Studies With Poly Functional Heteroaromatics: Recent Development and Tales of Unexpected

Mohamed Hilmy Elnagdi

Department of Chemistry, Faculty of Science; University of Kuwait:

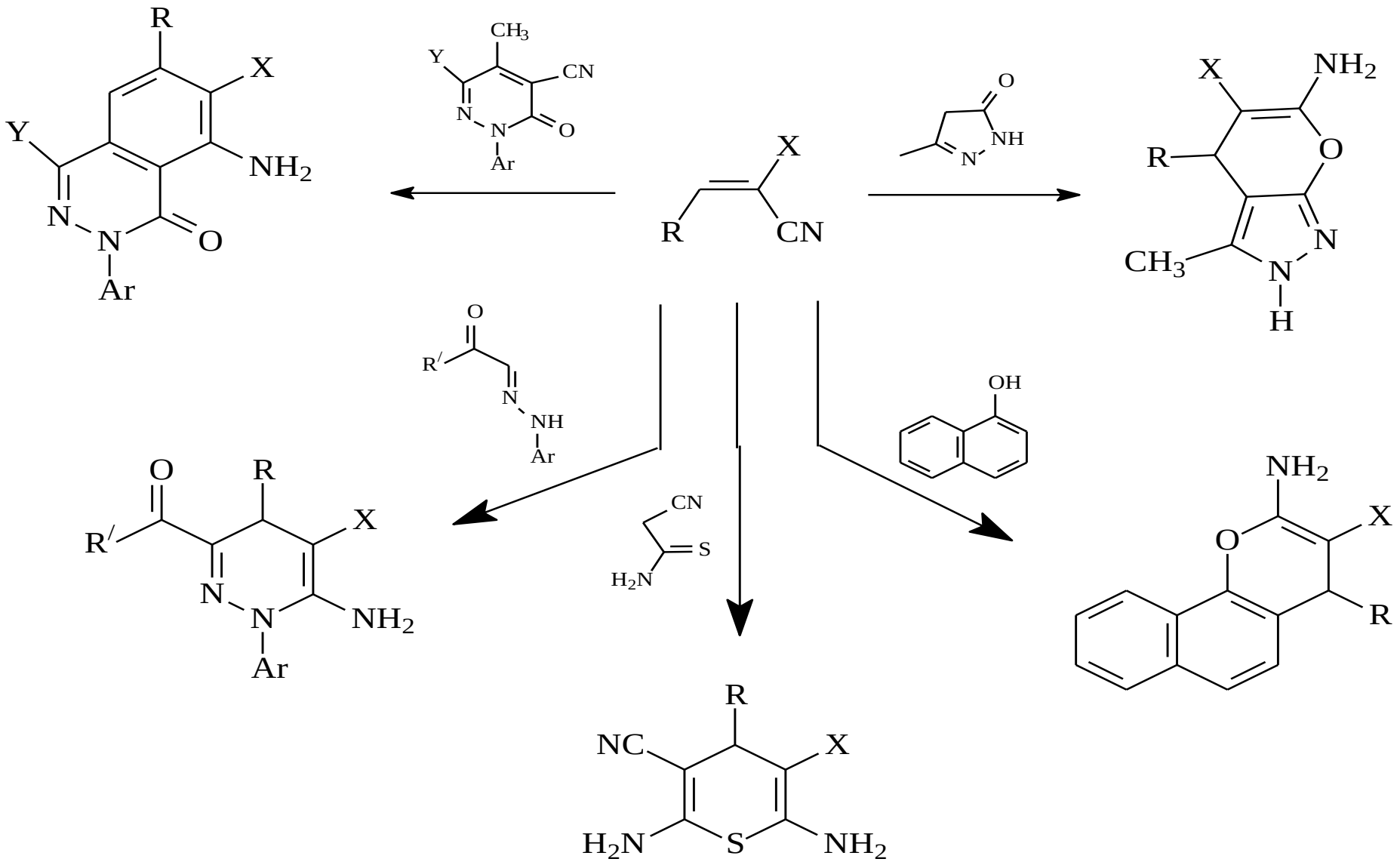
Safat; 13060: Kuwait, p.o. Box. 5969.

E-mail: sehelmy1941@yahoo.com

Abstract: Most significant results of my group work in the past fifty years in Kuwait; Egypt; Saudi Arabia and Syria will be presented. Emphasis will be placed on our work aimed at adopting unusual energy sources to initial our reactions including utility of microwaves, ultrasound and sunlight. Several tales for quite unexpected results well documented by X-ray and spectral data will be discussed. Mechanisms for the new rearrangements that led to unexpected product will be demonstrated.

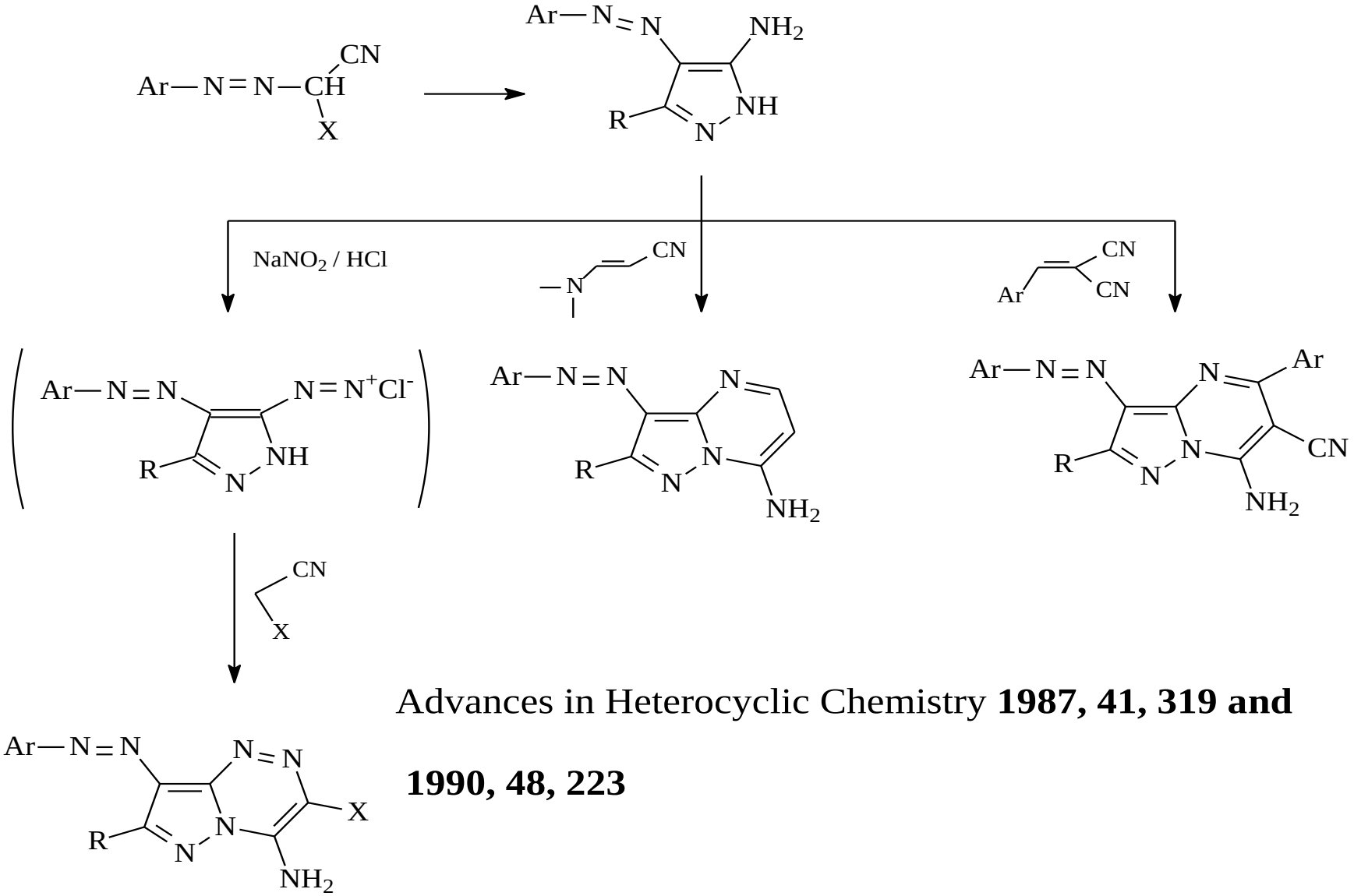
I started with organic synthesis on May 1962. It is thus almost fifty years in this area. Plenty could be produced and I am still keeping an average of 10 papers a year. The old work is now well cited perhaps because of patented diverse biological activities. Surely our most cited work of this period is

i) Addition of active methylenes to α,β-unsaturated nitriles demonstrated in scheme below.



