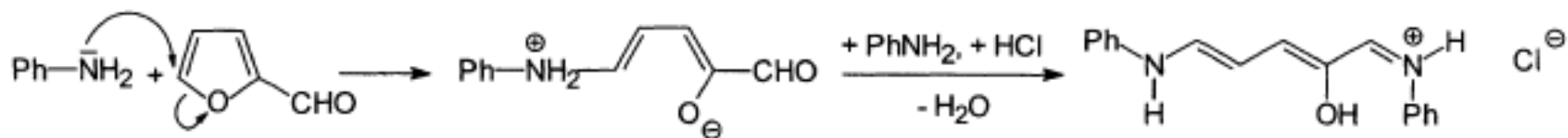
# REACCIONES CON ALDEHÍDOS



# REACCIONES CON ALDEHÍDOS

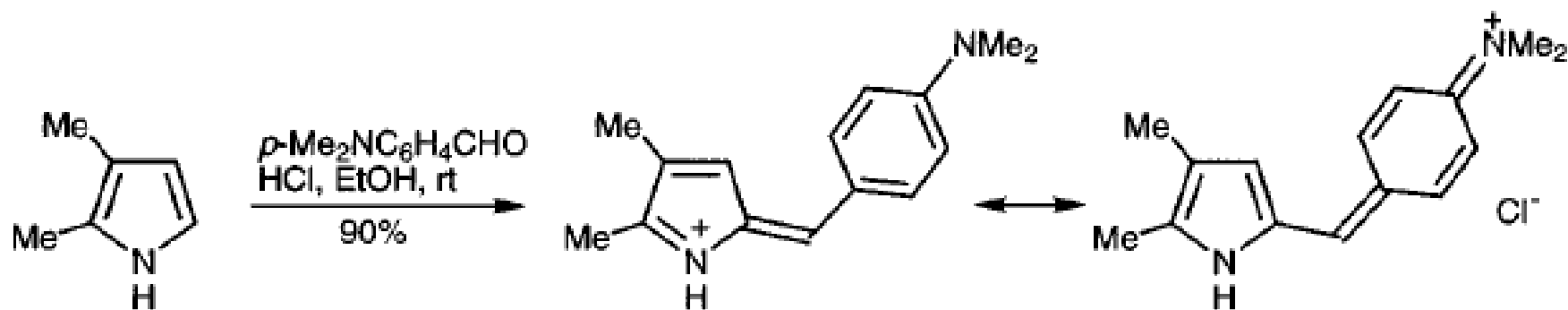


# REACCIONES CON ALDEHÍDOS

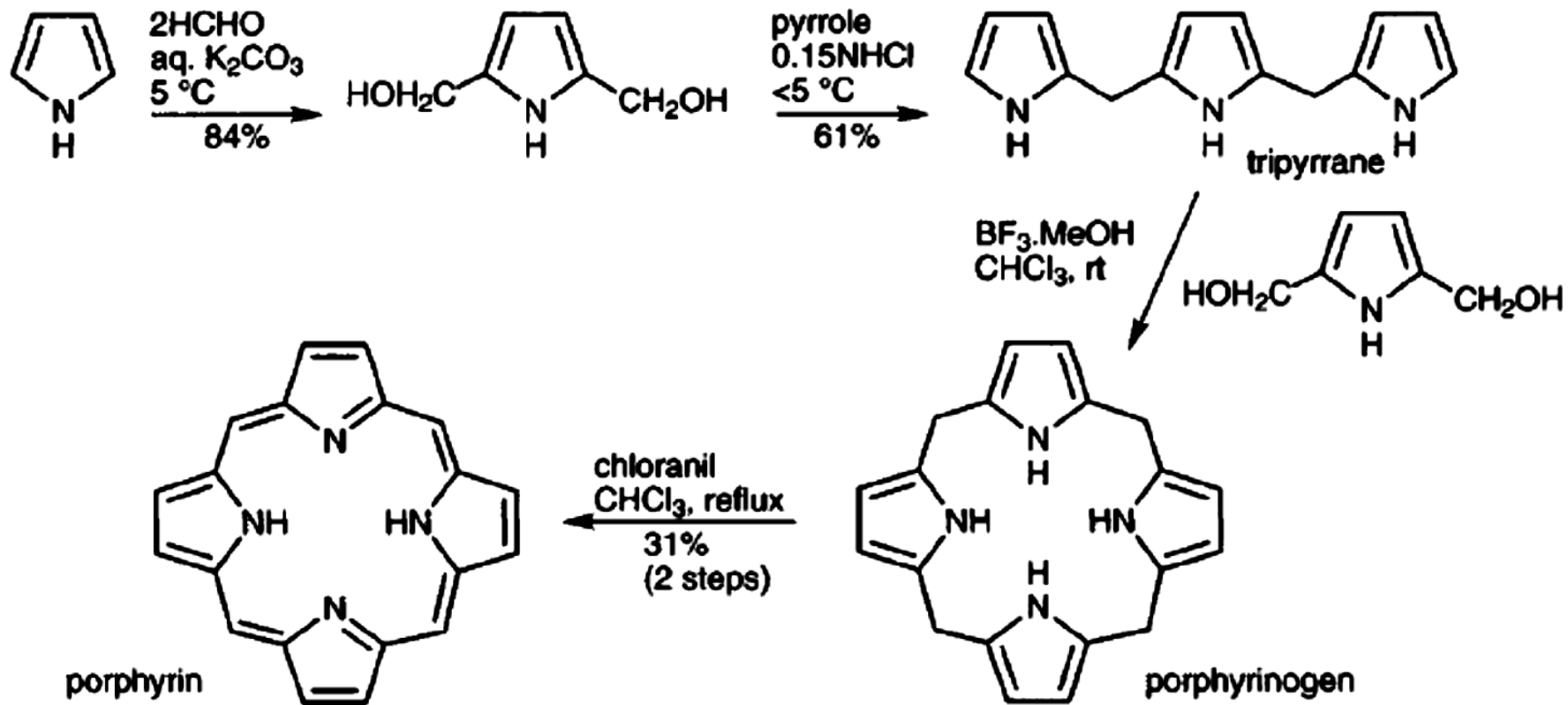


Colorante polimetino  
(rojo)

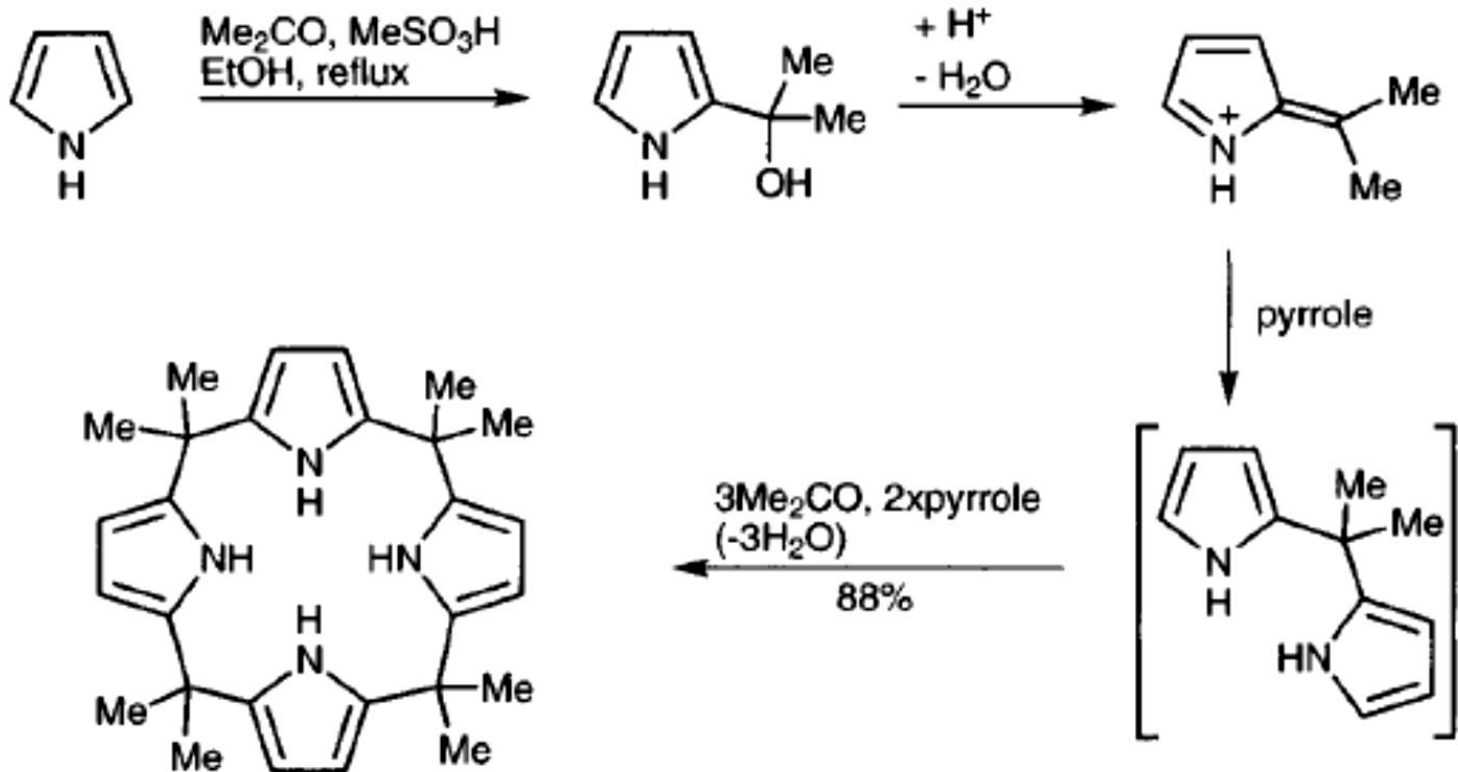
Con el reactivo de Ehrlich, *i.e.* una solución del 4-(dimetilamino)benzaldehído en presencia de HCl, la reacción procede para dar una sal de azafulvenio de color púrpura:  $\text{NMe}_2$



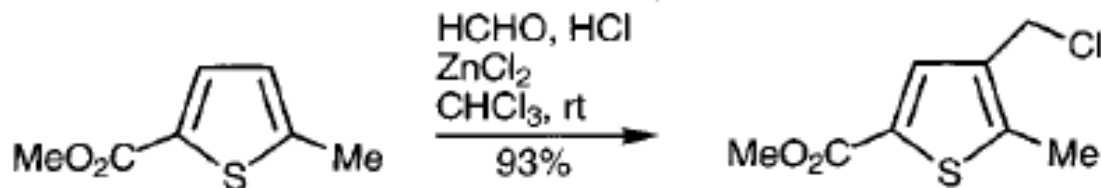
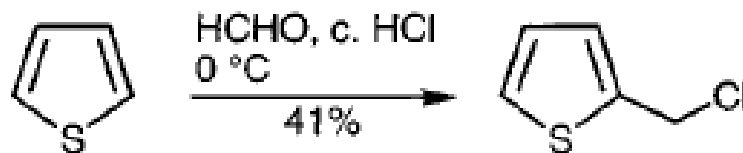
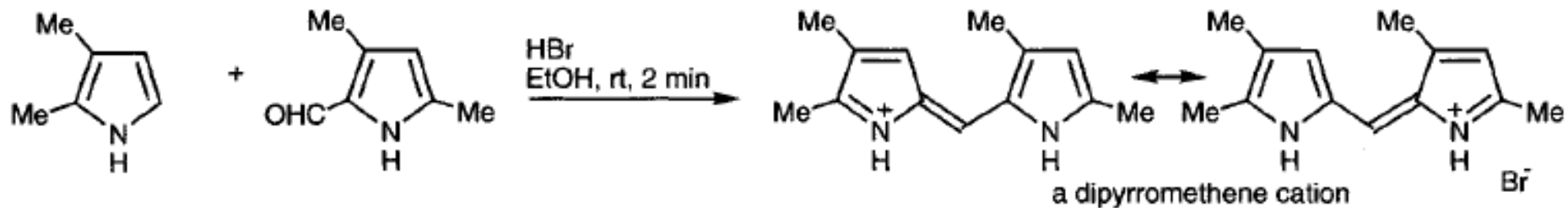
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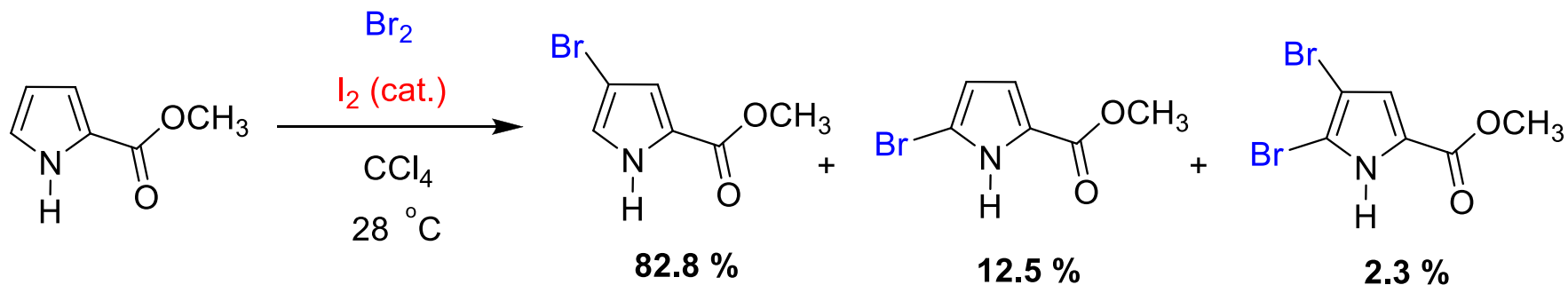
# REACCIONES CON CETONAS



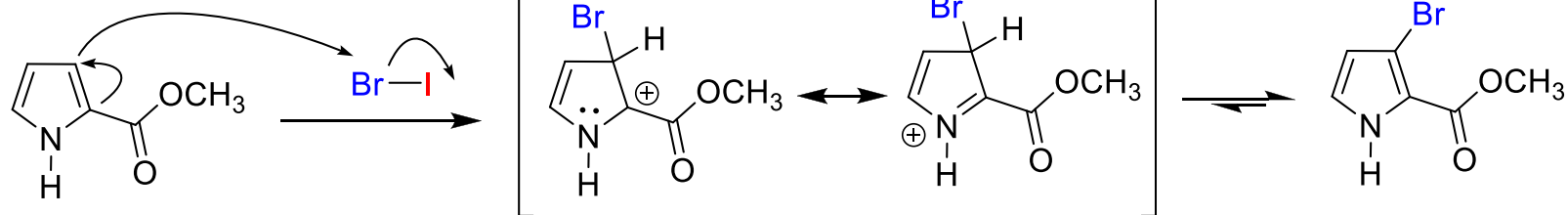
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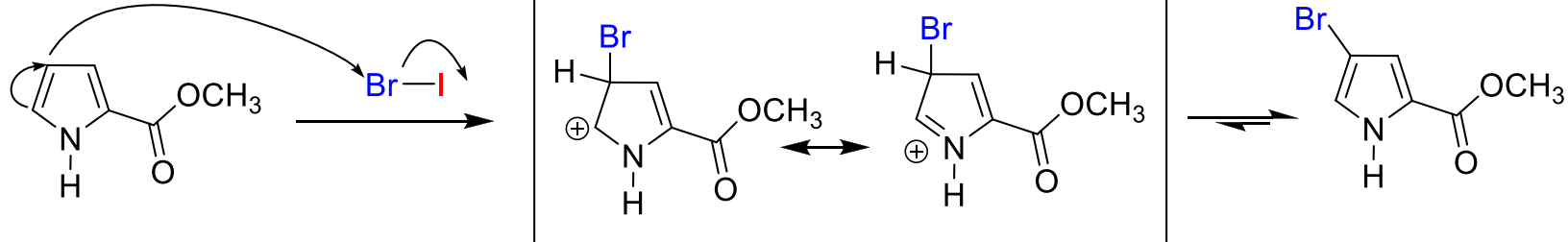
# REACCIONES DE DISUSTITUCIÓN (SEAr)