For a review see: Review in preparation

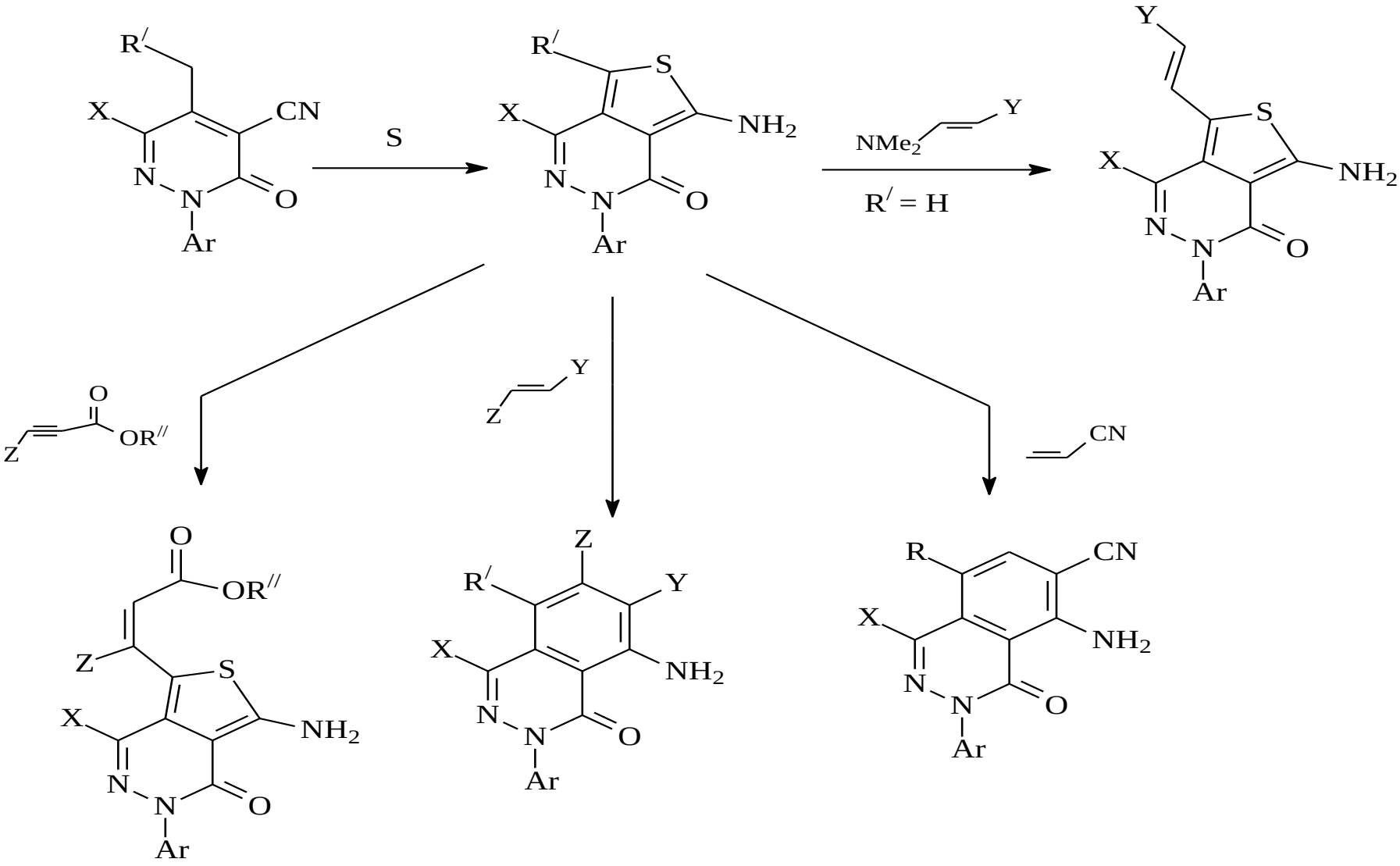
ii) Synthesis and chemistry of aminoazoles : Formation of azoloazines



Advances in Heterocyclic Chemistry **1987, 41, 319 and**

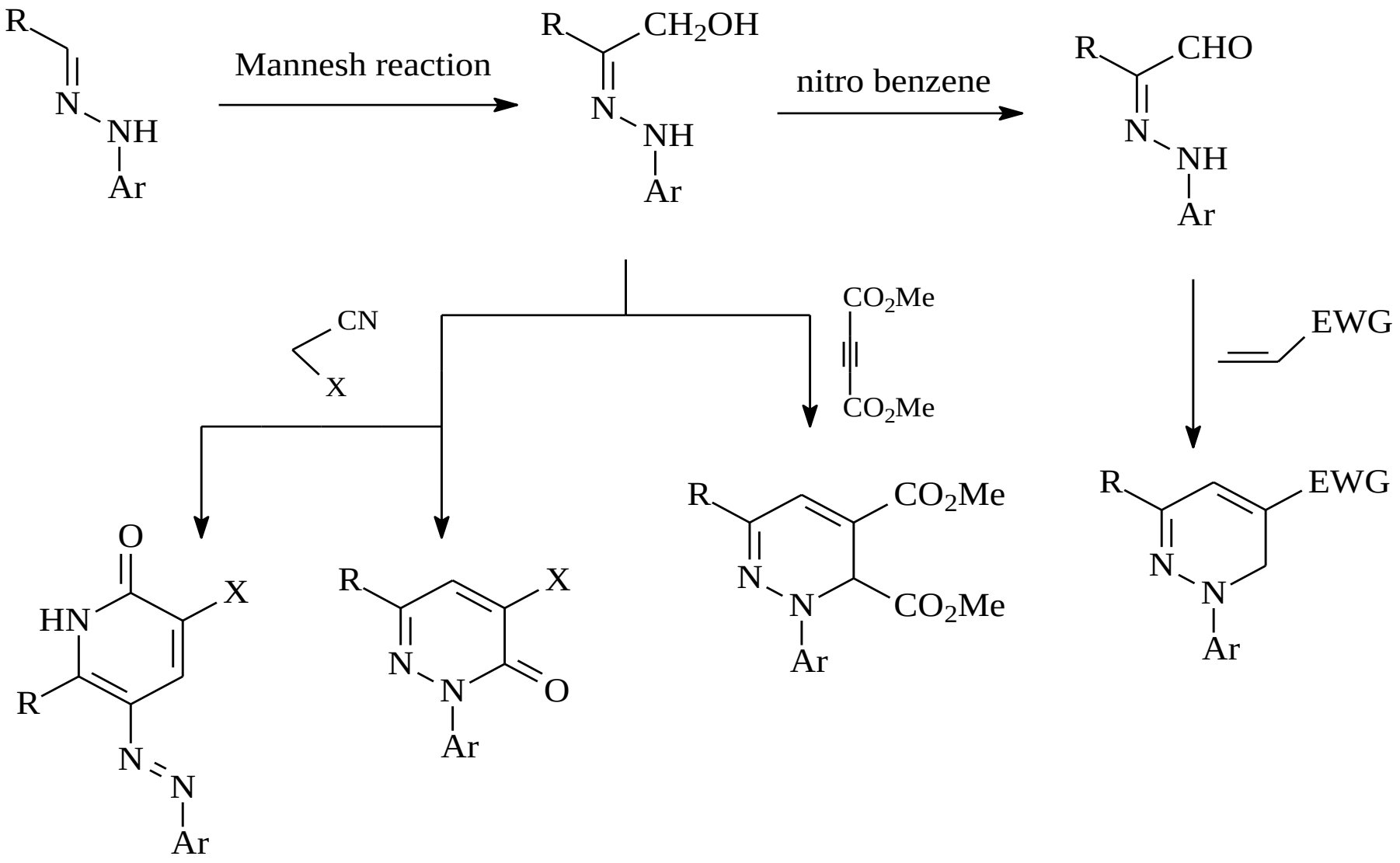
1990, 48, 223

iii) Cyclo addition with Thienoazines



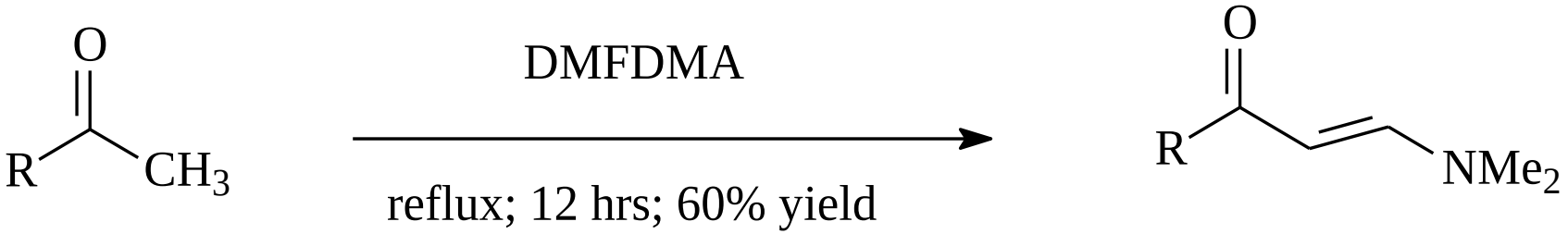
For review see Advances in Heterocyclic Chemistry **1997, 68, 181**

iv) Synthesis of pyridazines.



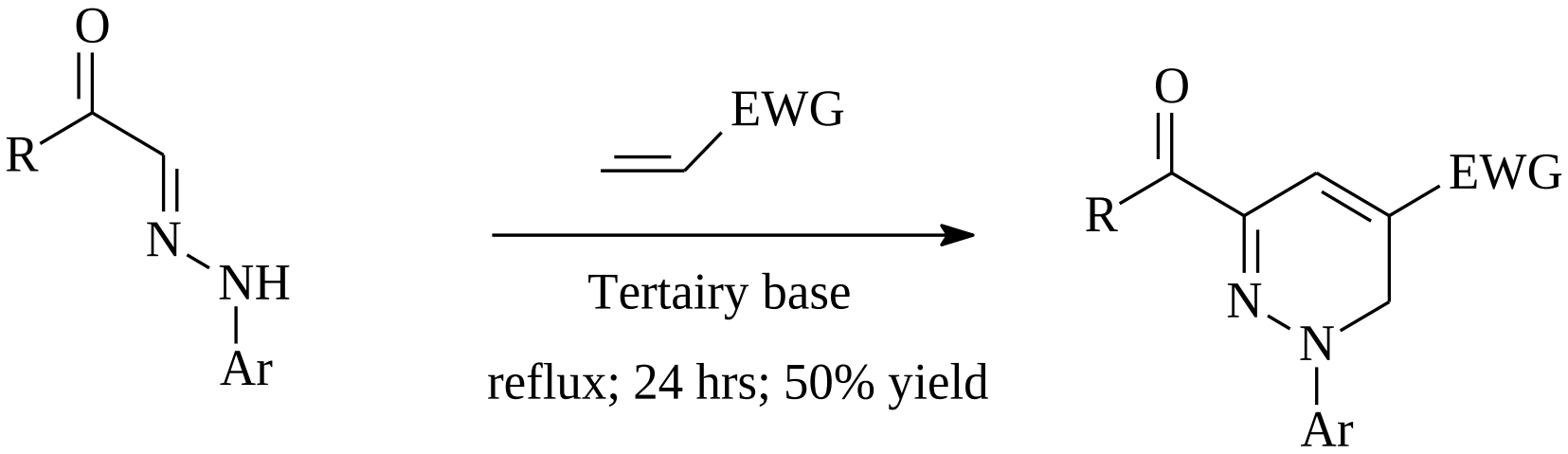
For review see Current Organic Chemistry **2011, 15, 3503**

- Since 2003 we shifted to green chemistry perhaps to clean plenty of Hazard we produced the since 1962; although we have been used to work as clean as possible as can bee realized from the fact that I am still okay at age of 70.
- Our first project was to adopt microwaves as energy source for reactions. We could produce about 20 papers in this area and could realized that microwave heating permit faster and cleaner reactions. Examples for most important contributions are shown.



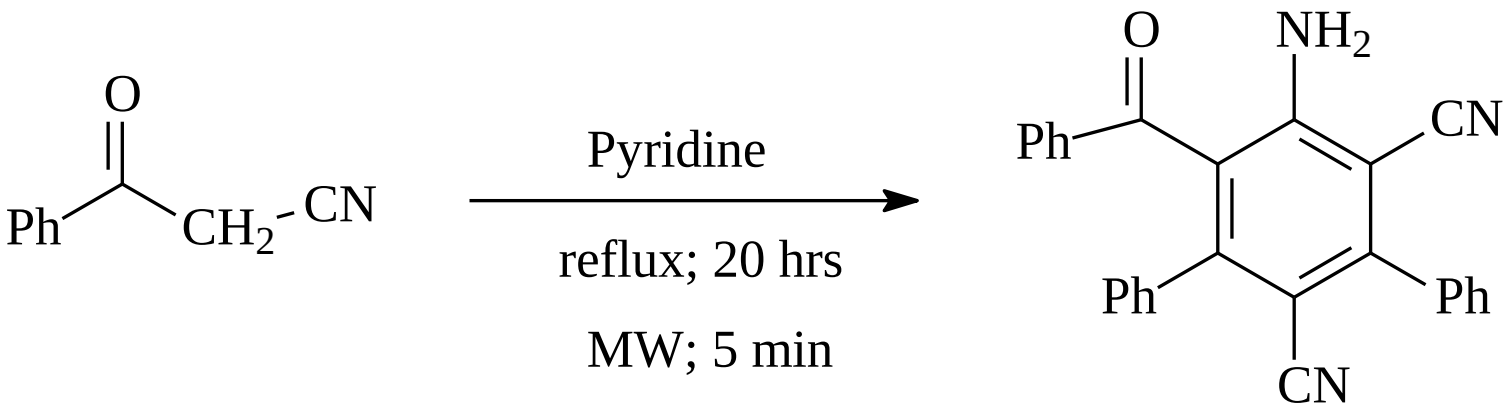
MW; 15 min ; more than 85 % yield

Elnagdi *et al* Molecules, **2010, 15, 58**

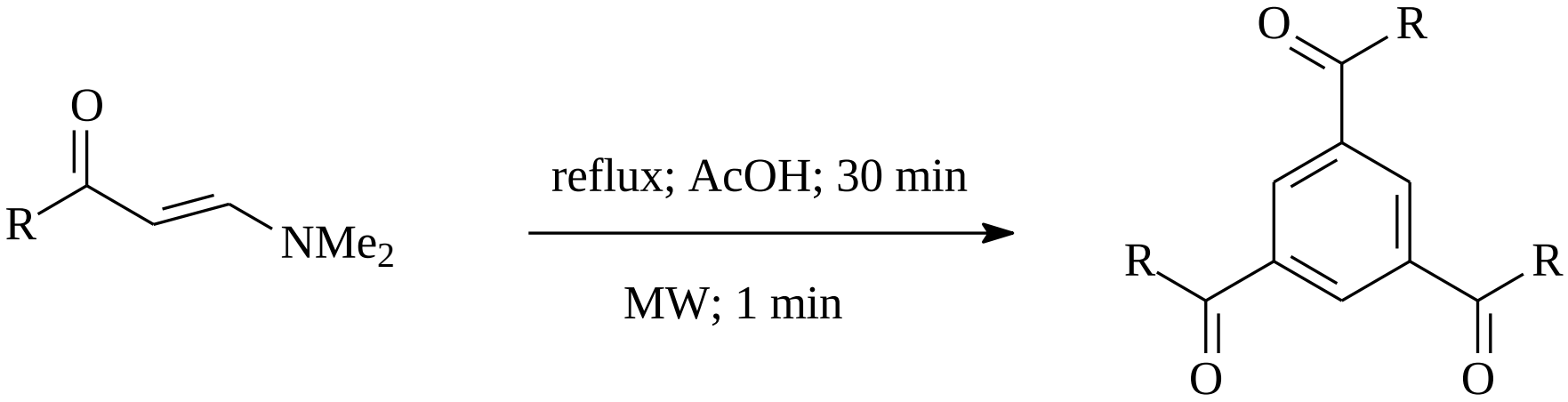


MW; 5 hrs ; more than 62 % yield

Elnagdi *et al* Tetrahedron, **2008, 64(35), 8202**



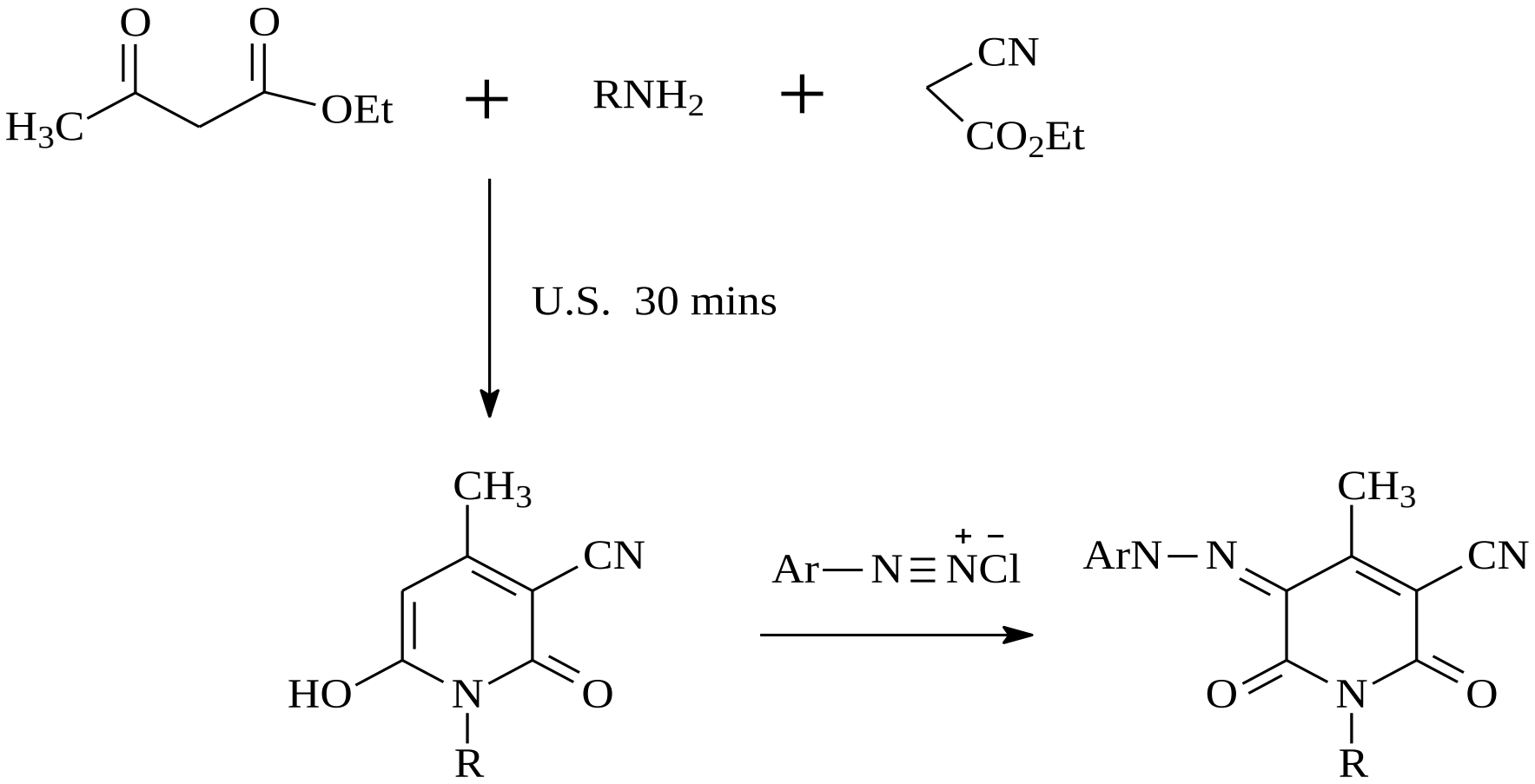
Elnagdi *et al* Synlett, **2007, (19), 2979**



Elnagdi *et al* Synthetic Communications,**2002, 32(22), 3493**

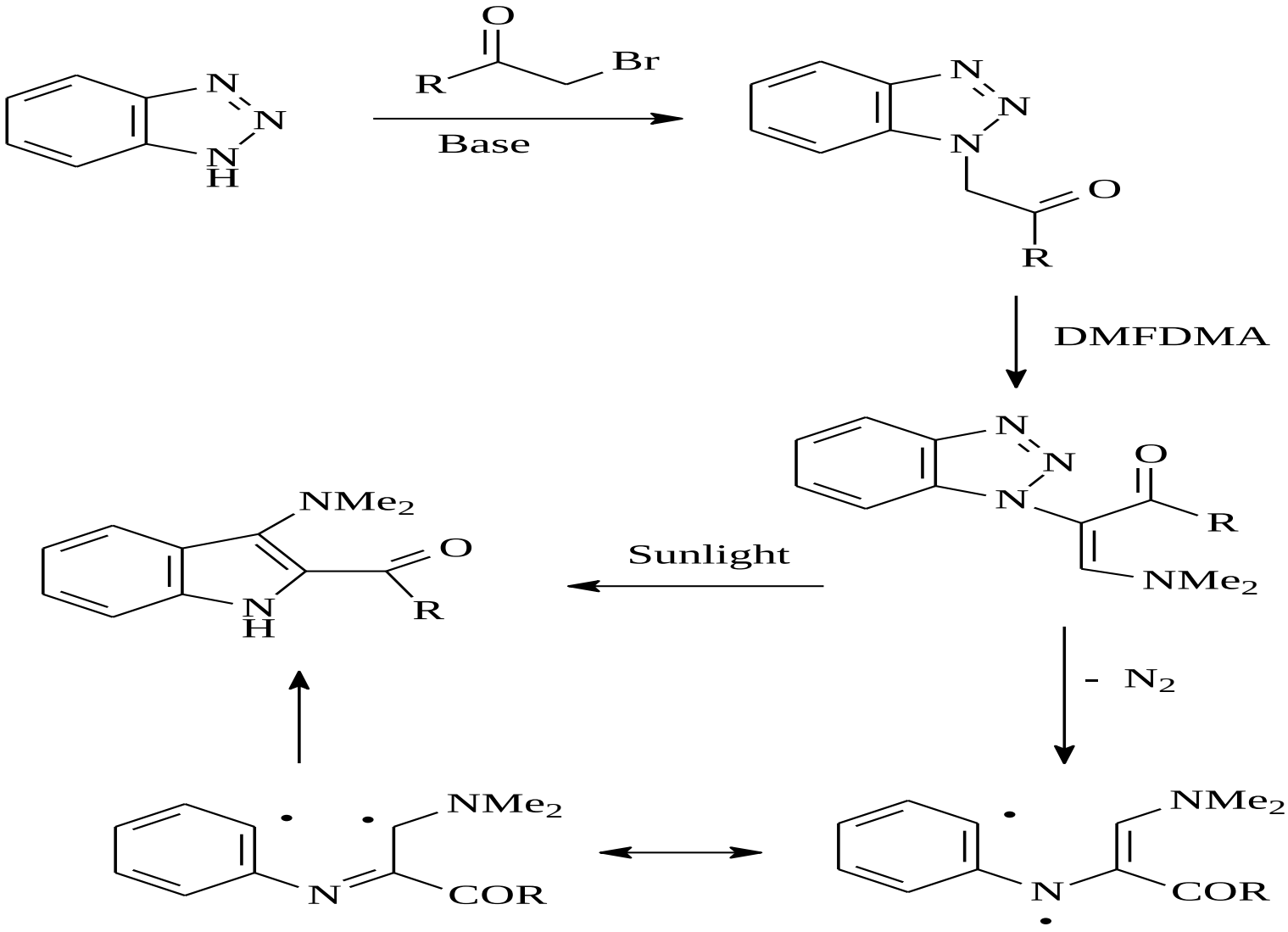
Elnagdi *et al* J.H.C, **2002, 39(5),1035**

- We turned then our attention to utility of ultrasound at ambient temperature were able to synthesis arylazo pyridines.