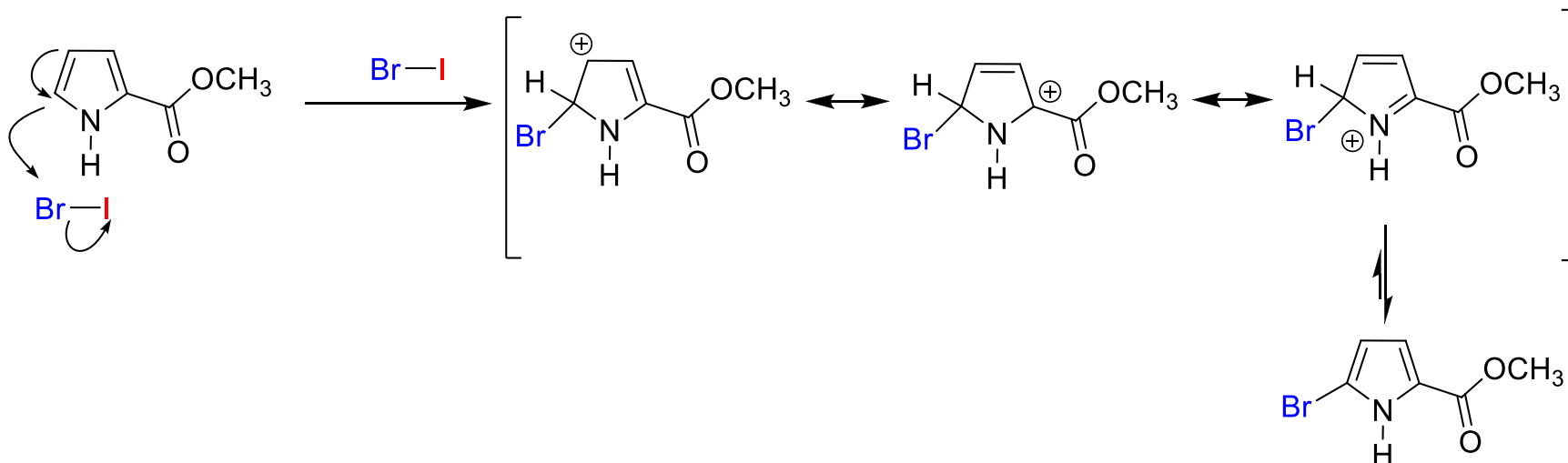
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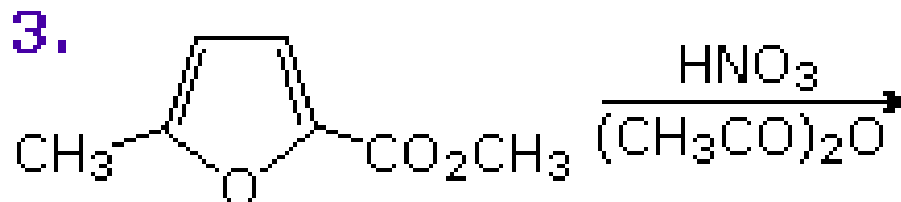
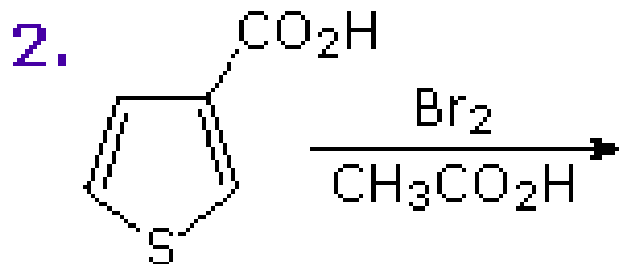
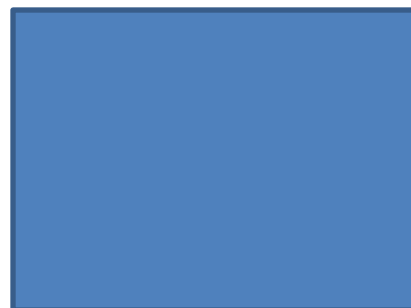
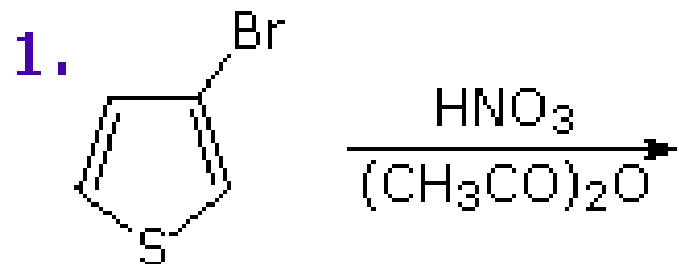
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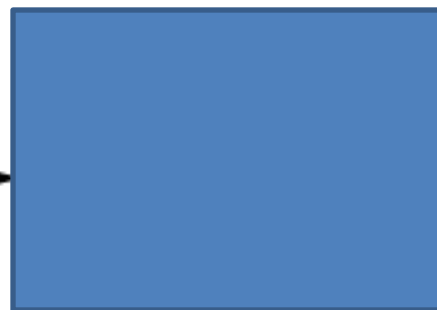
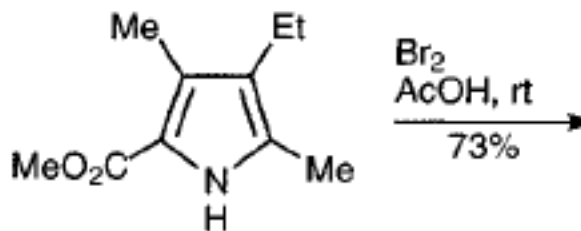
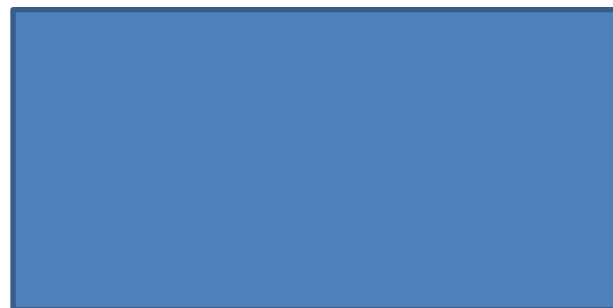
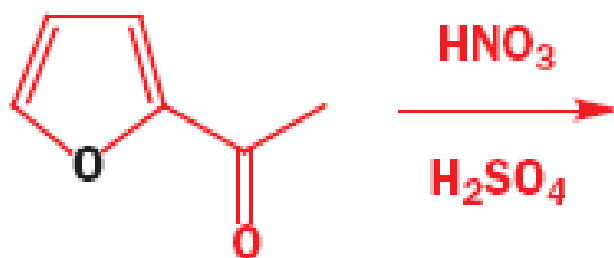
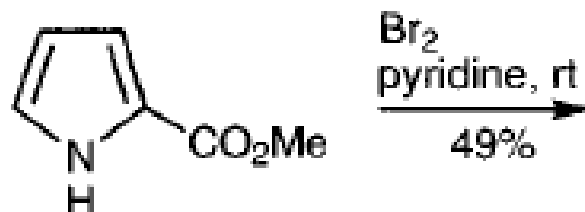
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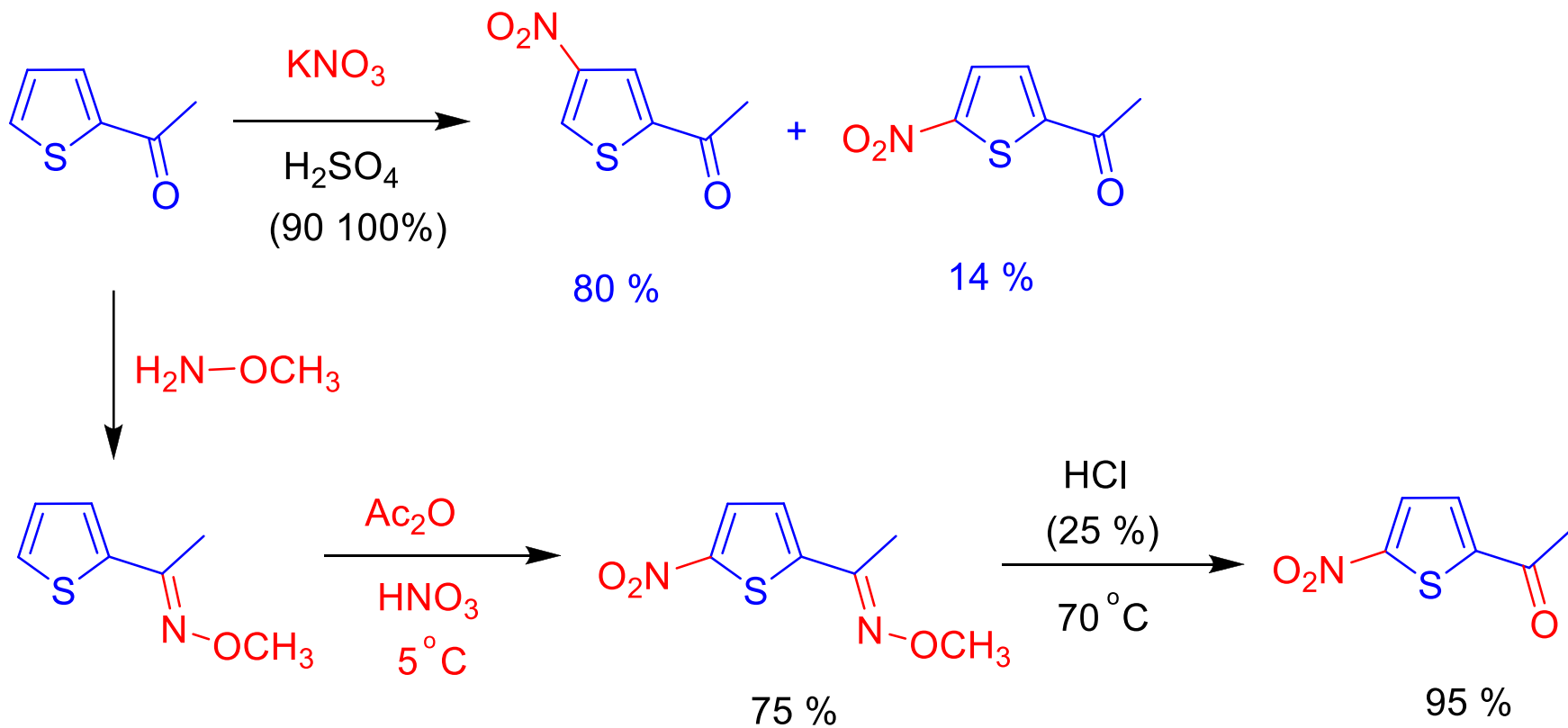


# REACCIONES DE DISUSTITUCIÓN (SEA)



# REACCIONES DE DISUSTITUCIÓN (SEA)

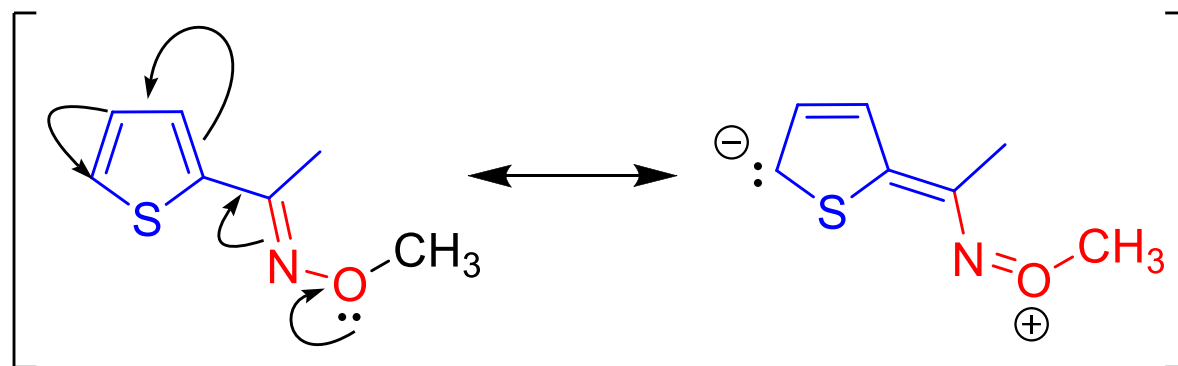
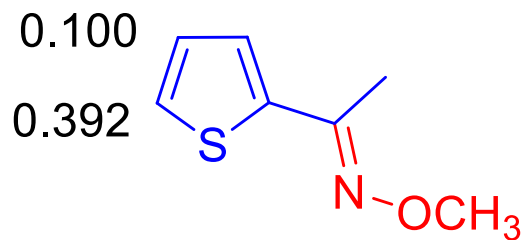
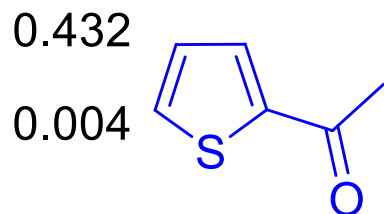




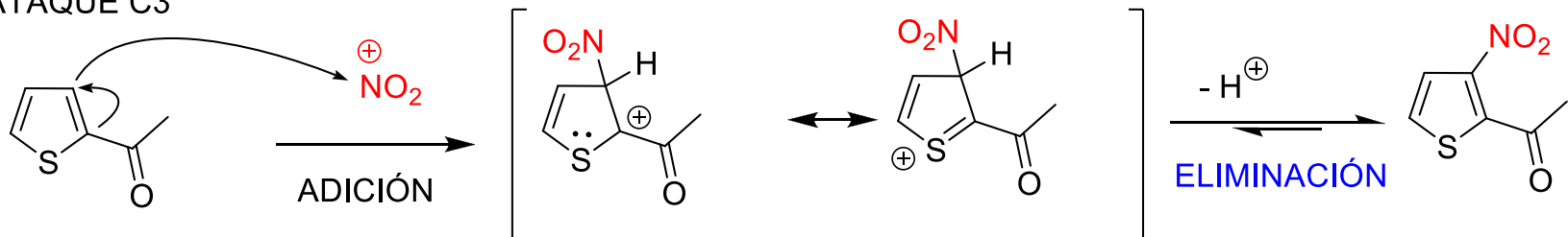
Goda, H.; et. al., *Synthesis*, 849(1992)



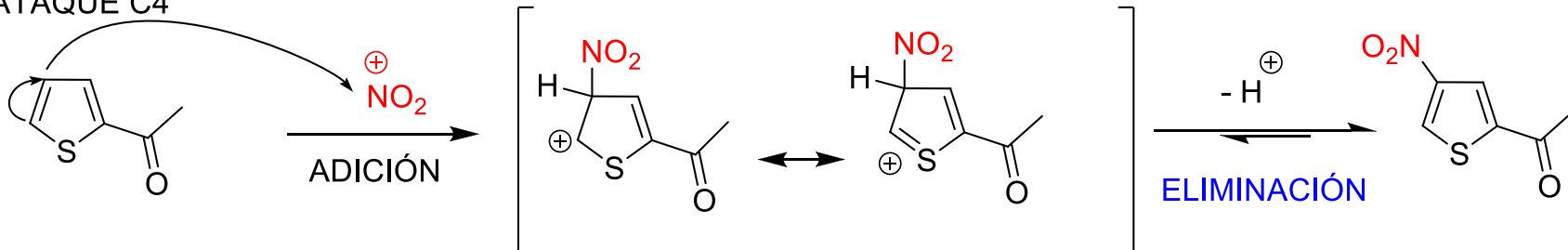
## ENERGÍA DE LOS HOMOS



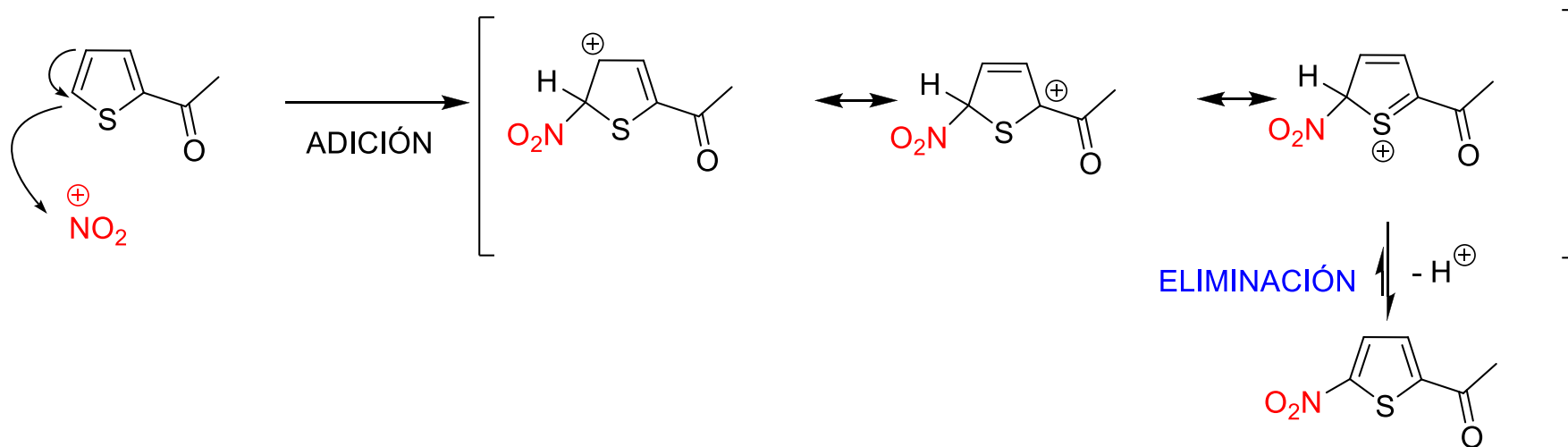
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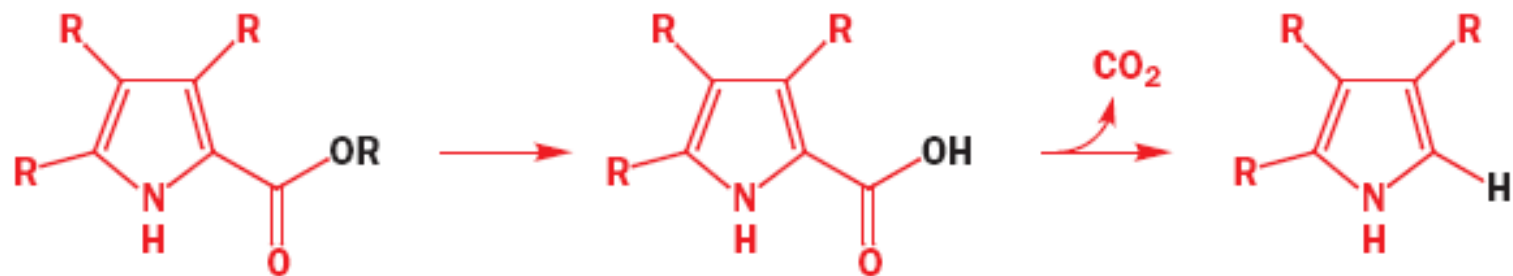