Elnagdi *et al* Ultrasonics Sonochemistry, **2010, 17(5), 909**

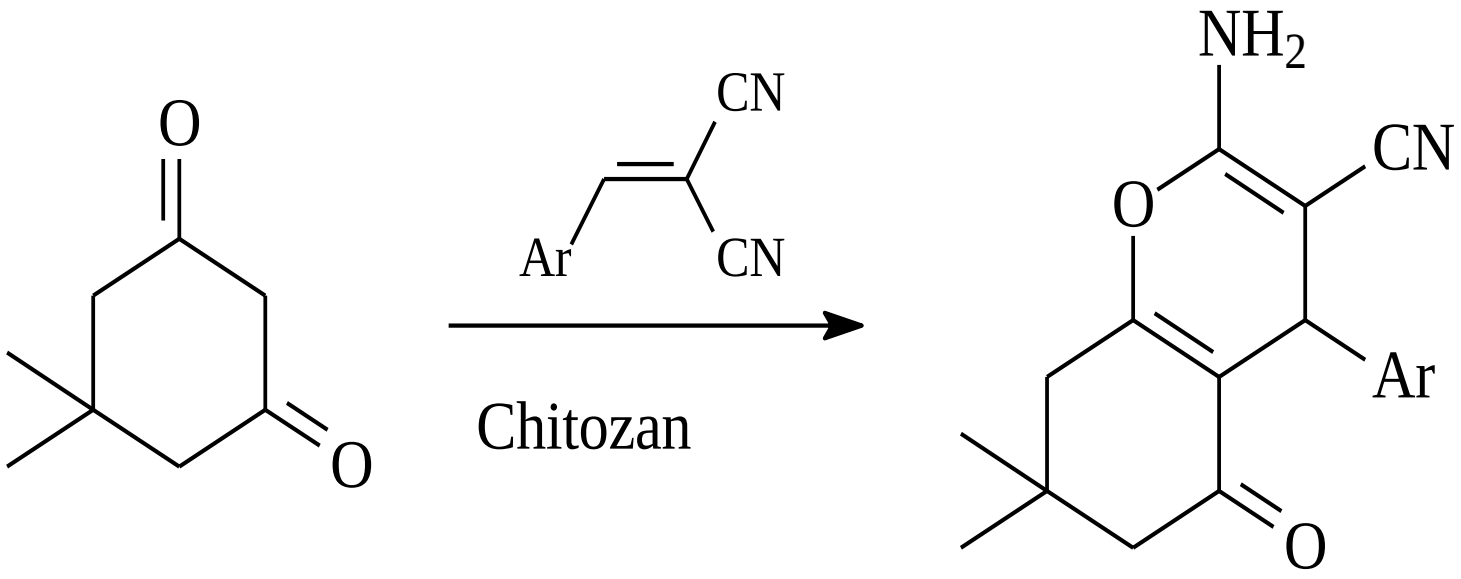
- Now we are looking for utility of sunlight both thermal and photochemical energy for producing polyfunctional heteroaromatics. One success recently reached is shown below.



Elnagdi *et al* Arkivoc, **2011, (x), 288**

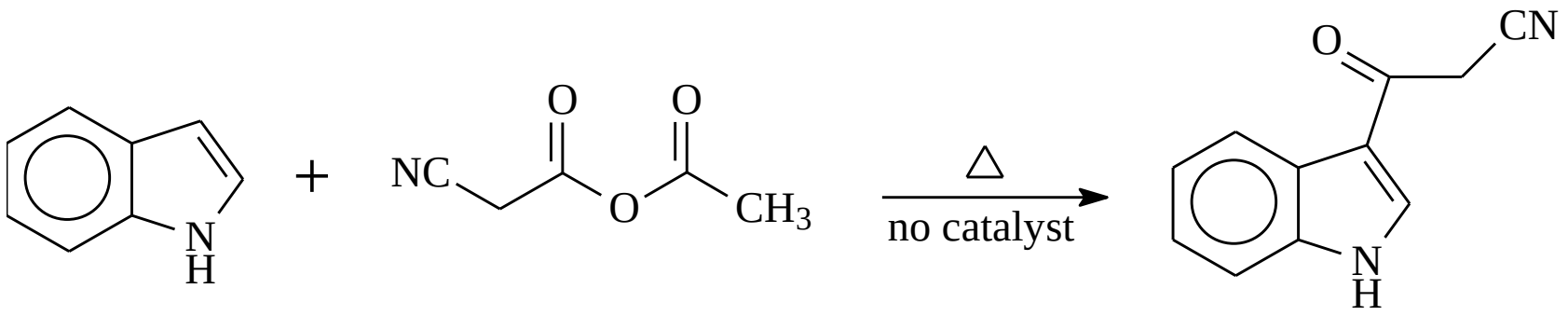
- We are now adopting sun thermal energy as energy source to activate Micheal additions.
- Replacing homogeneous catalysis by heterogeneous ecofriendly catalysts is of great Green value. In this respect we could show that chitozan, that can be readily obtained from chetin; a nature biopolymer can be used to replace piperidine and or pyridine in Micheal additions.

- We reported earlier yields were found to be the almost the same and more than those obtained by nanoparticulated MgO that has been recently suggested an example to compare.

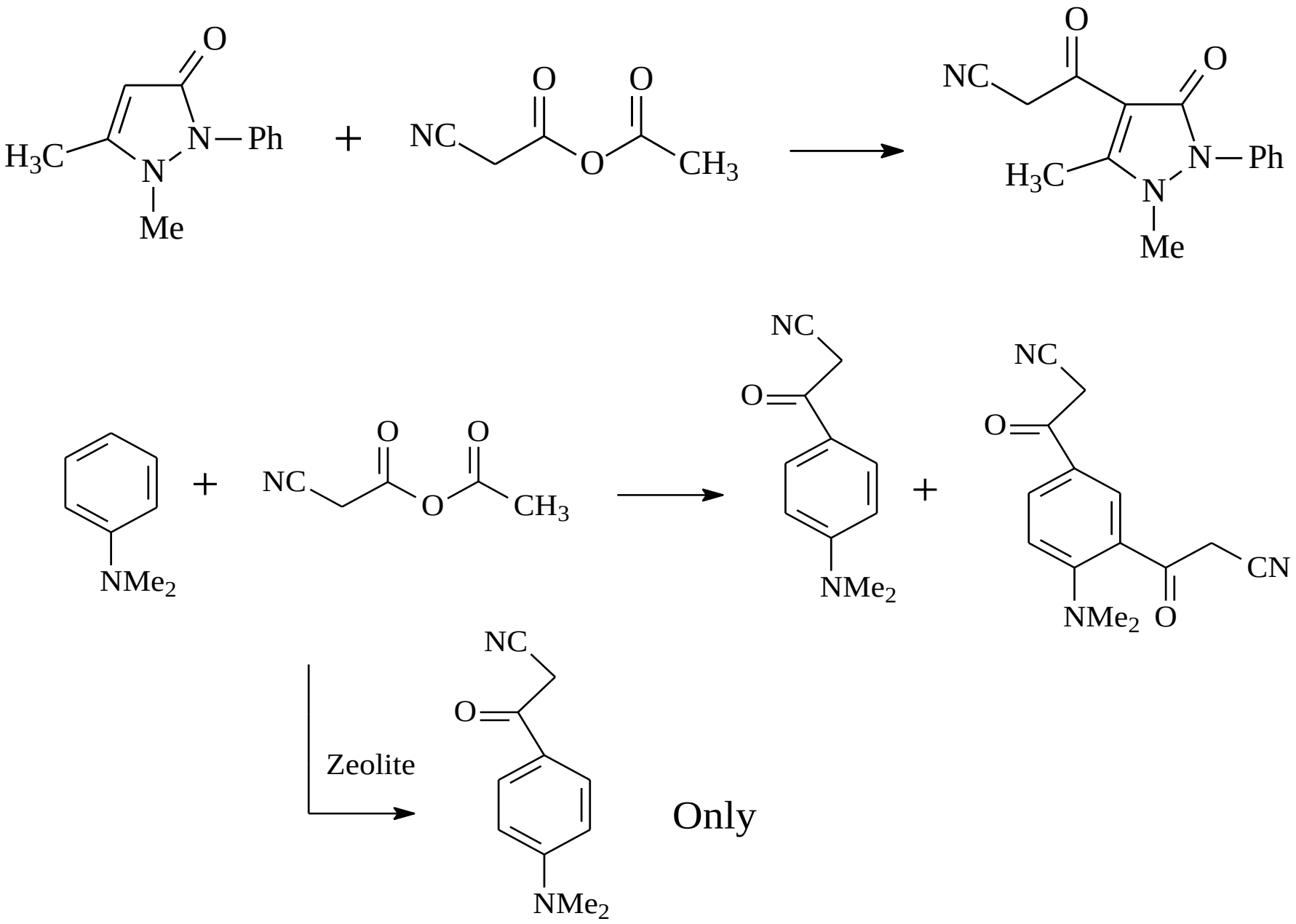


Elnagdi *et al* Arkivoc, **2008**, **(16)**, **288**

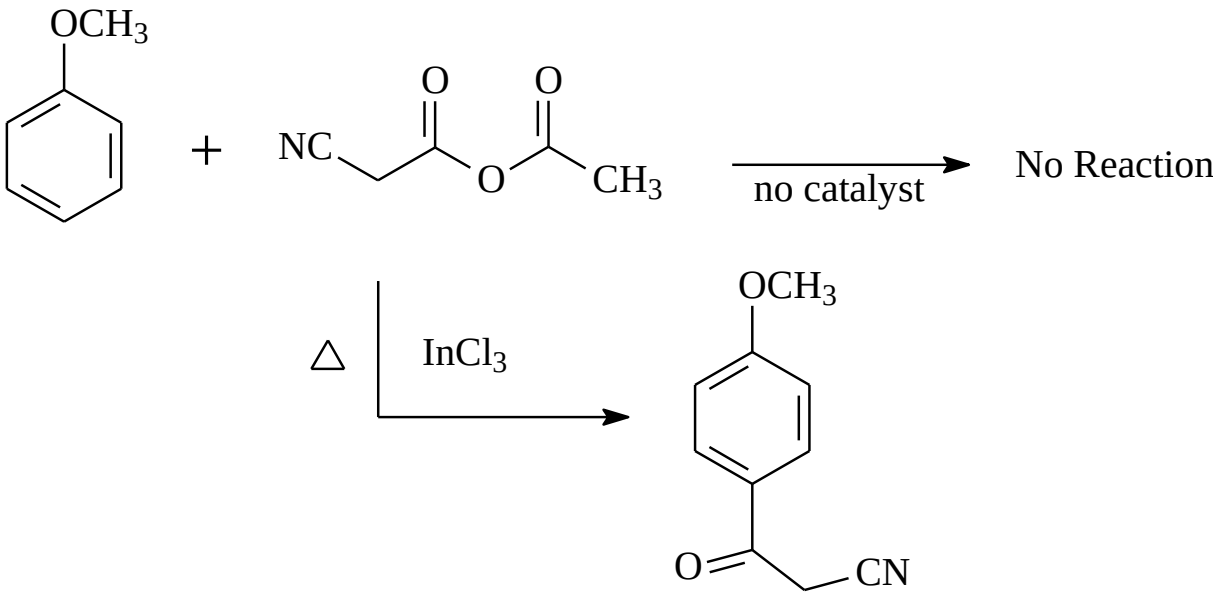
- We have also looked at utility of $InCl_3$ as water tolerant lewis acid catalyst to replace hazardous $AlCl_3$ in Friedel Craft's cyanoacetylation of electron rich aromatics



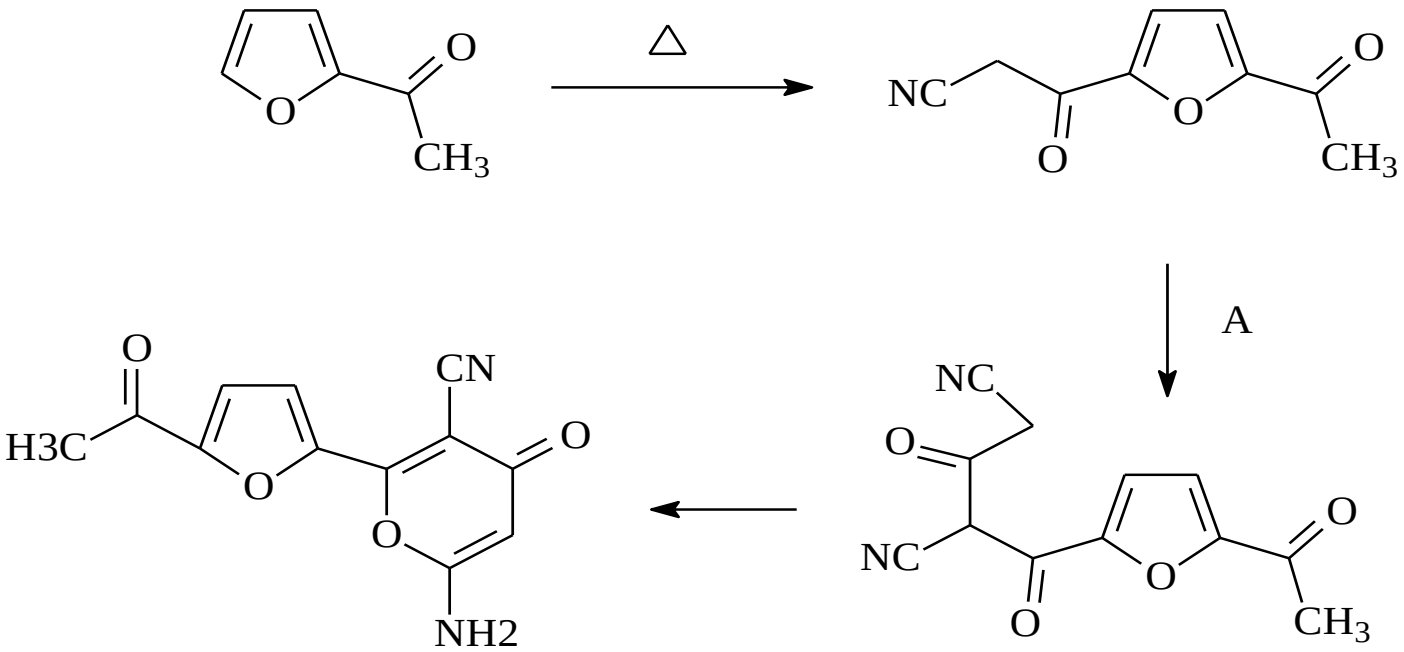
Elnagdi *et al* Heterocycles **(2007), 71(9), 1951**



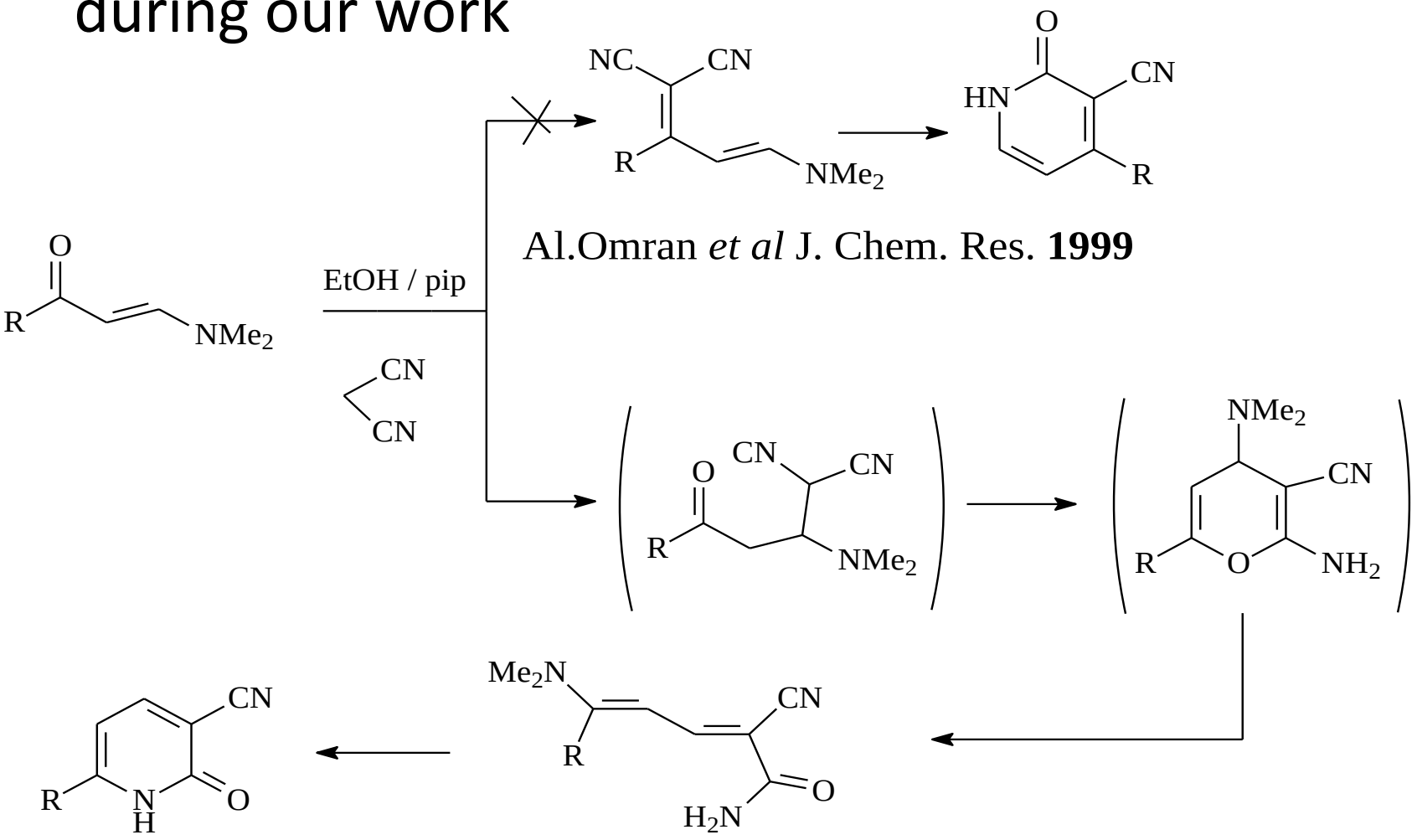
Elnagdi *et al* Submitted for publication