### ATAQUE C4

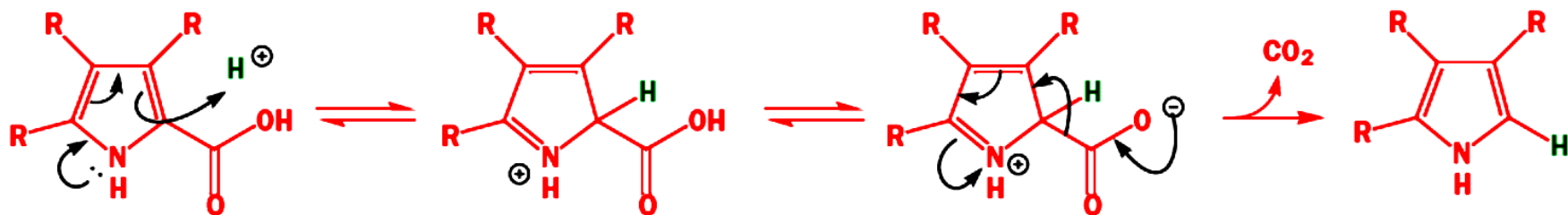


### ATAQUE C5

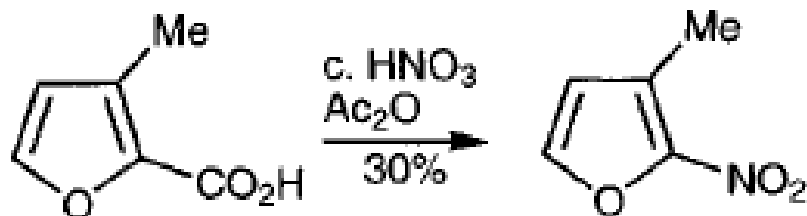
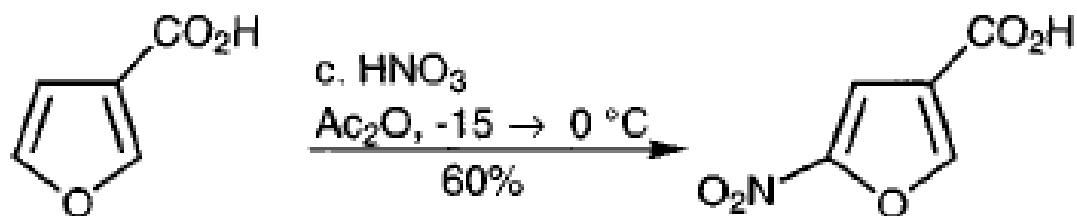
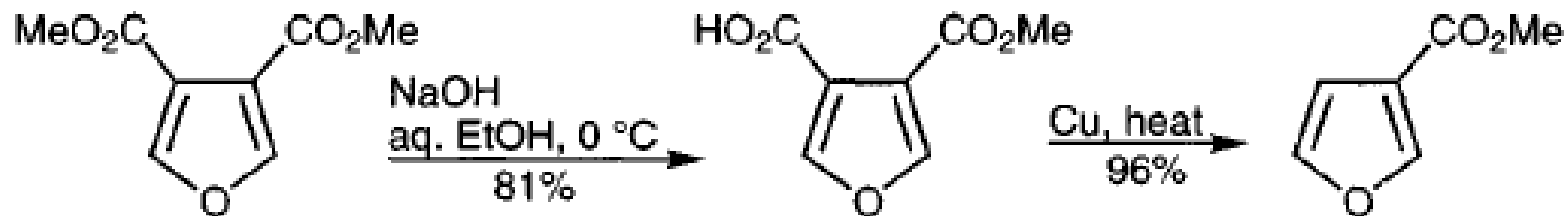


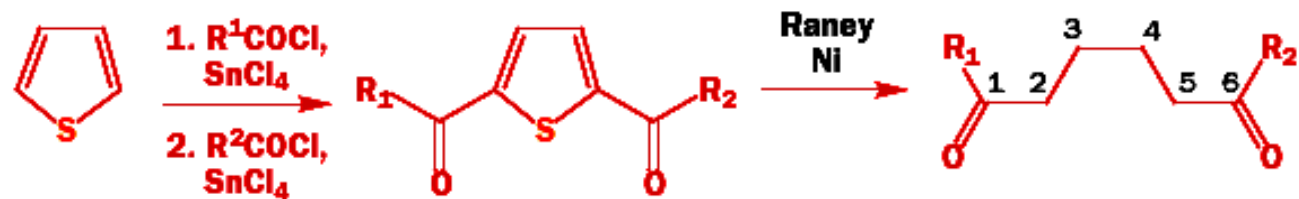
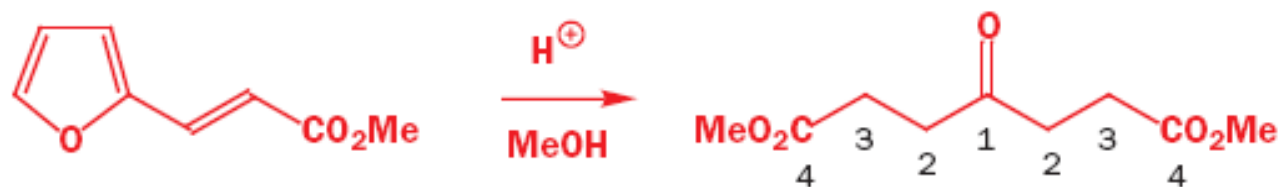
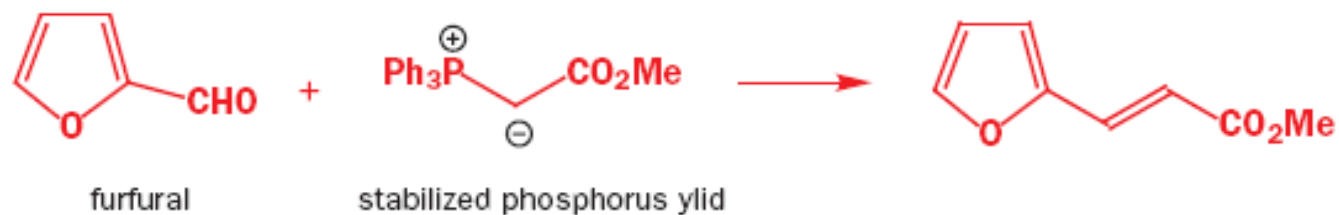


## MECANISMO DE LA REACCIÓN DE DESCARBOXILACIÓN

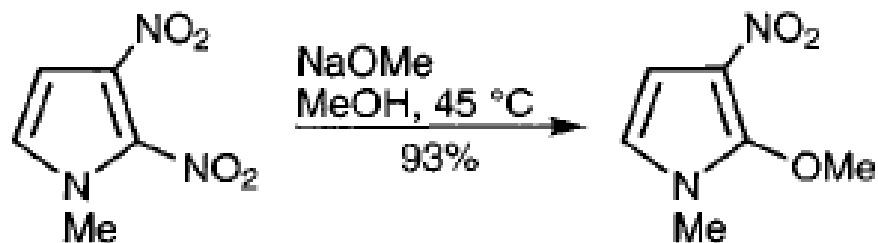
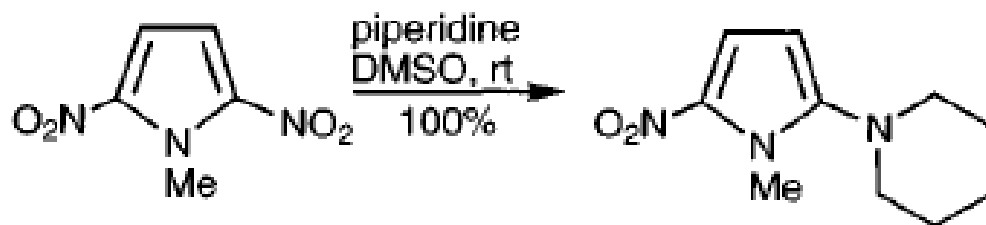
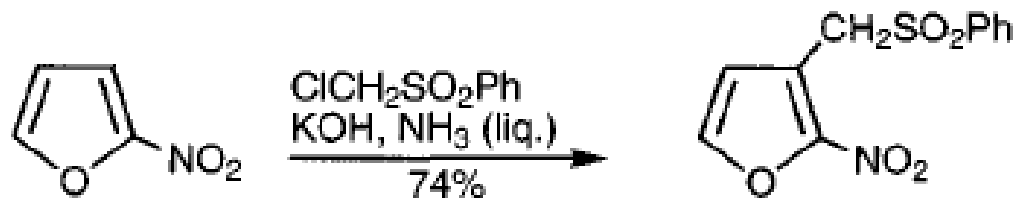


# REACCIONES DE DISUSTITUCIÓN (SEA)





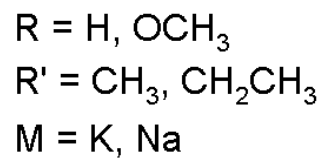
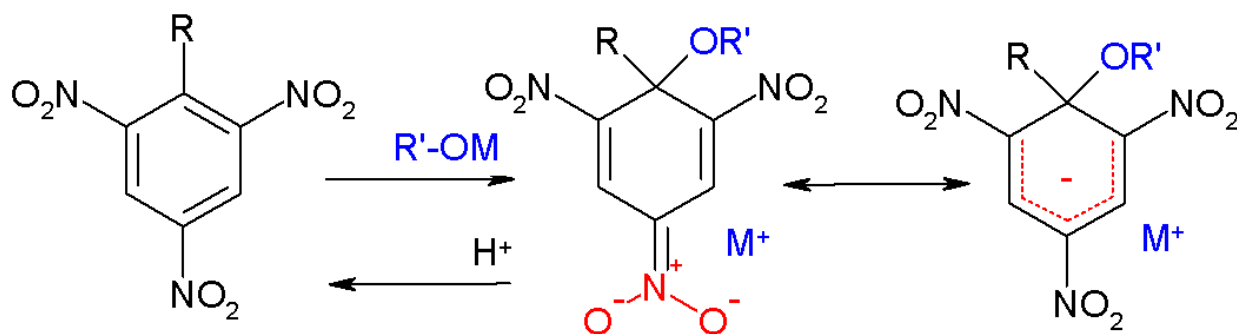
## REACCIONES CON REACTIVOS NUCLEOFÍLICOS (S<sub>N</sub>Ar)



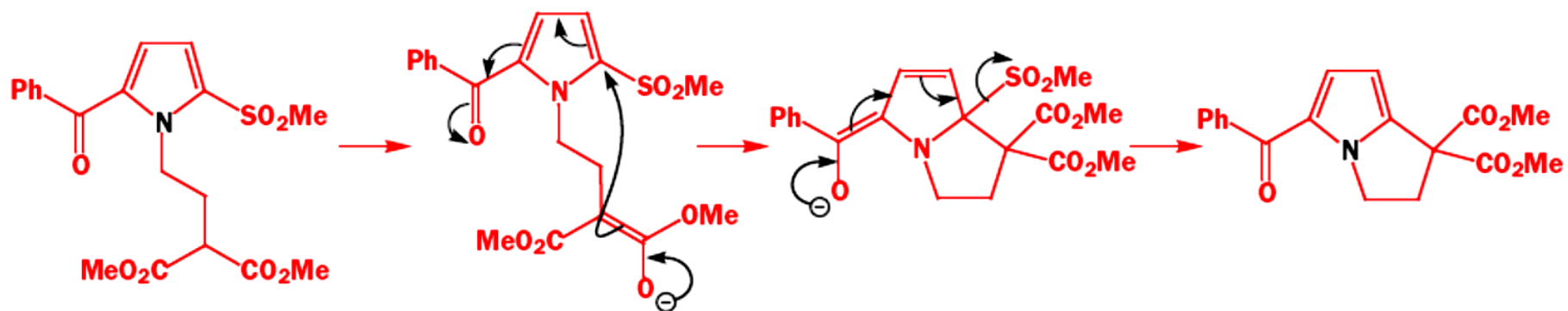
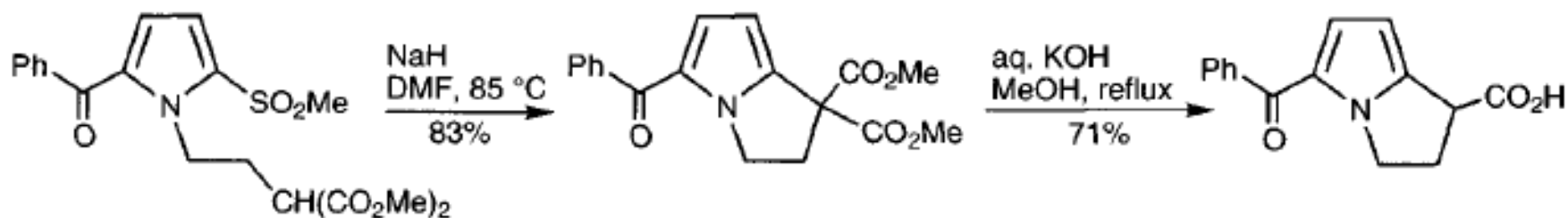


Jakob Meisenheimer  
(1876 –1934)  
Químico alemán

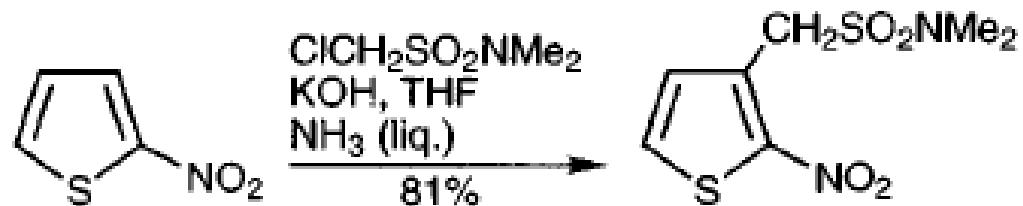
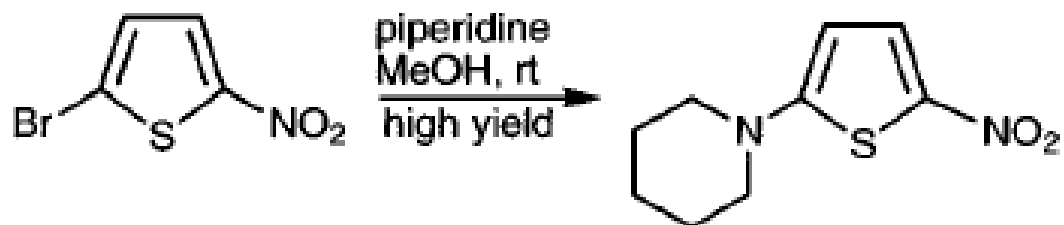
## Reacción de Meisenheimer (SNAr)



## REACCIONES CON REACTIVOS NUCLEOFÍLICOS (SNA)



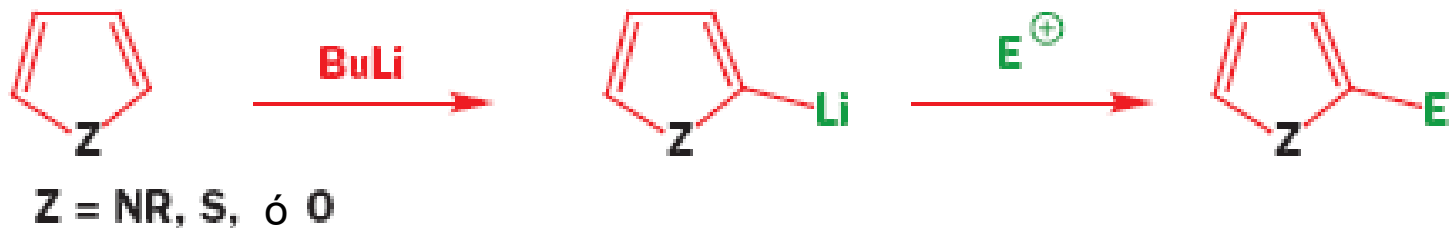
## REACCIONES CON REACTIVOS NUCLEOFÍLICOS ( $S_NAr$ )



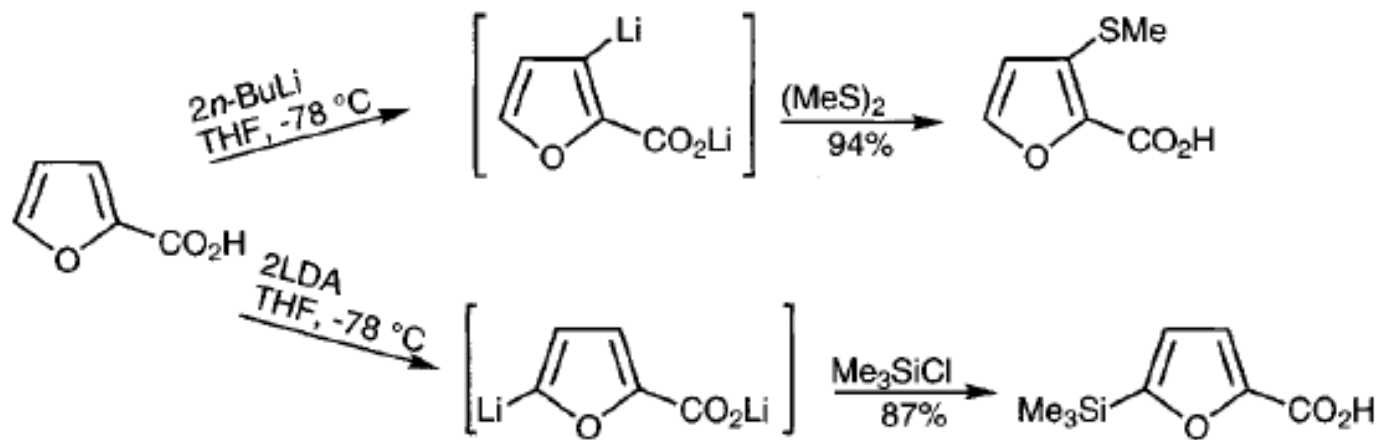
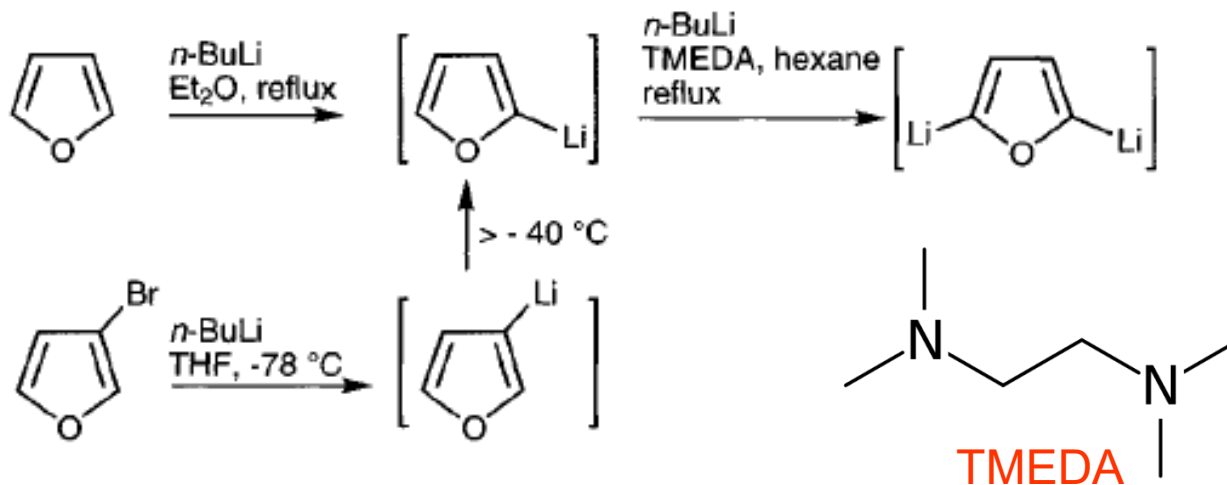
$S_NAr$  Vicaria