Elnagdi *et al* Tetrahedron **(2009), 65(45), 9421**

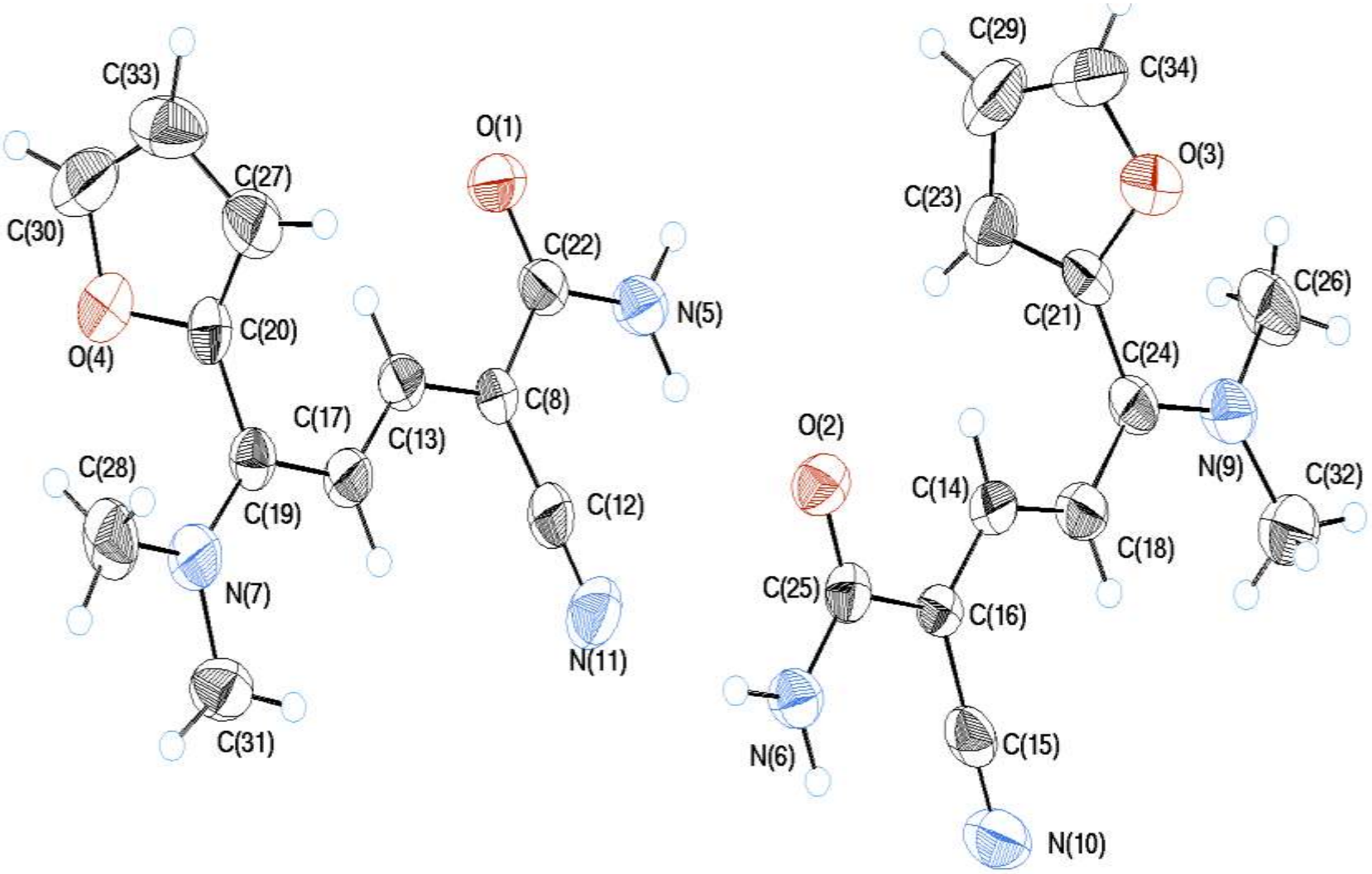


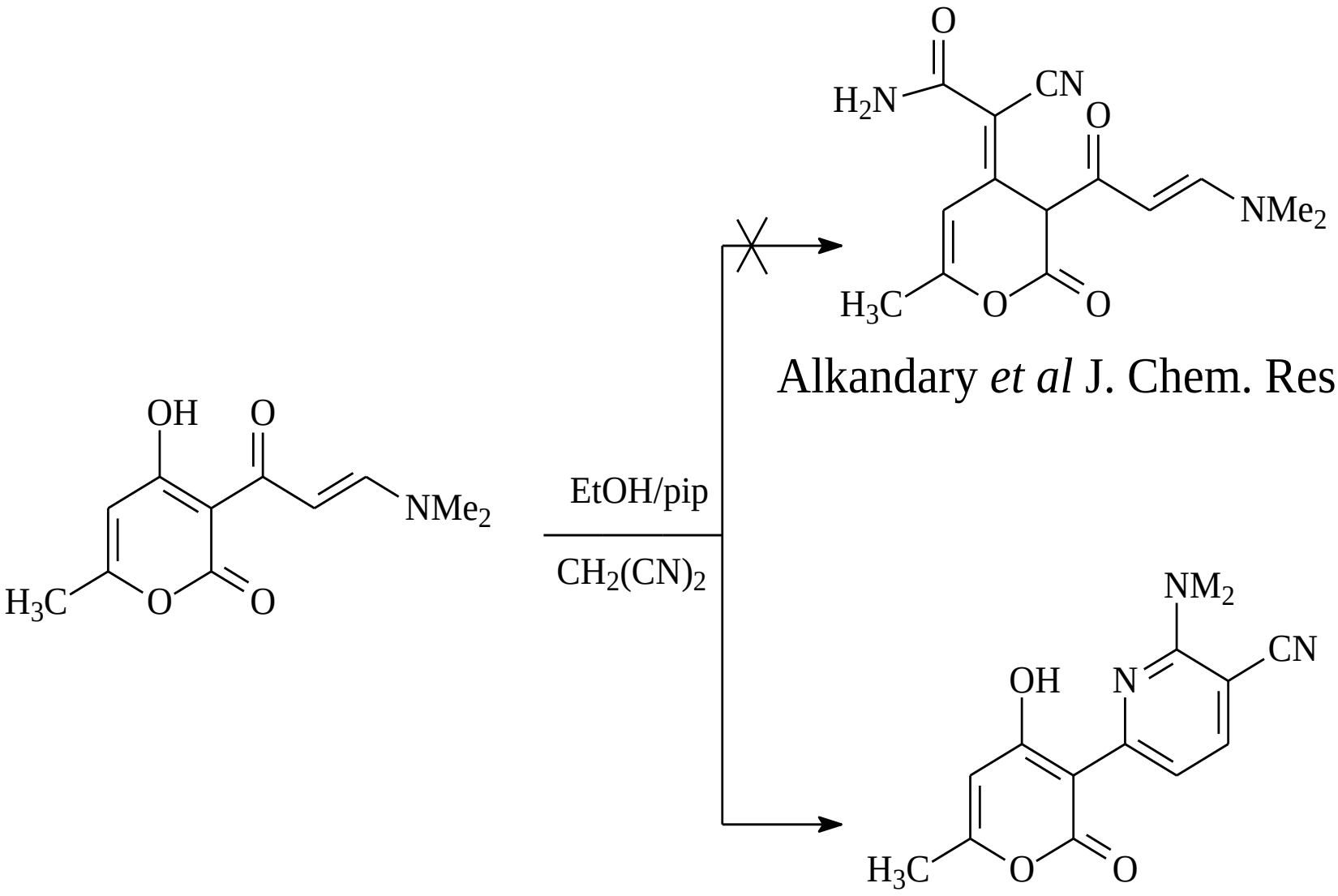
- Now I will tell several unexpected tales we noted during our work



Elnagdi *et al* Arkivoc **2009, 11, 1**

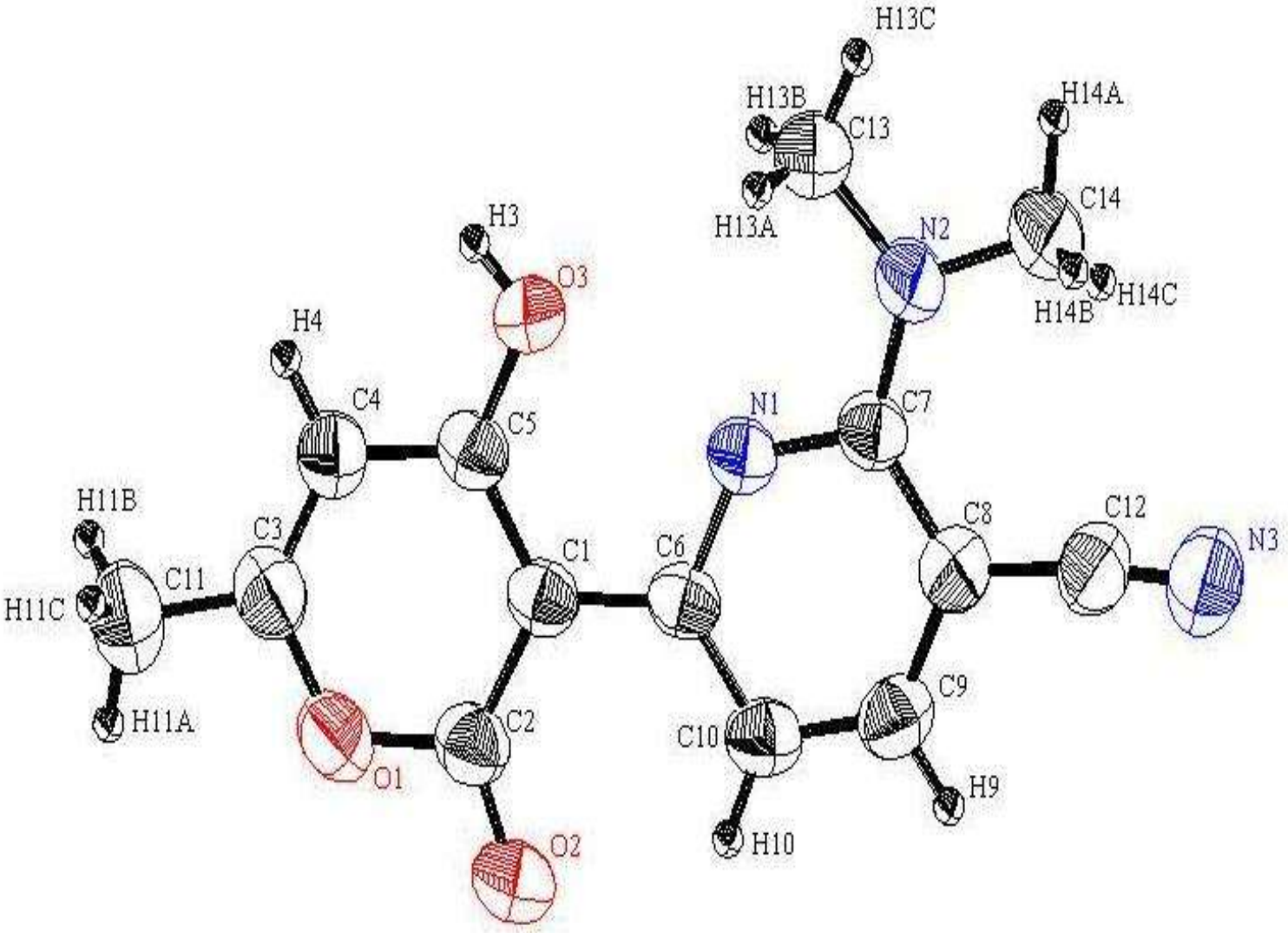
Elnagdi *et al* Molecules **2009, 14, 68**

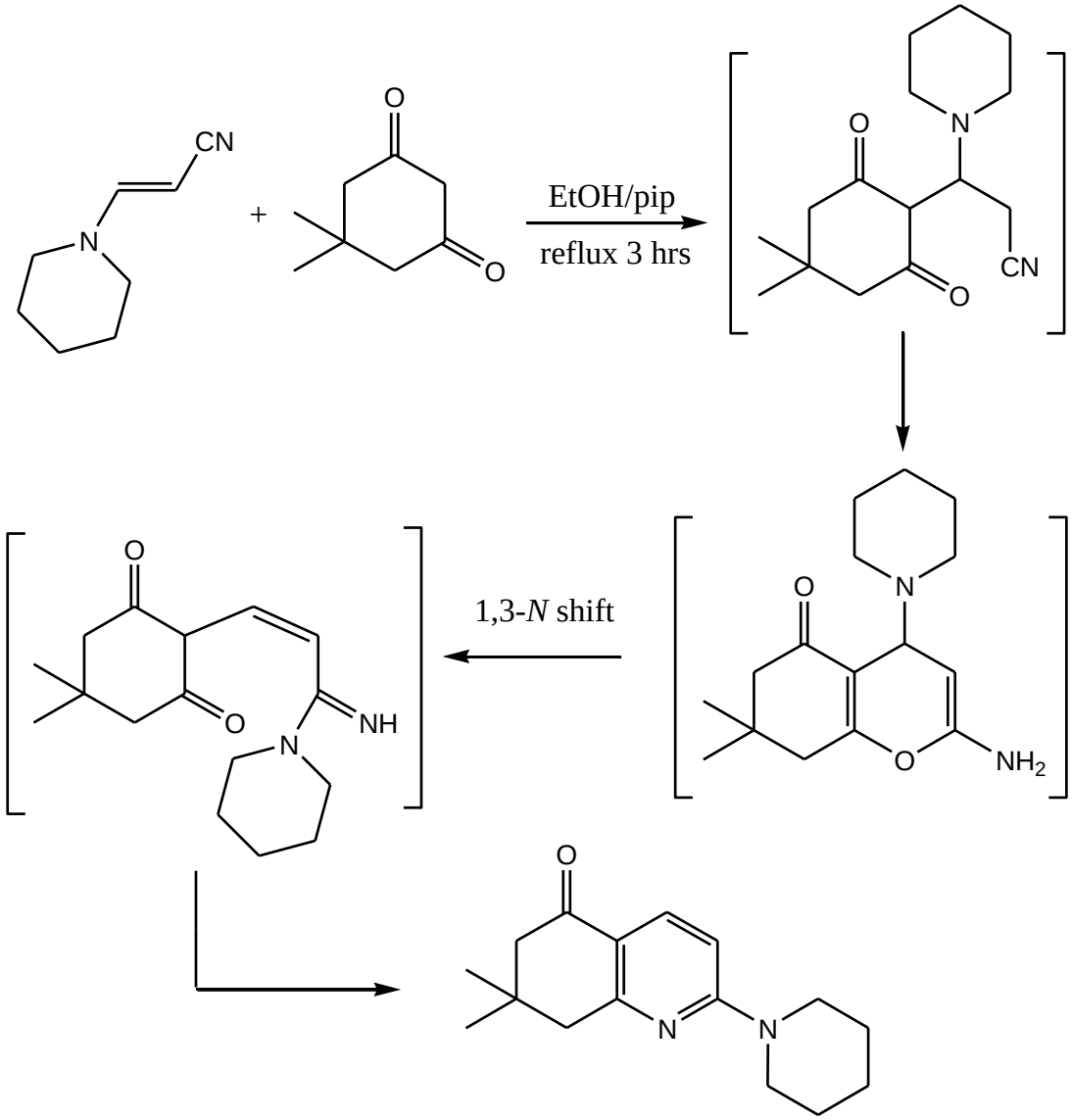

C(33)
C(27)
C(30)
O(4)
C(20)
C(28)
C(19)
N(7)
C(31)
C(17)
C(13)
O(1)
C(22)
N(5)
C(8)
C(12)
N(11)
C(29)
C(34)
O(3)
C(23)
C(21)
C(26)
C(24)
N(9)
C(32)
O(2)
C(14)
C(18)
C(25)
C(16)
N(6)
C(15)
N(10)



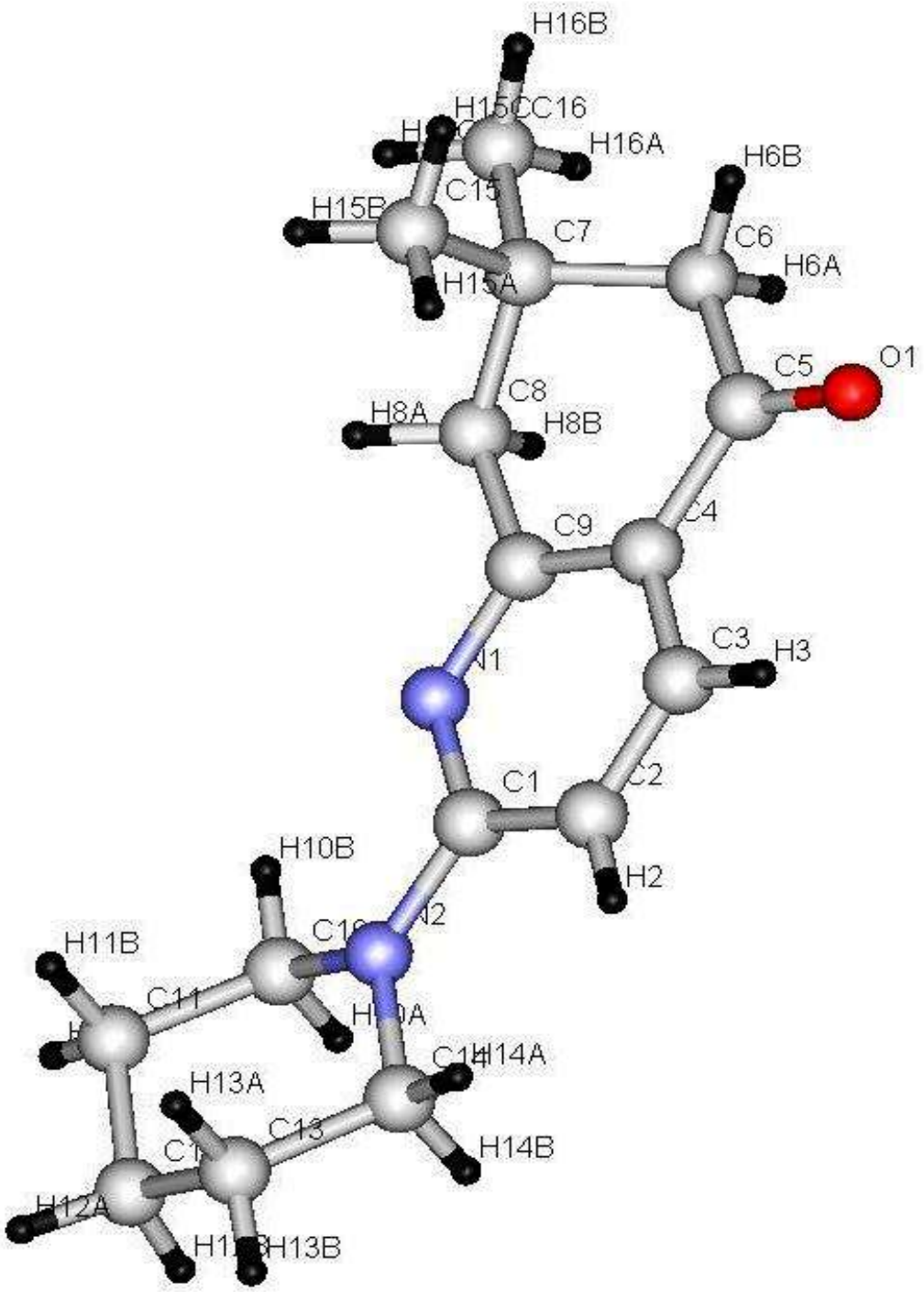
Alkandary *et al* J. Chem. Res. 2000

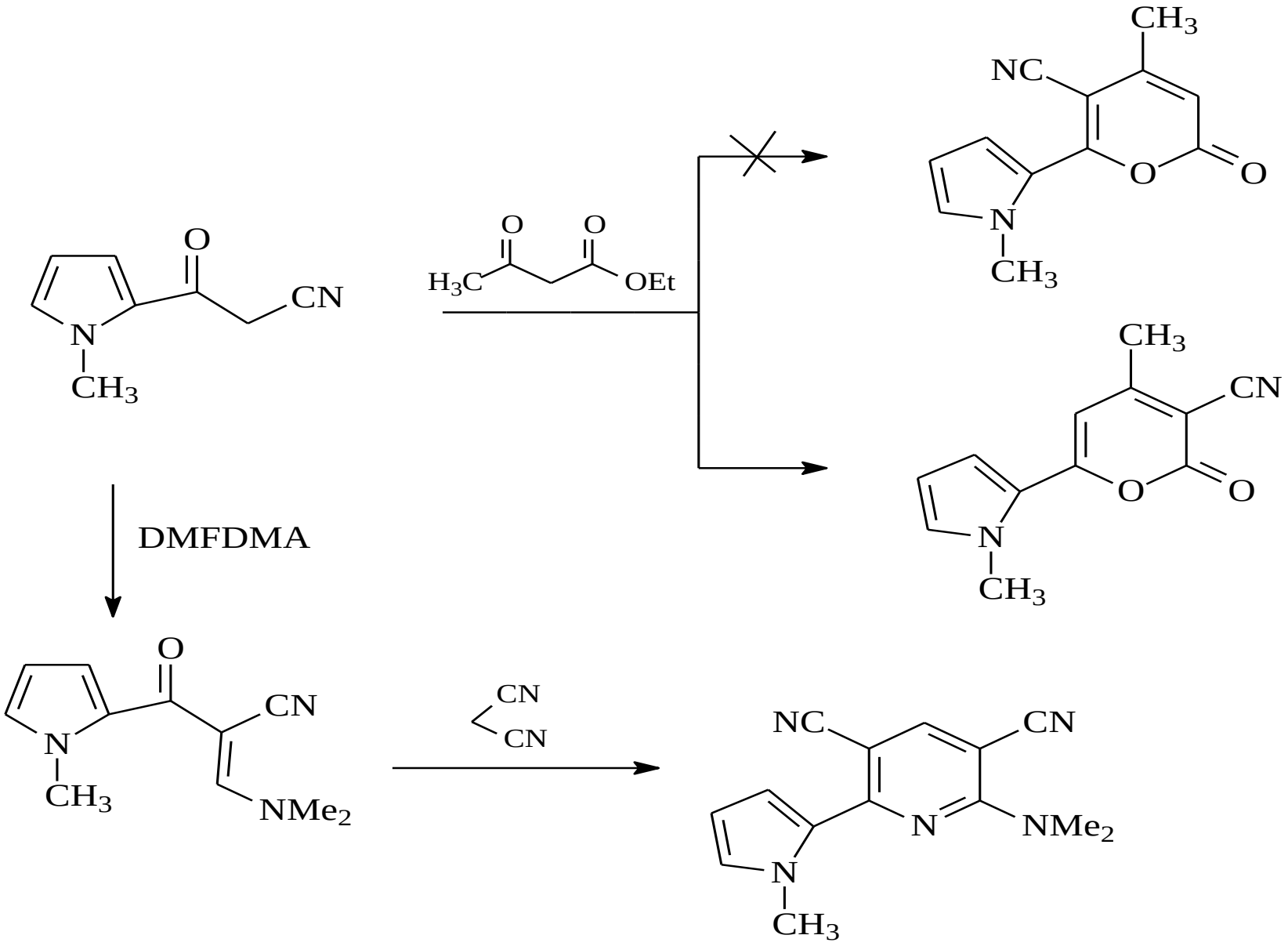
Synlett **2011, 15, 2237**


H13C
H13B
C13
H14A
H13A
N2
C14
H3
O3
H14B
H14C
H4
C4
C5
N1
C7
H11B
C3
C1
C6
C8
C12
N3
C11
H11C
C9
H11A
C2
C10
O1
H9
O2
H10