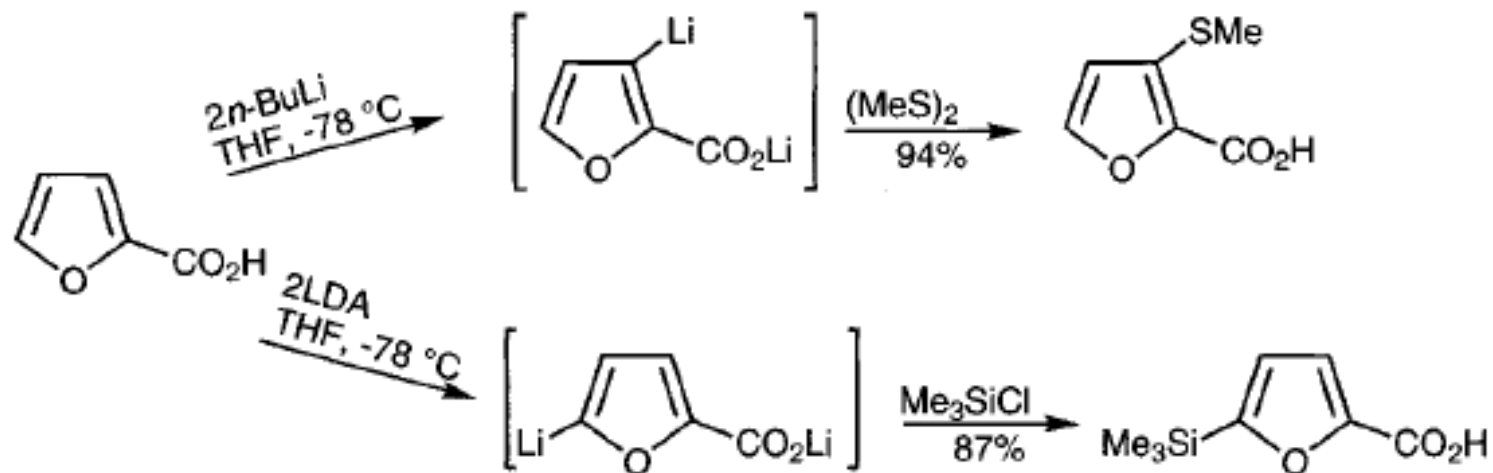
# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES



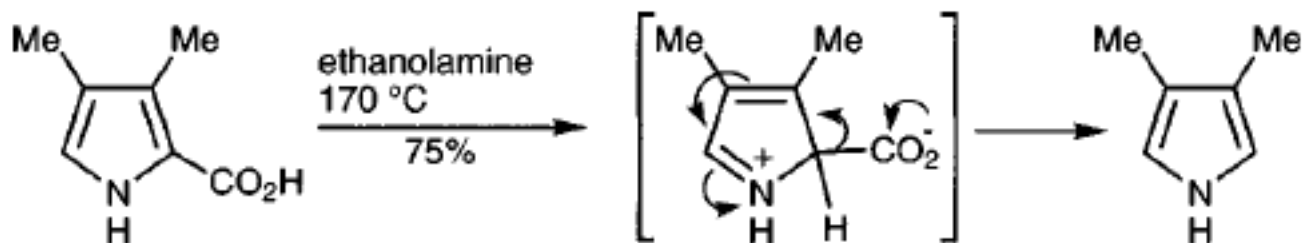
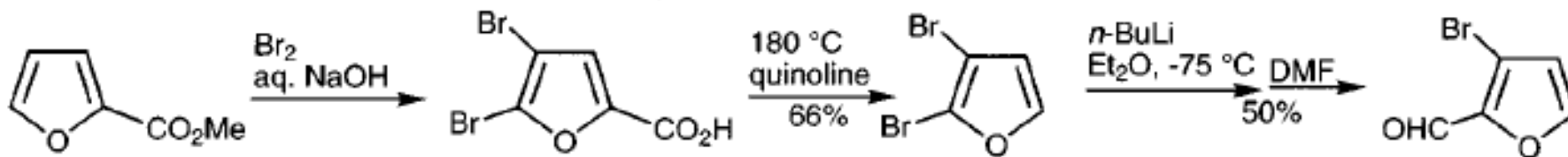
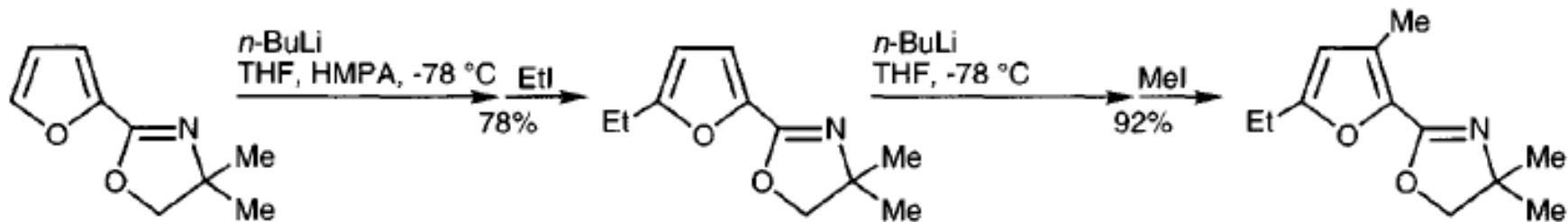
# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES



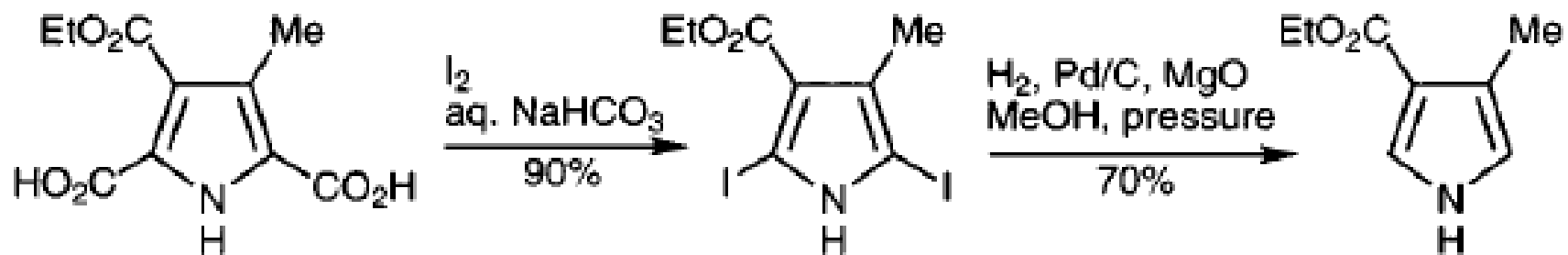
# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES



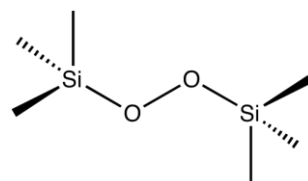
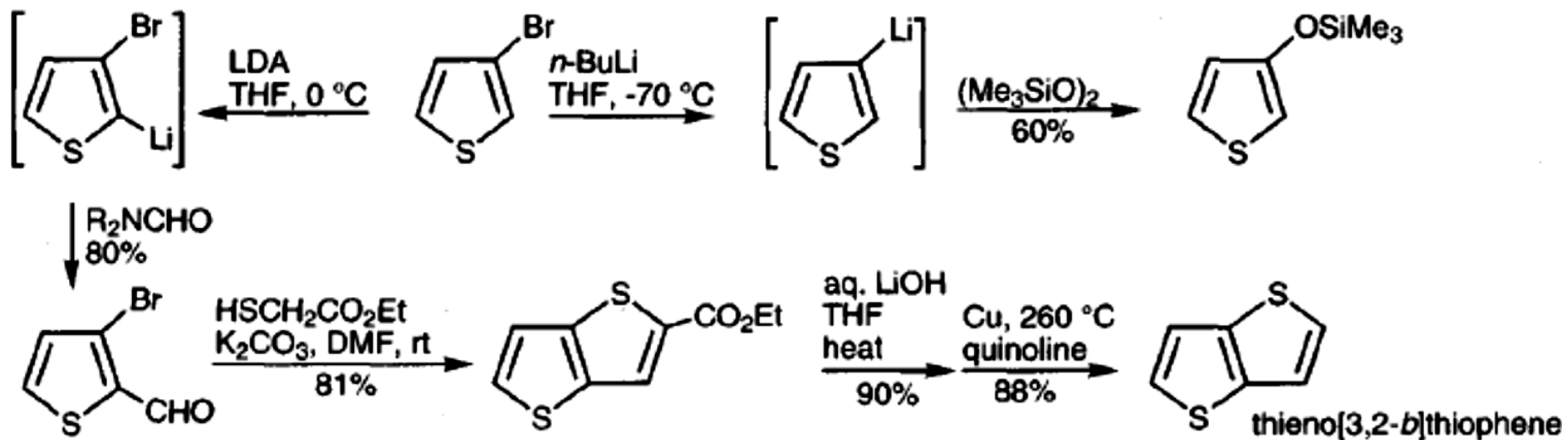
# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES



## REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES

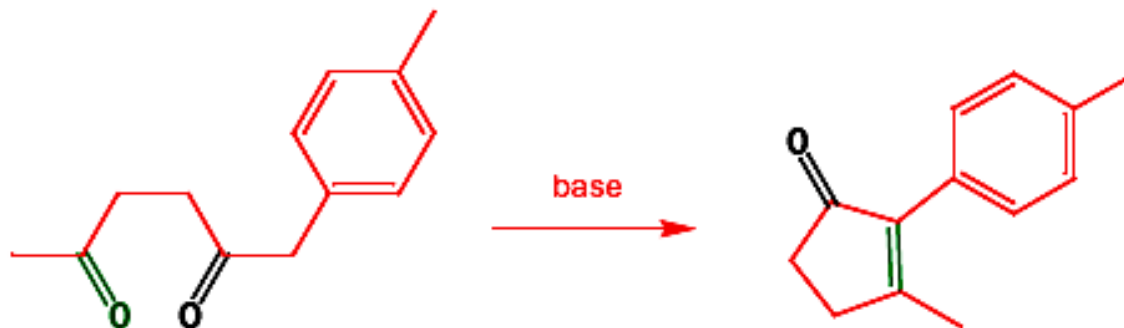
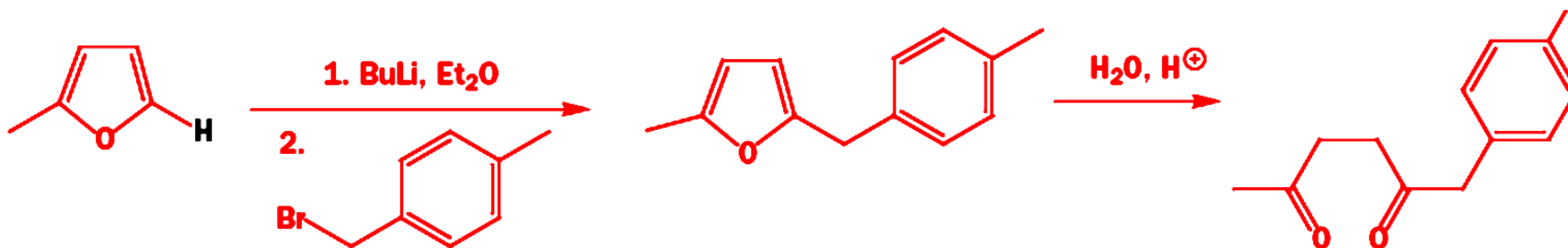
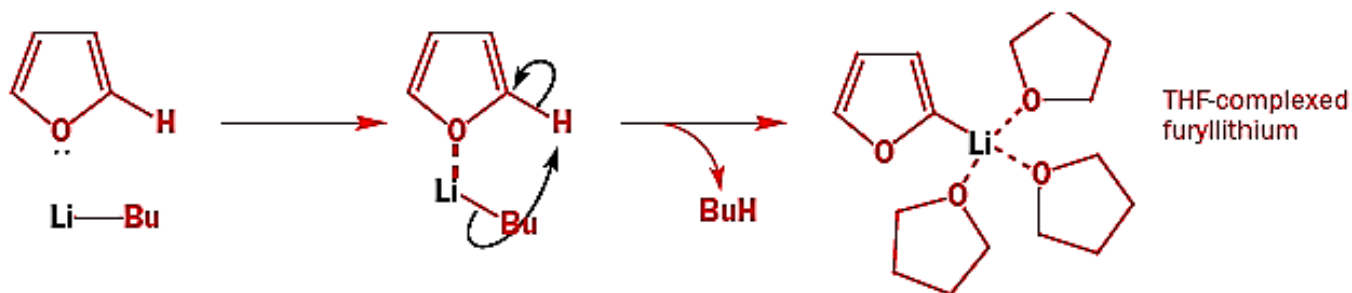


# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES

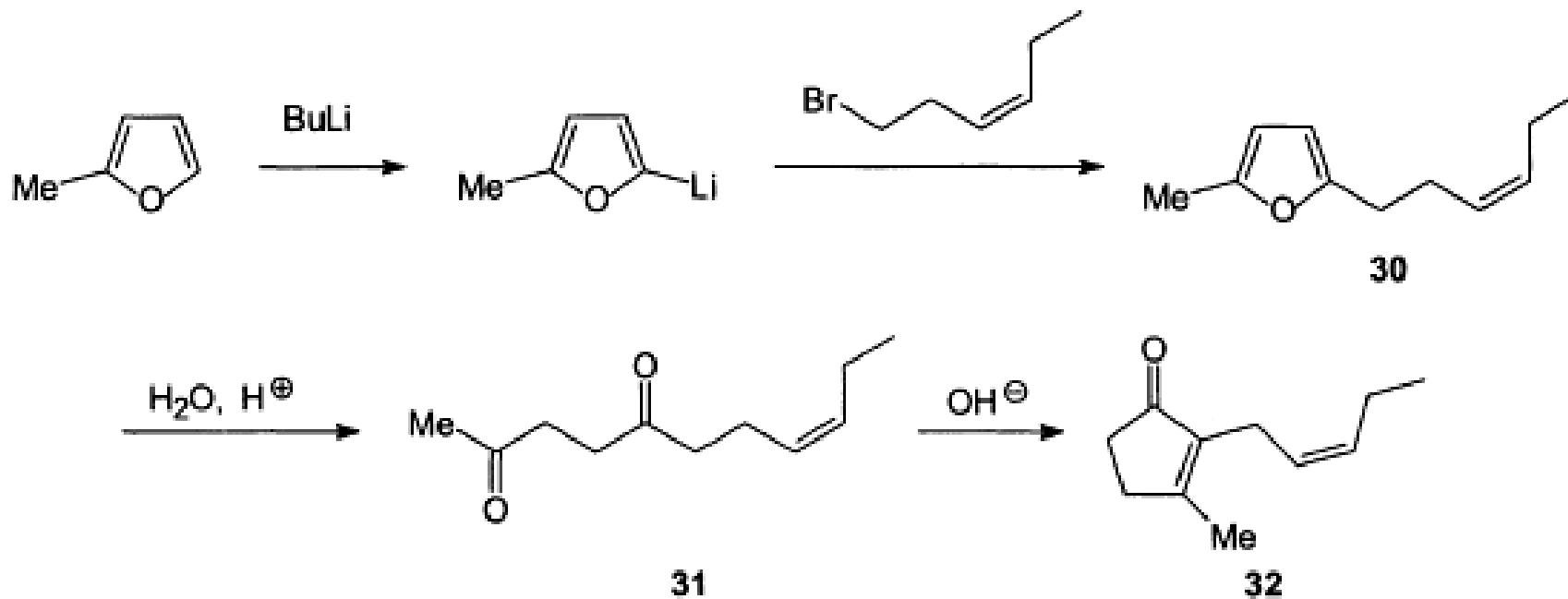


Bis(trimethylsilyl) peroxide

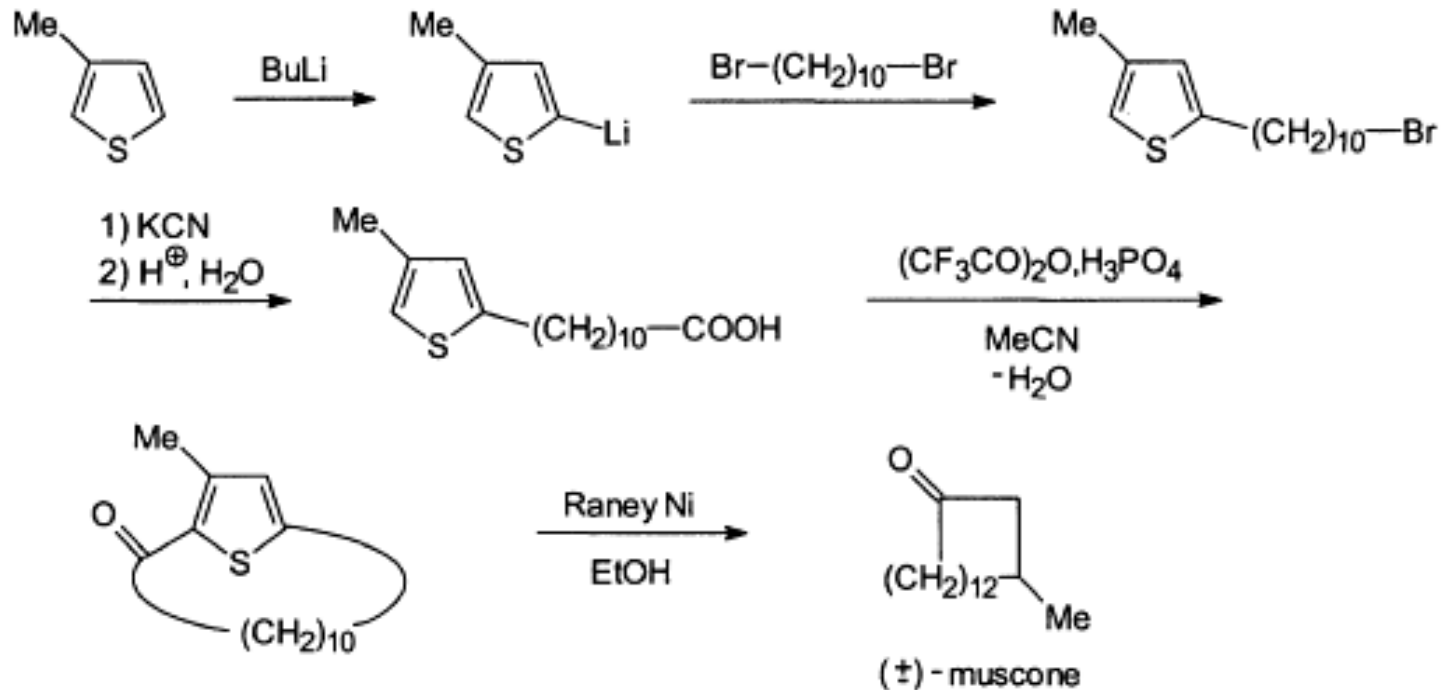
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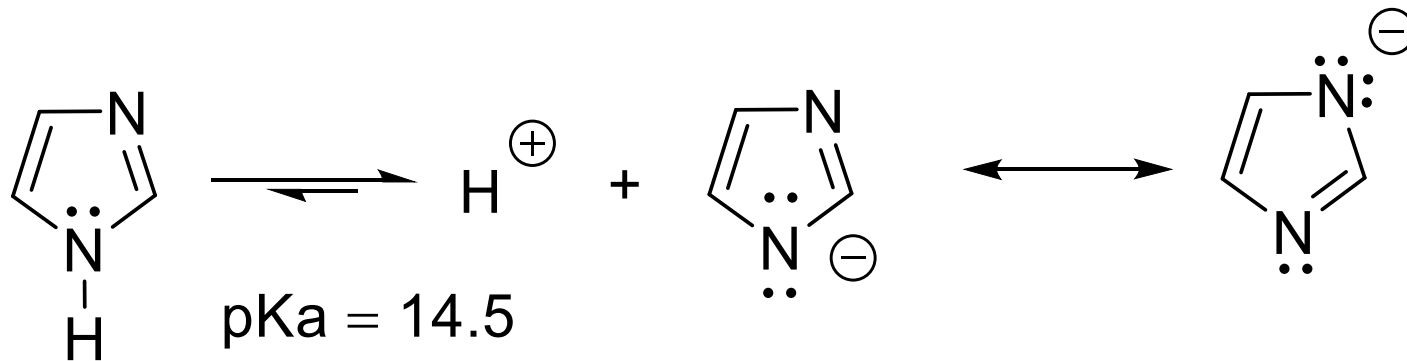
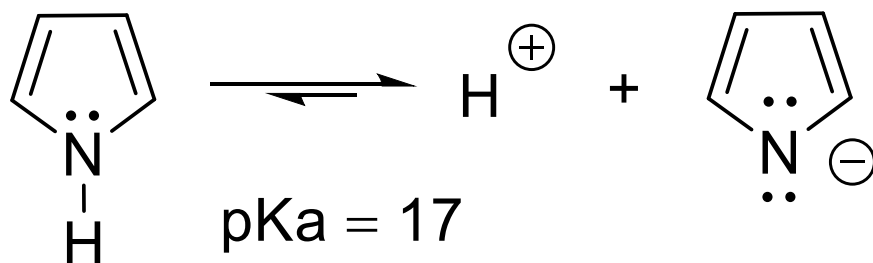
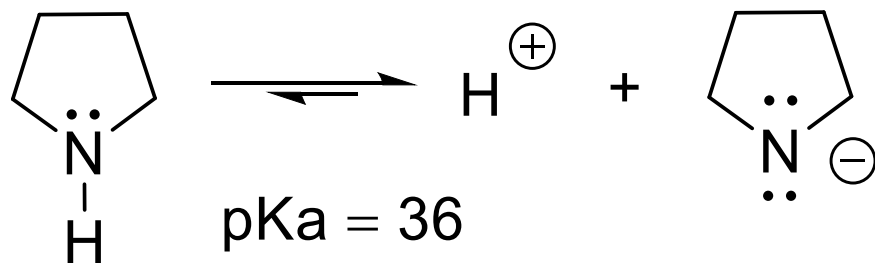
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# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES

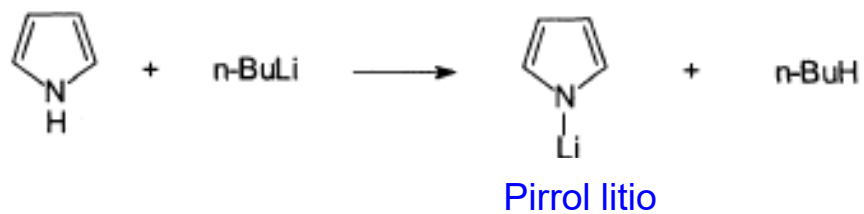
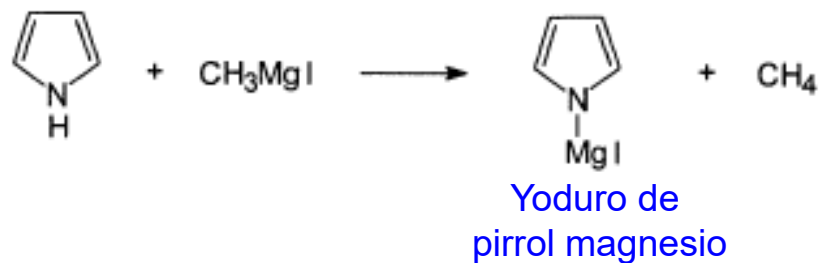


## Ácidez anillos heterocíclicos derivados del N

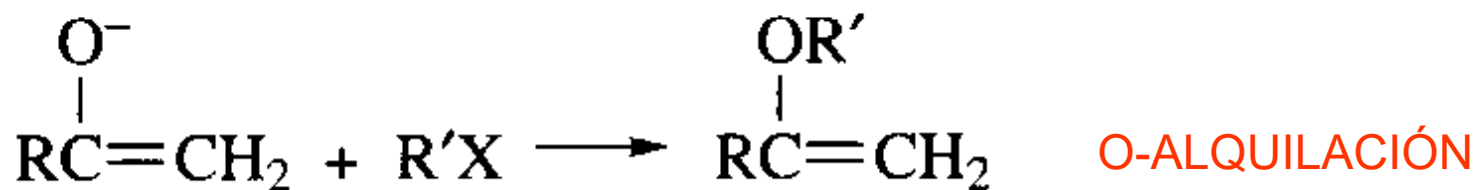
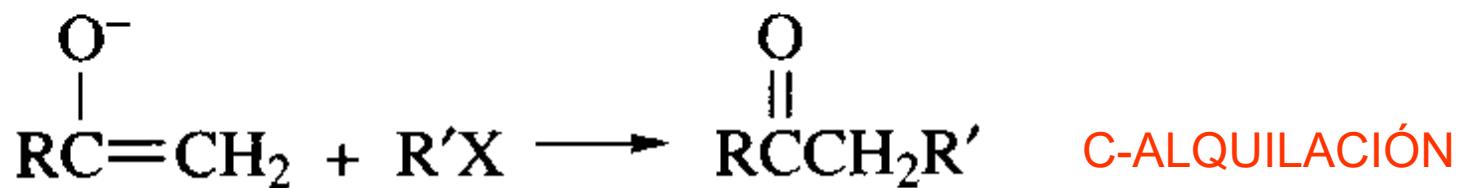
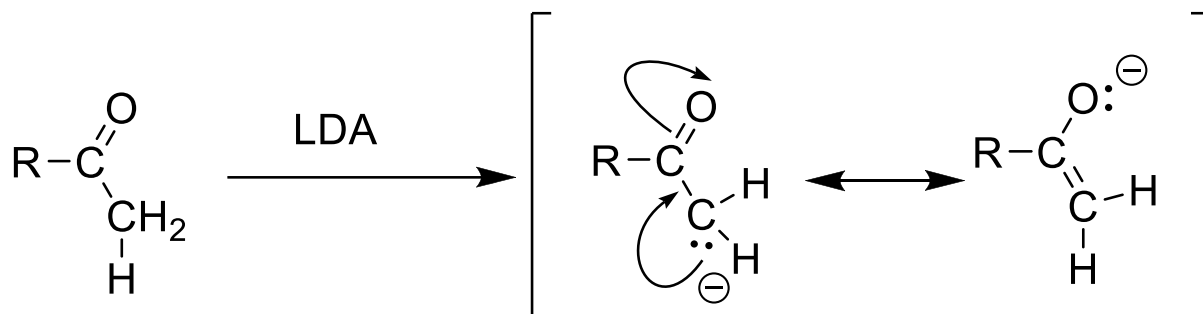


# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES

## ANIONES AMBIVALENTES



## ANIONES AMBIVALENTES



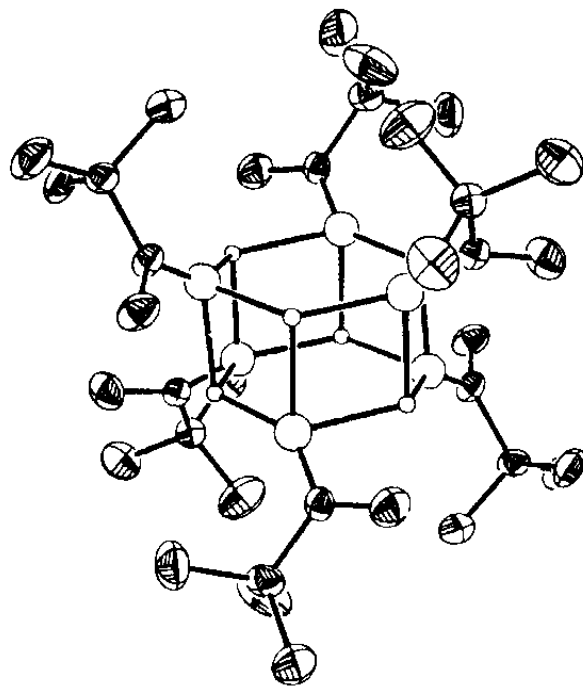


Fig. 1.1. Unsolvated hexameric aggregate of lithium enolate of methyl *t*-butyl ketone; large circles = oxygen, small circles = lithium. (Reproduced with permission from Ref. 44. Copyright 1986 American Chemical Society.)



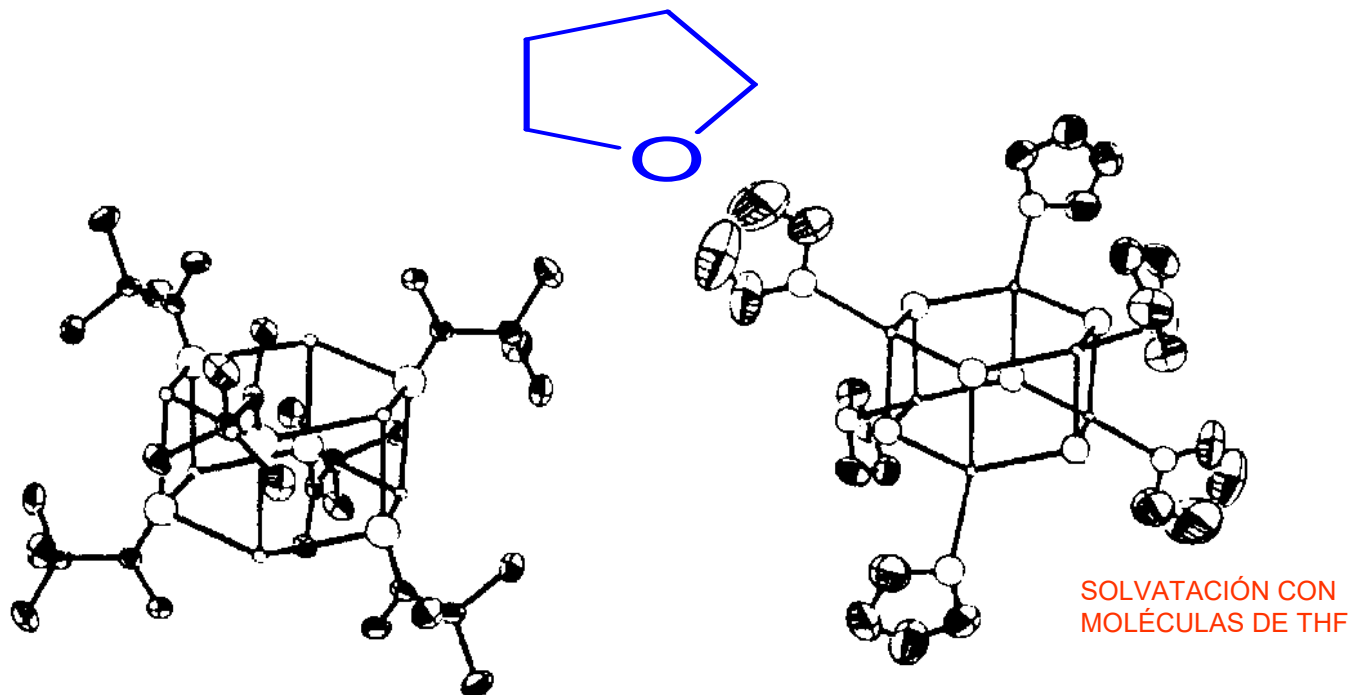
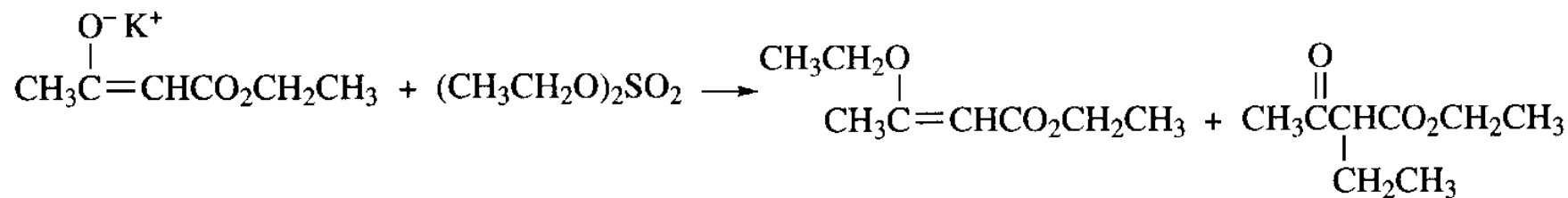


Fig. 1.2. Potassium enolate of methyl *t*-butyl ketone; large circles = oxygen, small circles = potassium. (a) Left-hand plot shows only methyl *t*-butyl ketone residues. (b) Right-hand plot shows only the solvating THF molecules. The crystal is a composite of these two structures. (Reproduced with permission from Ref. 44. Copyright 1986 American Chemical Society.)

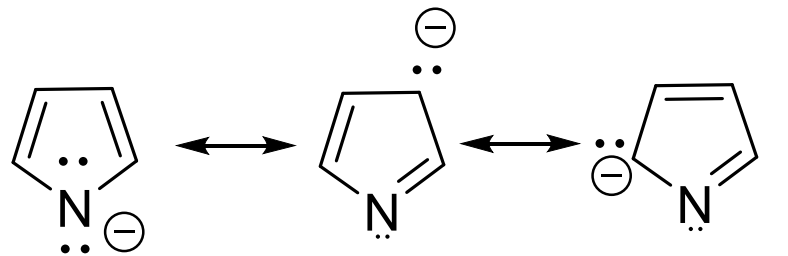




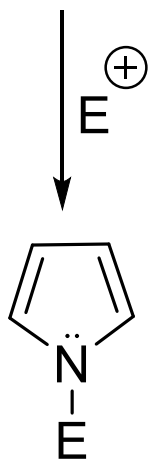
<b>EN HMPA</b>	<b>83 %</b>	<b>15 %</b>
<b>EN t-BuOH</b>	<b>0 %</b>	<b>94 %</b>
<b>EN THF</b>	<b>0 %</b>	<b>94 %</b>



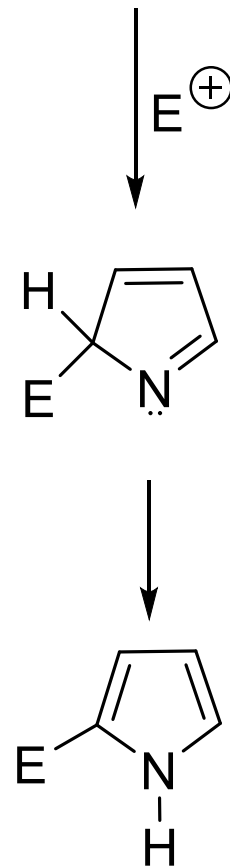
# ANIÓN PIRROL



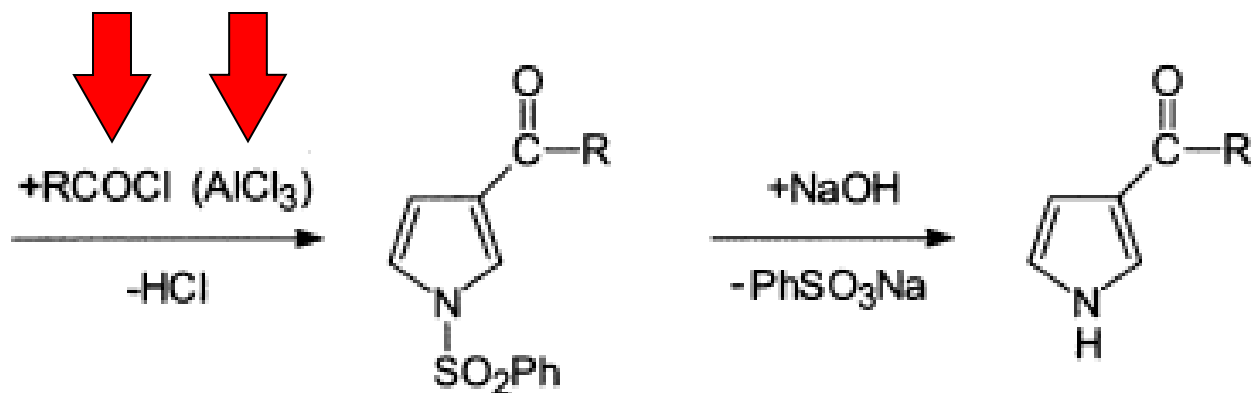
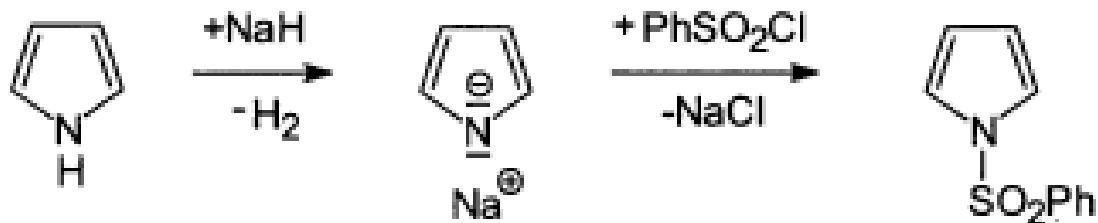
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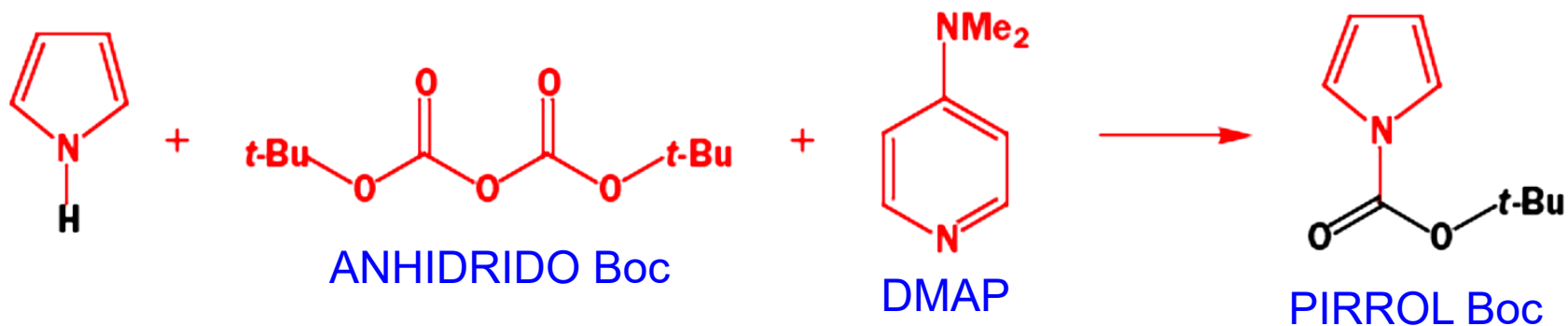
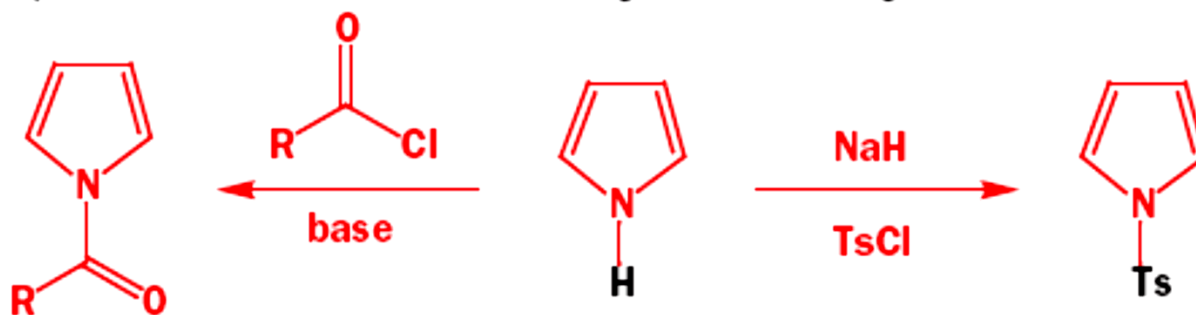
**C-SUSTITUCIÓN**



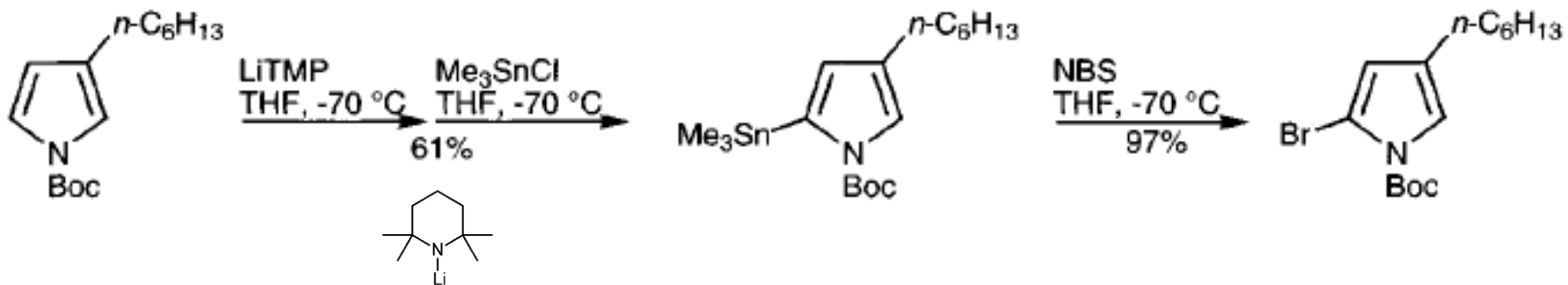
# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES



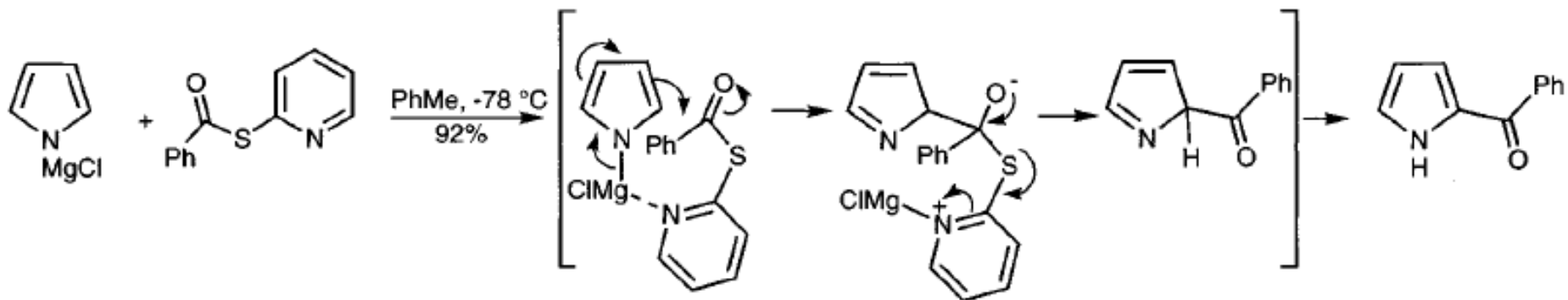
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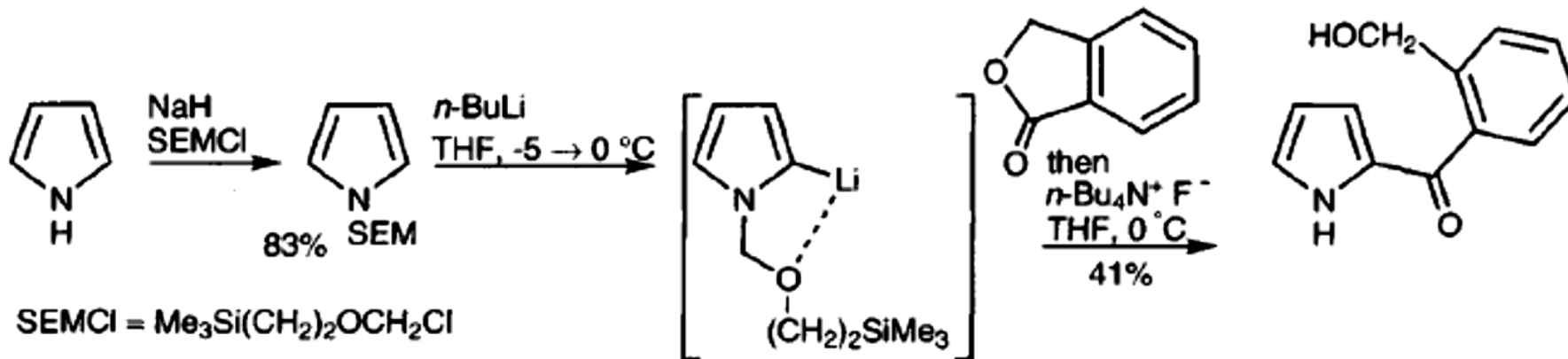
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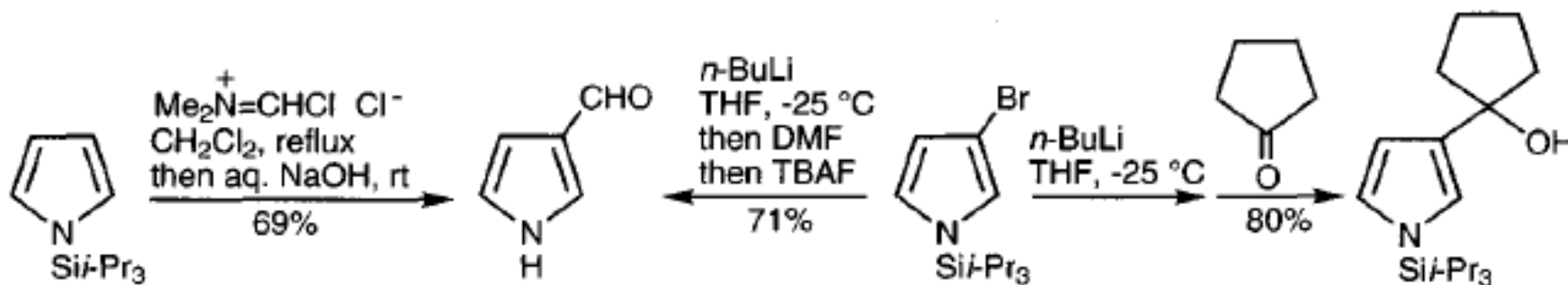
LiTMP = tetrametilpiperiduro de litio



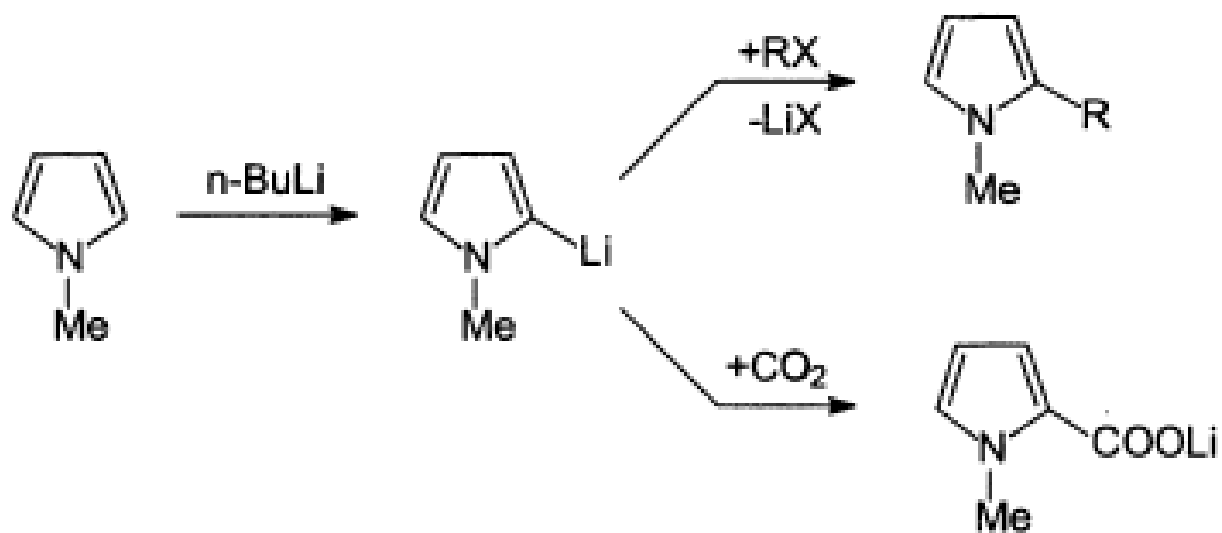
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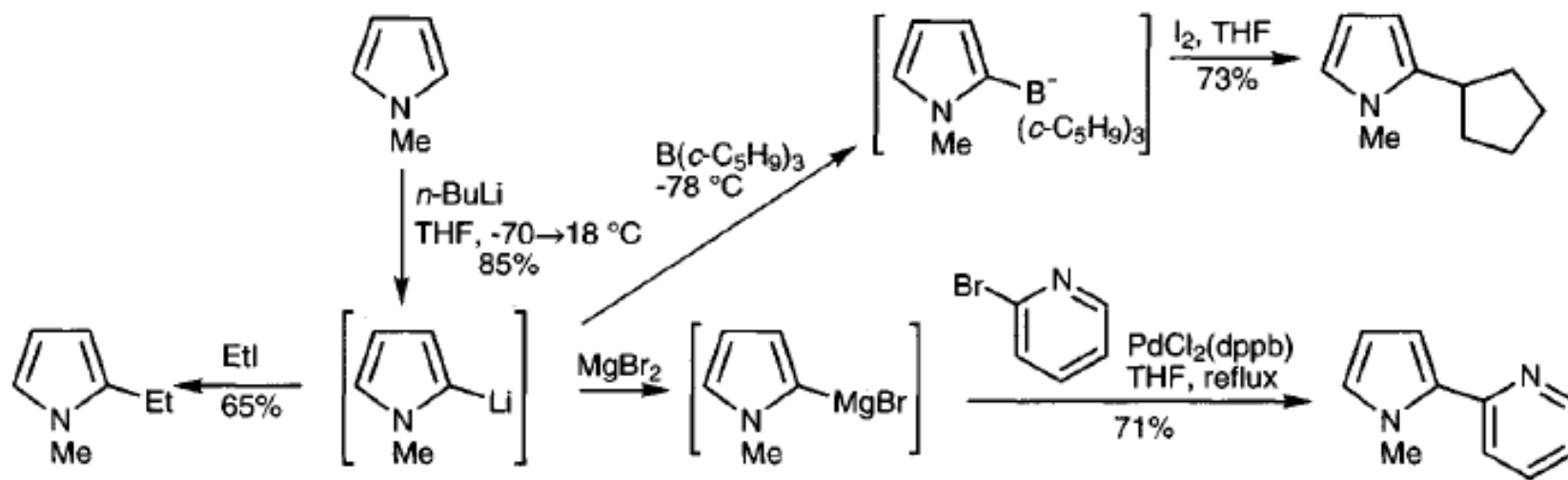
## CLORURO DE 2-(TRIMETILSILIL)-ETOXIMETILO



# REACCIONES CON BASES FUERTES. FORMACIÓN DE CARBANIONES

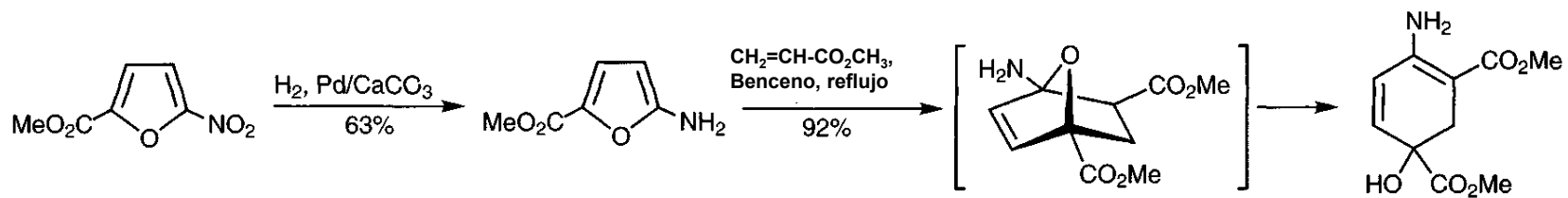
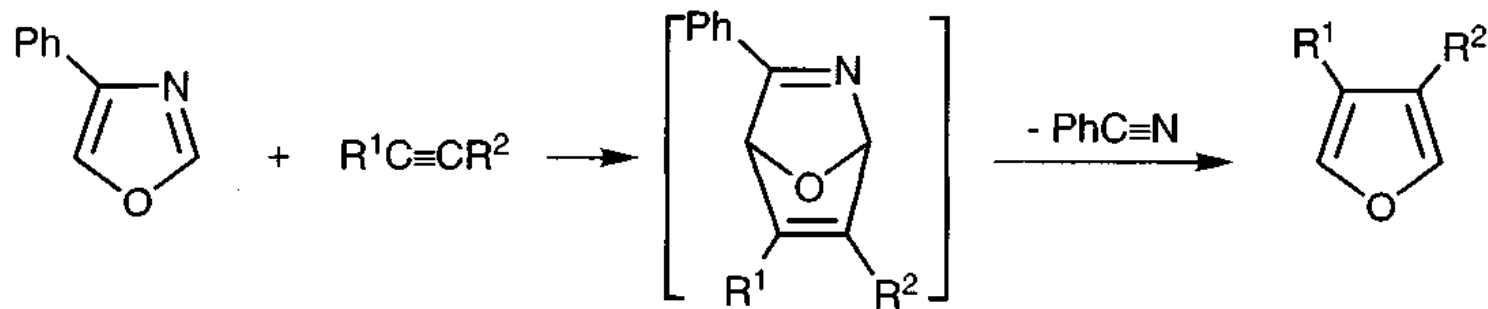


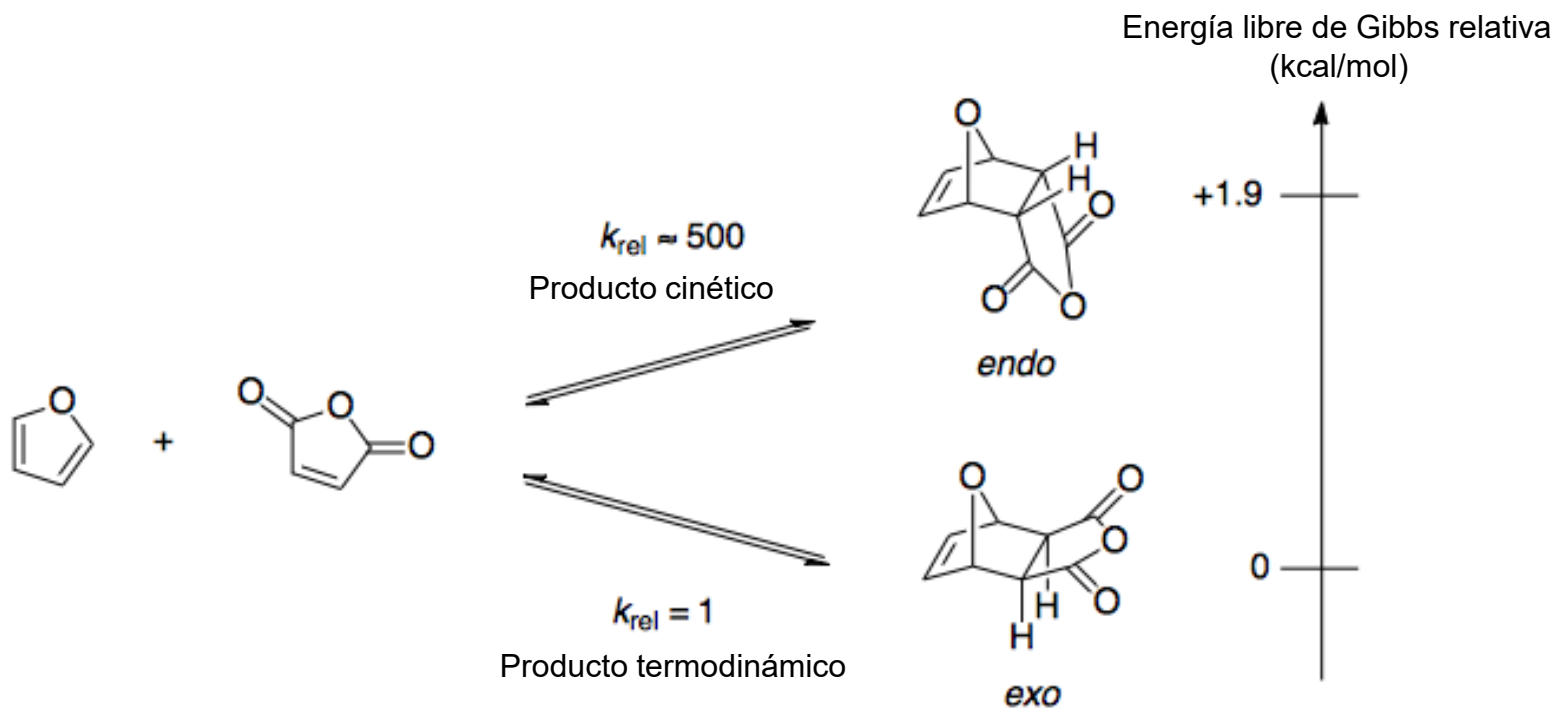
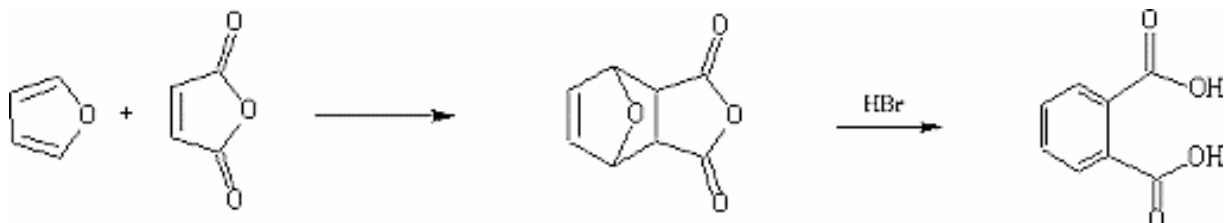
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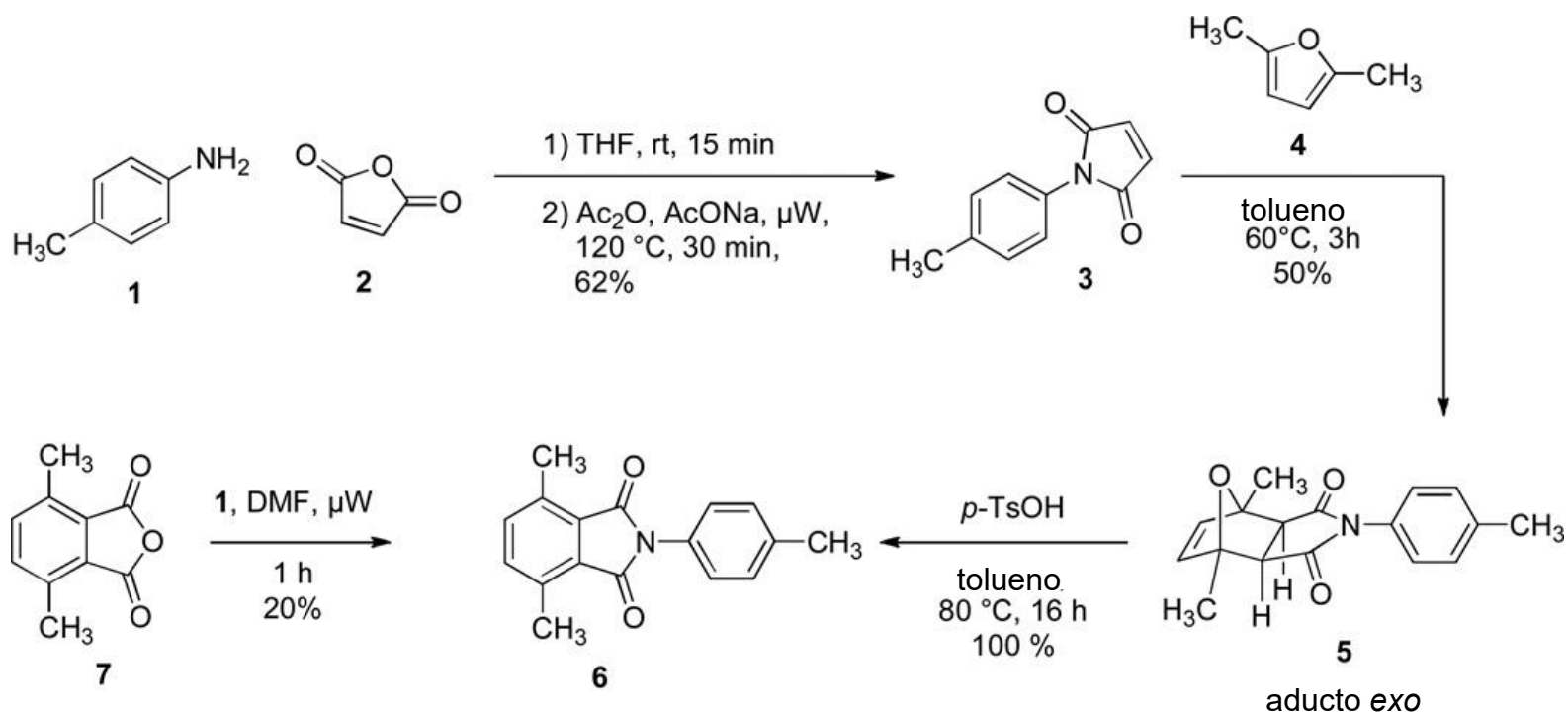
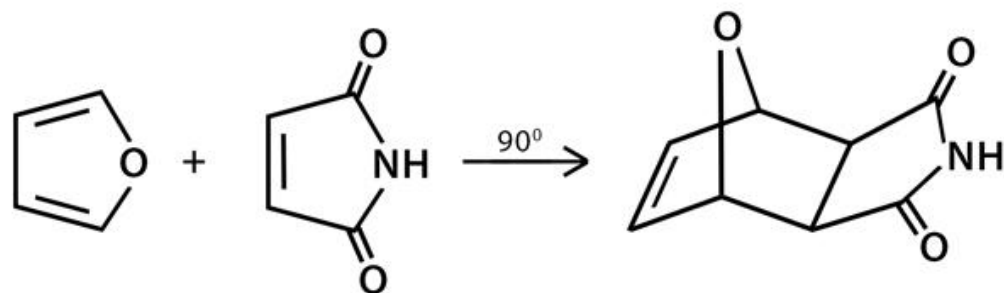


# Reacción de Diels-Alder





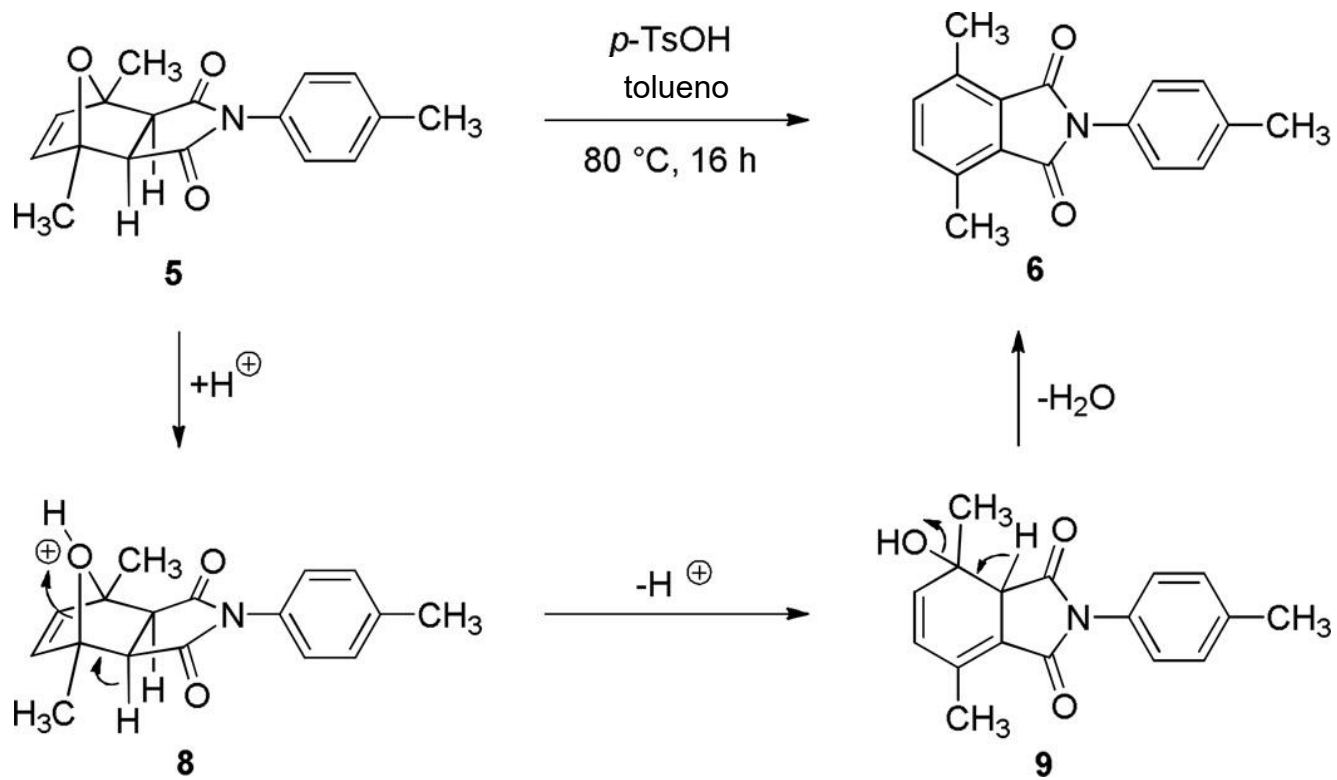


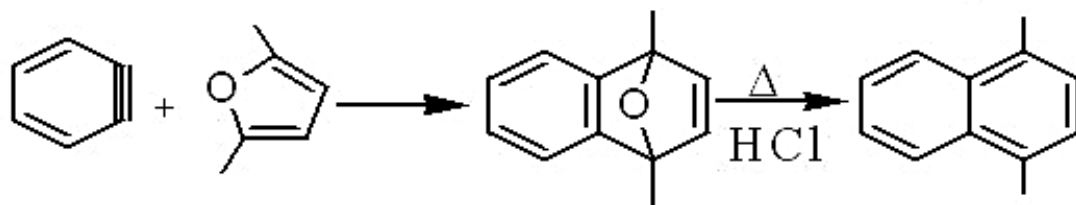
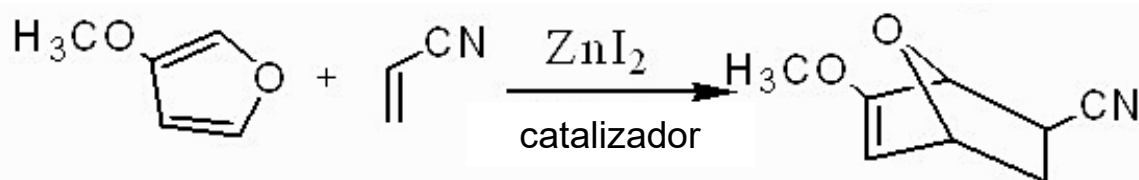
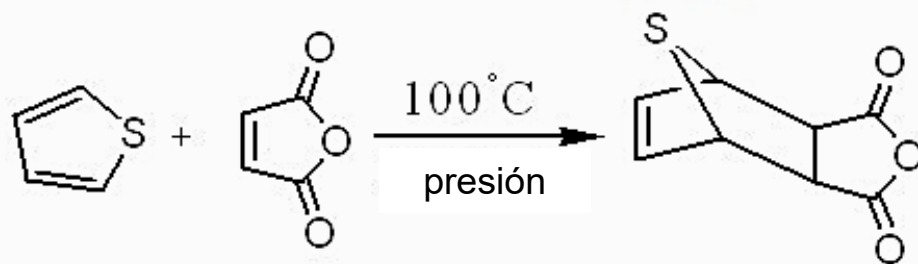


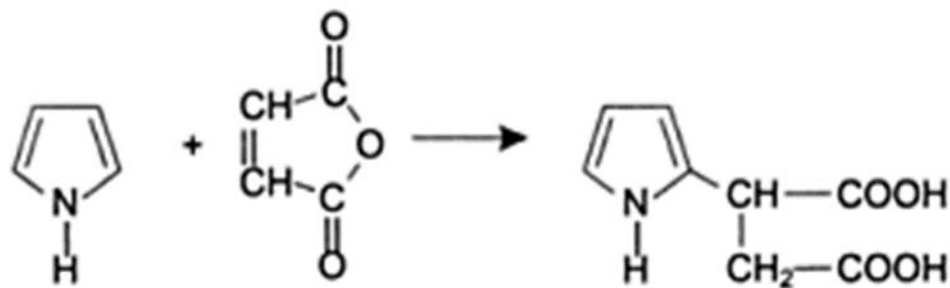
Xiaoyuan Ding, Son T. Nguyen, John D. Williams, Norton P. Peet  
 Diels-Alder reactions of five-membered heterocycles containing one heteroatom

*Tetrahedron Lett.* **2014**, *17*; 55(51): 7002–7006.  
 doi: [10.1016/j.tetlet.2014.10.114](https://doi.org/10.1016/j.tetlet.2014.10.114)

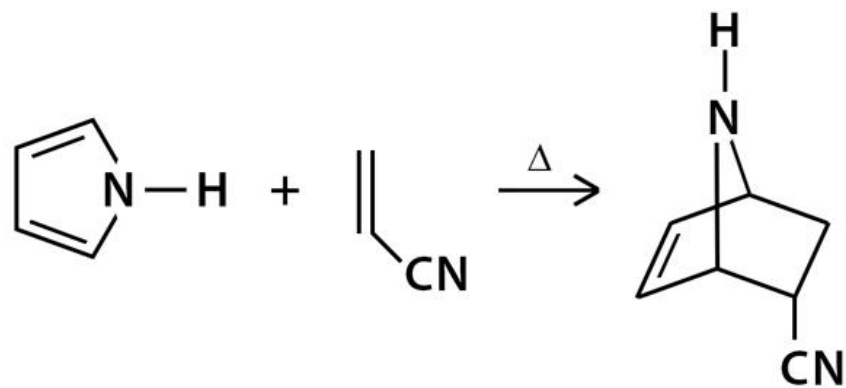


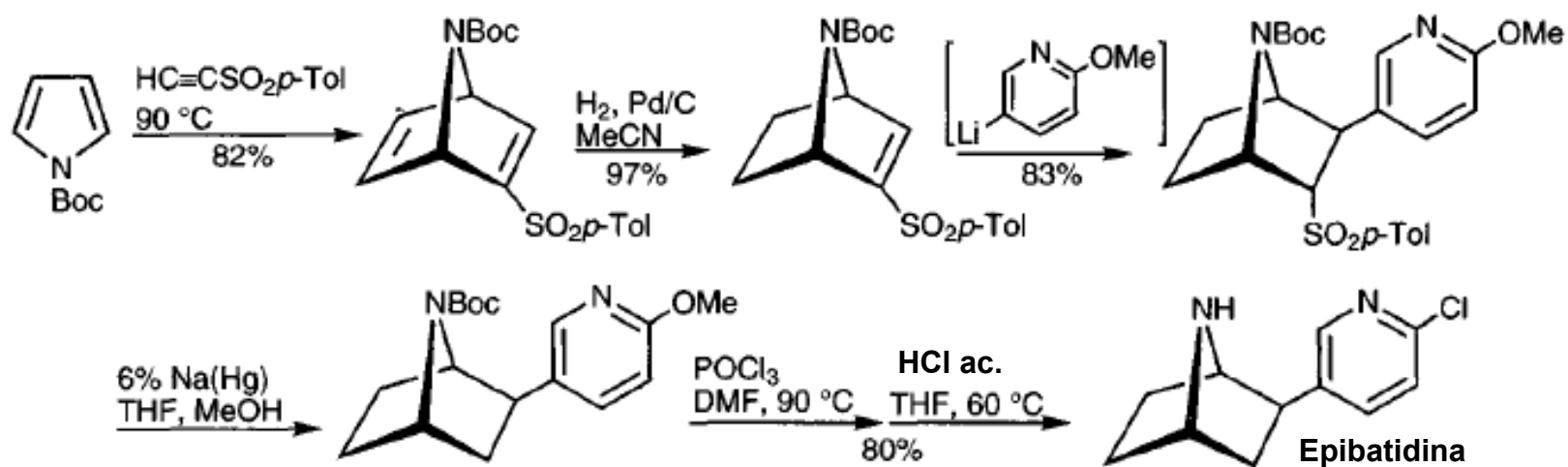
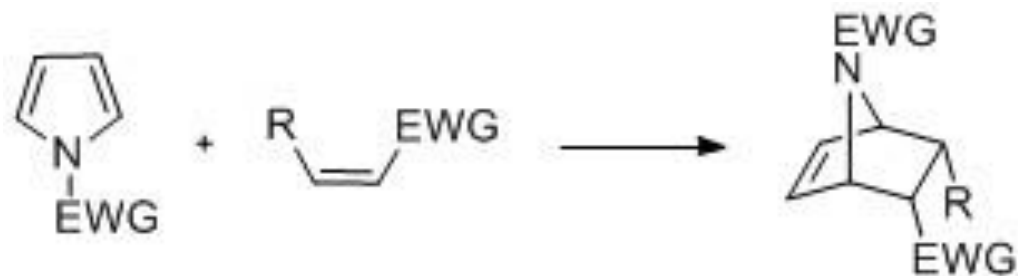


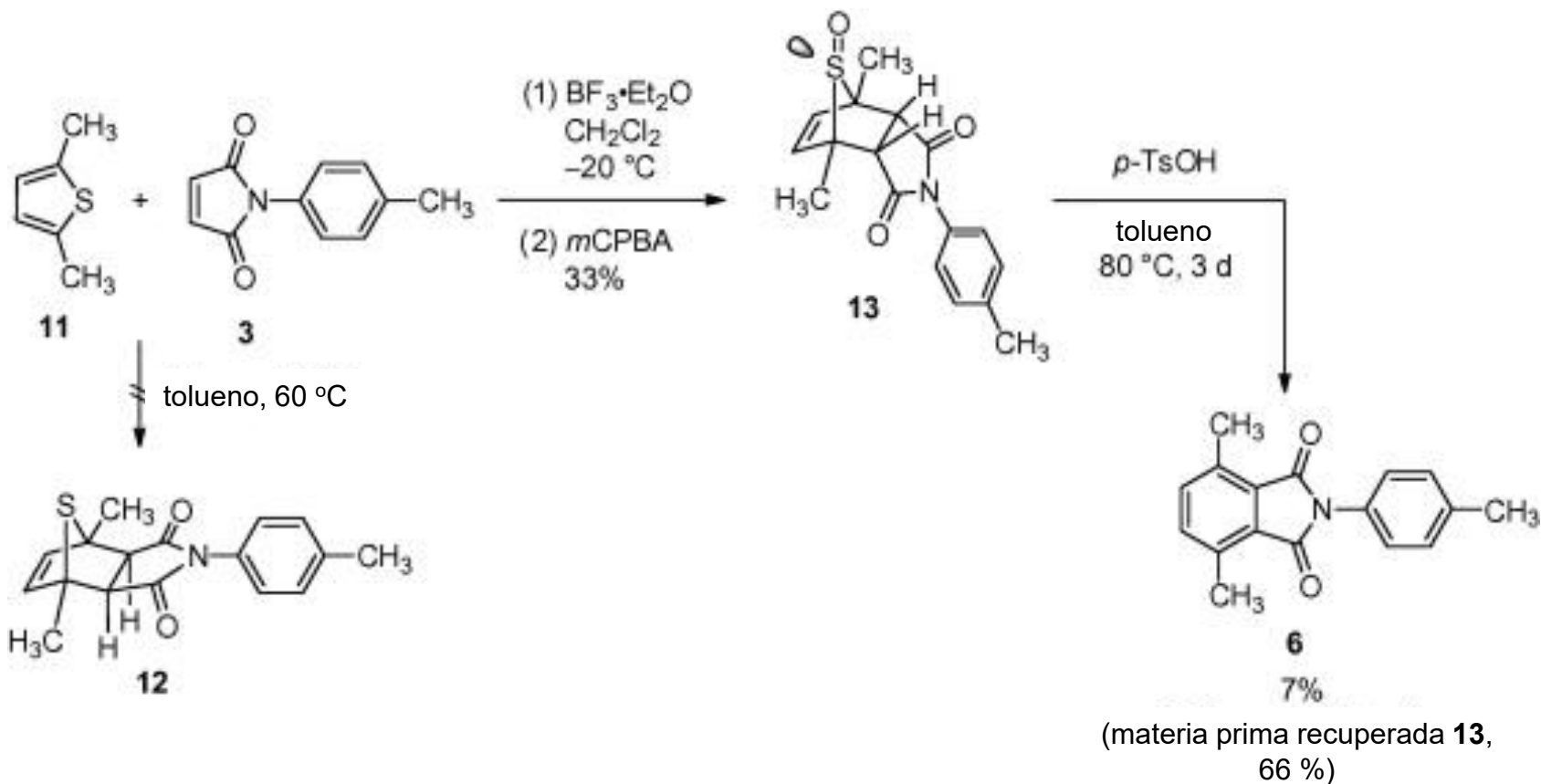




### Reacción de Diels-Alder con el pirrol

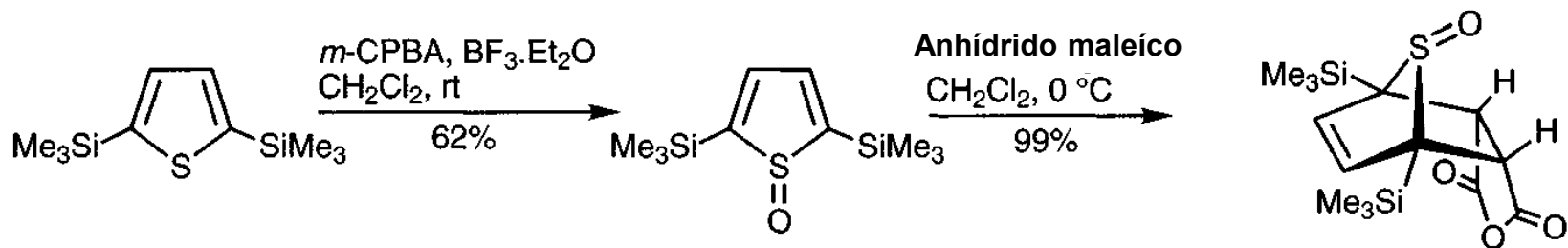
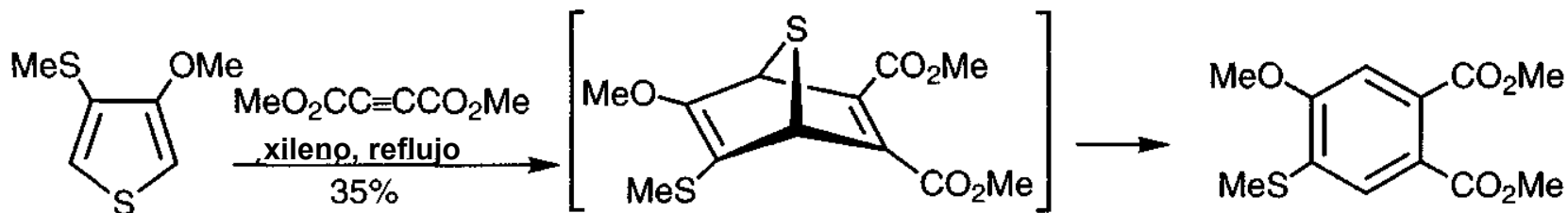
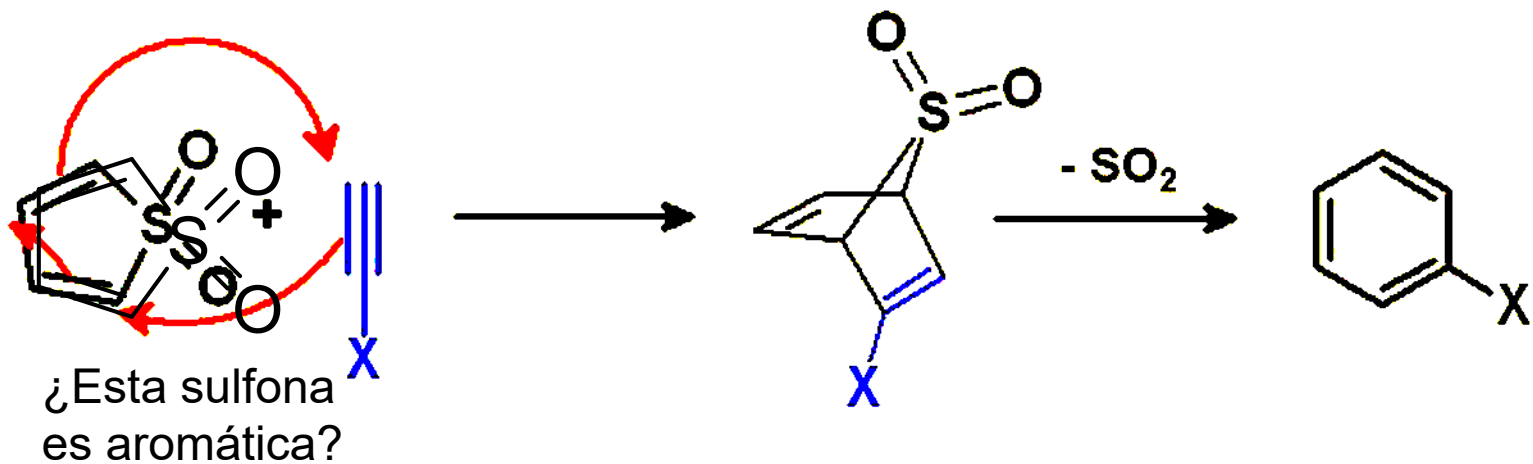




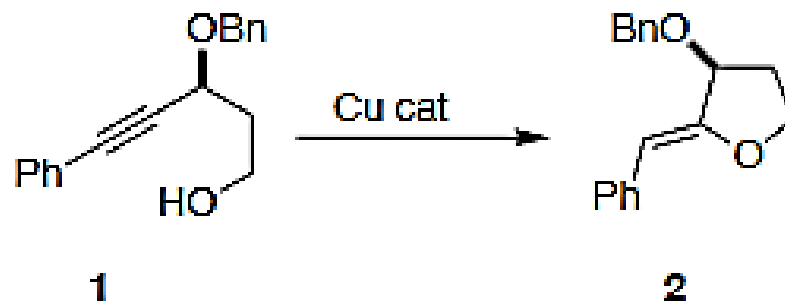


Diels–Alder Reaction of Thiophene: Dramatic Effects  
 of High-Pressure/Solvent-Free Conditions<sup>‡</sup>  
 Koji Kumamoto, Isao Fukada, Hiyoshizo Kotsuki  
 30 March 2004  
<https://doi.org/10.1002/anie.200353487>

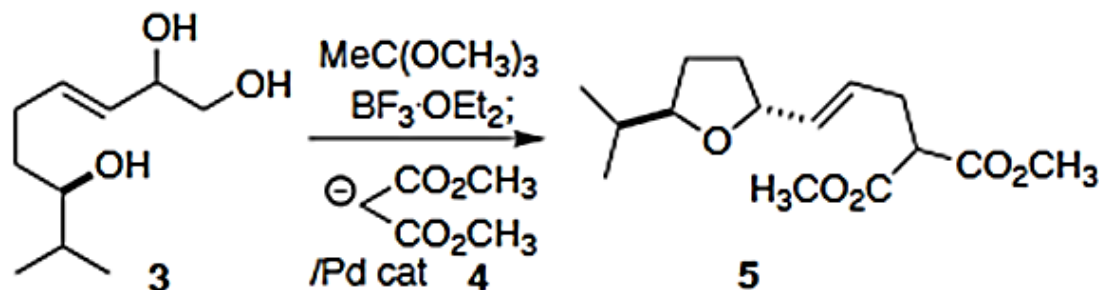




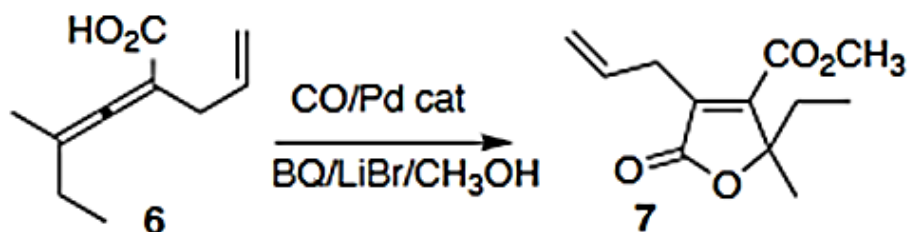
Silvia Díez-González del Imperial College London cicló el alquino 1 al enol éter 2 (Adv. Synth. Catal. 2024, 366, 806. DOI: 10.1002/adsc.202301181).



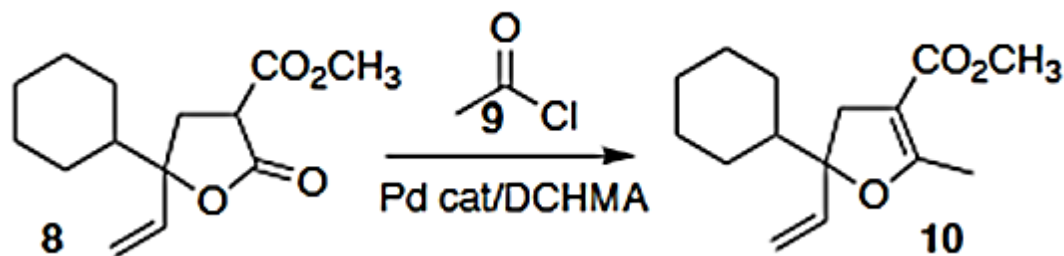
Sébastien Prévost de la Ecole Polytechnique y Aurélien de la Torre de la Université Paris-Saclay construyeron el tetrahidrofurano 5 acoplando el triol 3 con la sal de sodio 4 del malonato de dimetilo (Org. Lett. 2024, 26, 2393. DOI: 10.1021/acs.orglett.4c00495).



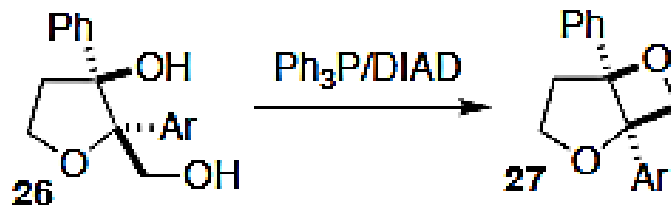
Xin Mu y Bin Yang de la Universidad Xi'an Jiaotong y Jan-E. Bäckvall, de la Universidad de Estocolmo, carboniló el aleno 6 en condiciones oxidativas para dar la lactona 7 (Org. Lett. 2024, 26, 2430. DOI: 10.1021/acs.orglett.4c00572).



Hongchao Guo de la Universidad Agrícola de China ensambló el dihidrofurano 10 combinando la lactona 8 con cloruro de acetilo (9) (Org. Lett. 2024, 26, 2057. DOI: 10.1021/acs.orglett.4c00315



Indrajeet Sharma, de la Universidad de Oklahoma, cicló el diol 26 al oxetano 27 (ACS Catal. 2024, 14, 1292. DOI: 10.1021/acscatal.3c05040).



Se aisló etromyroxol (3) de > 106 litros de agua de mar acondicionada con larvas de lamprea marina, *Petromyzon marinus*. Rodney A. Fernandes del Instituto Indio de Tecnología de Bombay ensambló el núcleo de 3 ciclando selectivamente el diol 1 al tetrahidrofurano 2 (Chem. Commun. 2023, 59, 2007, DOI: 10.1039/D2CC04579F; Chem. Commun. 2022, 58, 11921, DOI: 10.1039/D2CC04574E).