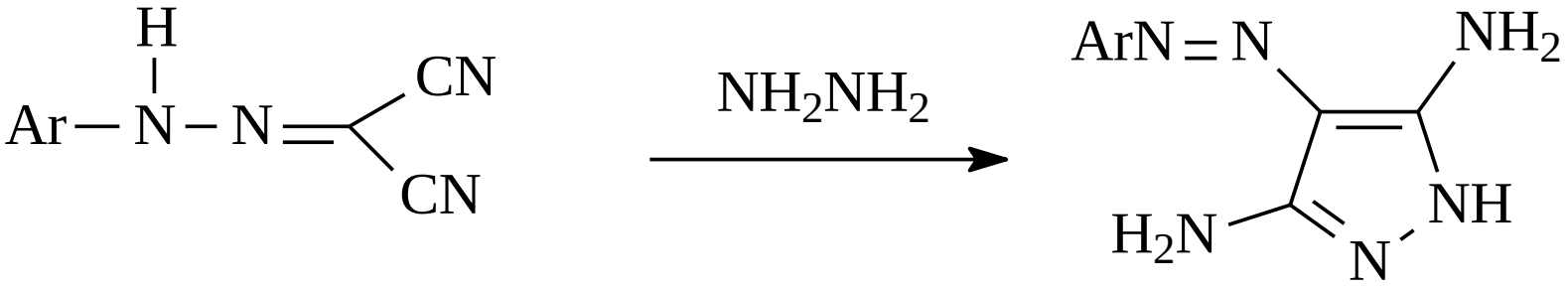
Synlett 2011, 15, 2237


H16B
H15C
C16
H16A
H6B
C15
H15B
C7
C6
H6A
H15A
C5
O1
C8
H8A
H8B
C9
C4
C3
H3
C1
C2
H10B
H2
H11B
C11
H14A
H13A
C13
H14B
H12A
H13B



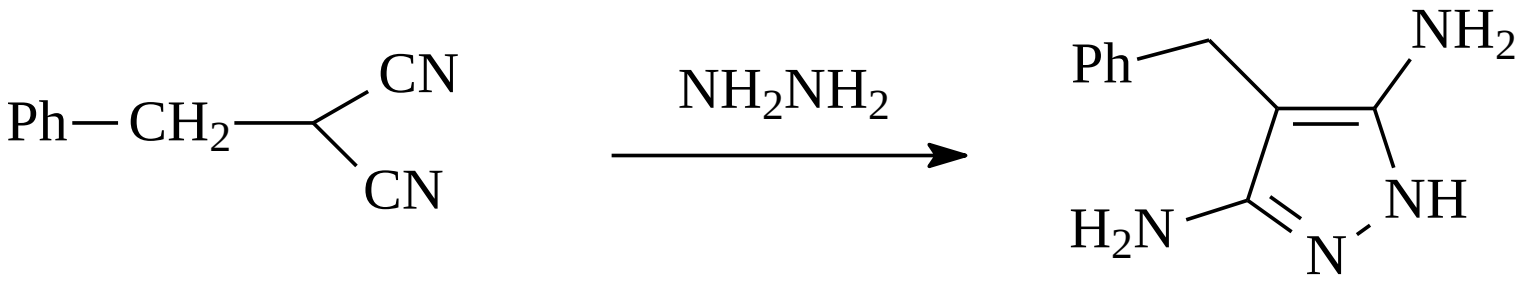
Arkivoc in press

- I have mentioned earlier plenty of our compounds have found their way to patent literature. Trials to coordinate with some cosmetic company on diaminopyrazoles for utility in hair dye formulations led us to discover that plenty of old reports in this area are in fact incorrect.



Elnagdi *et al*, J. Prakt. Chem. **1973, 317, 1009**

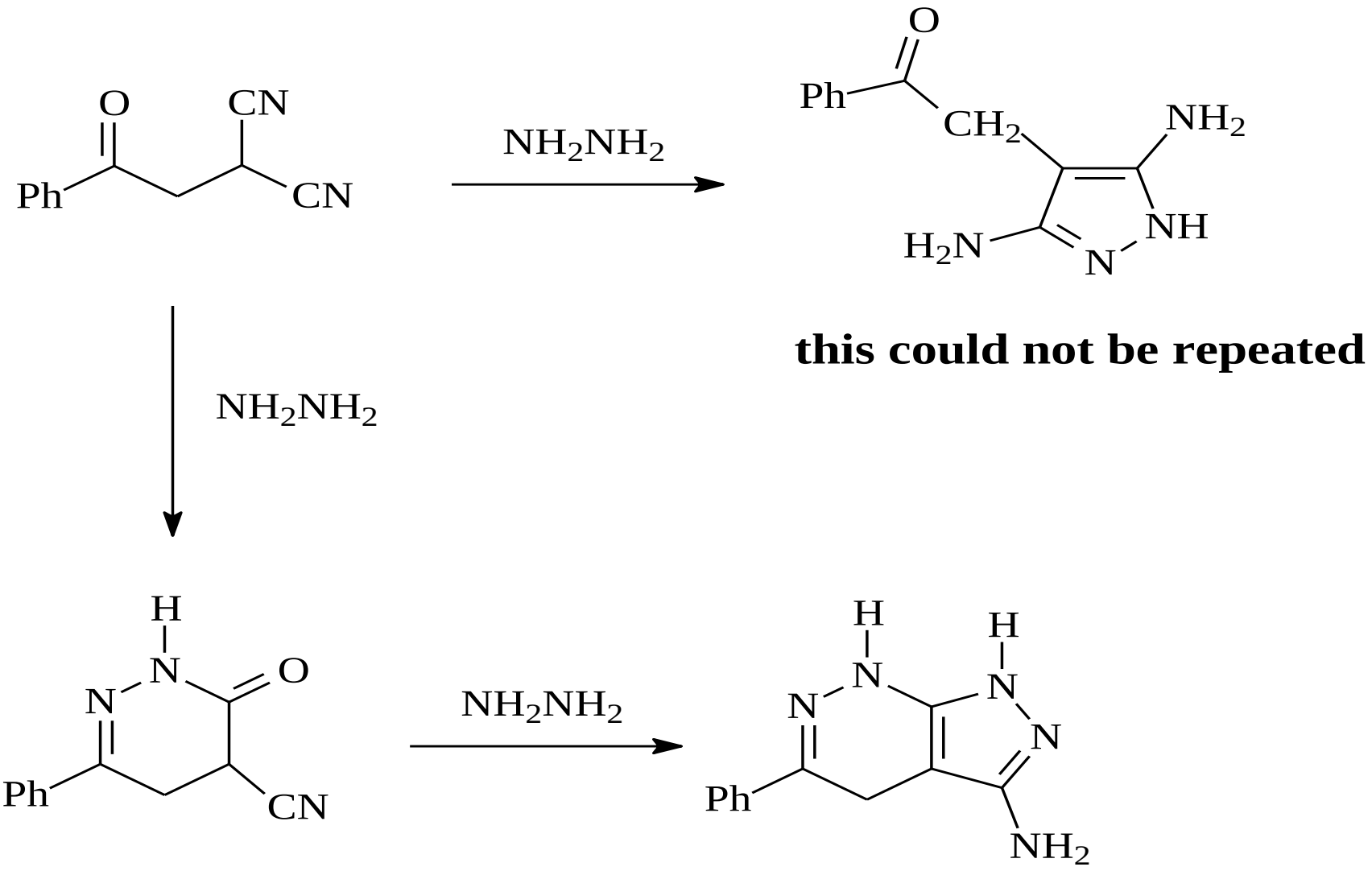
- Elguero reported also formation of other diaminopyrazoles



Elnagdi *et al* Heterocycles **(2008), 75(6), 1371**

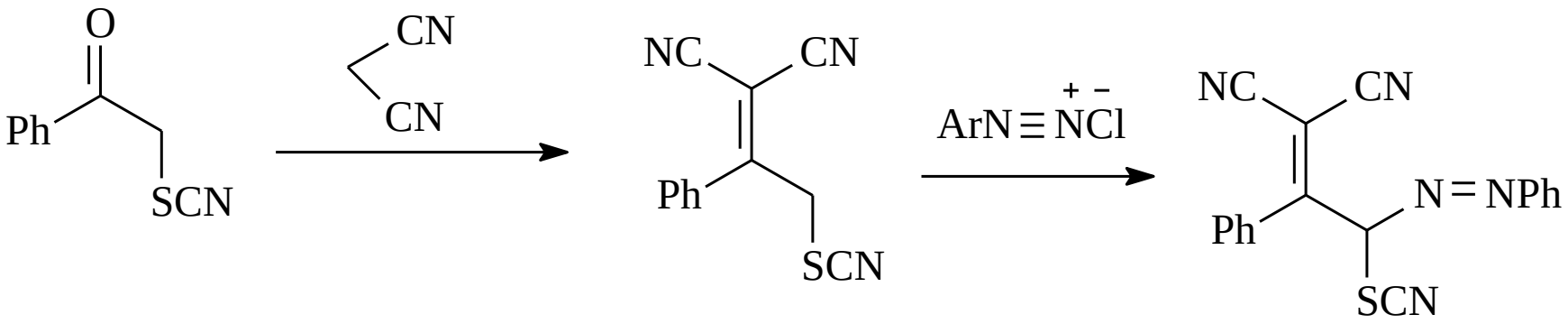
We checked this reported and is correct one

- Then we looked into Egyptian reported that



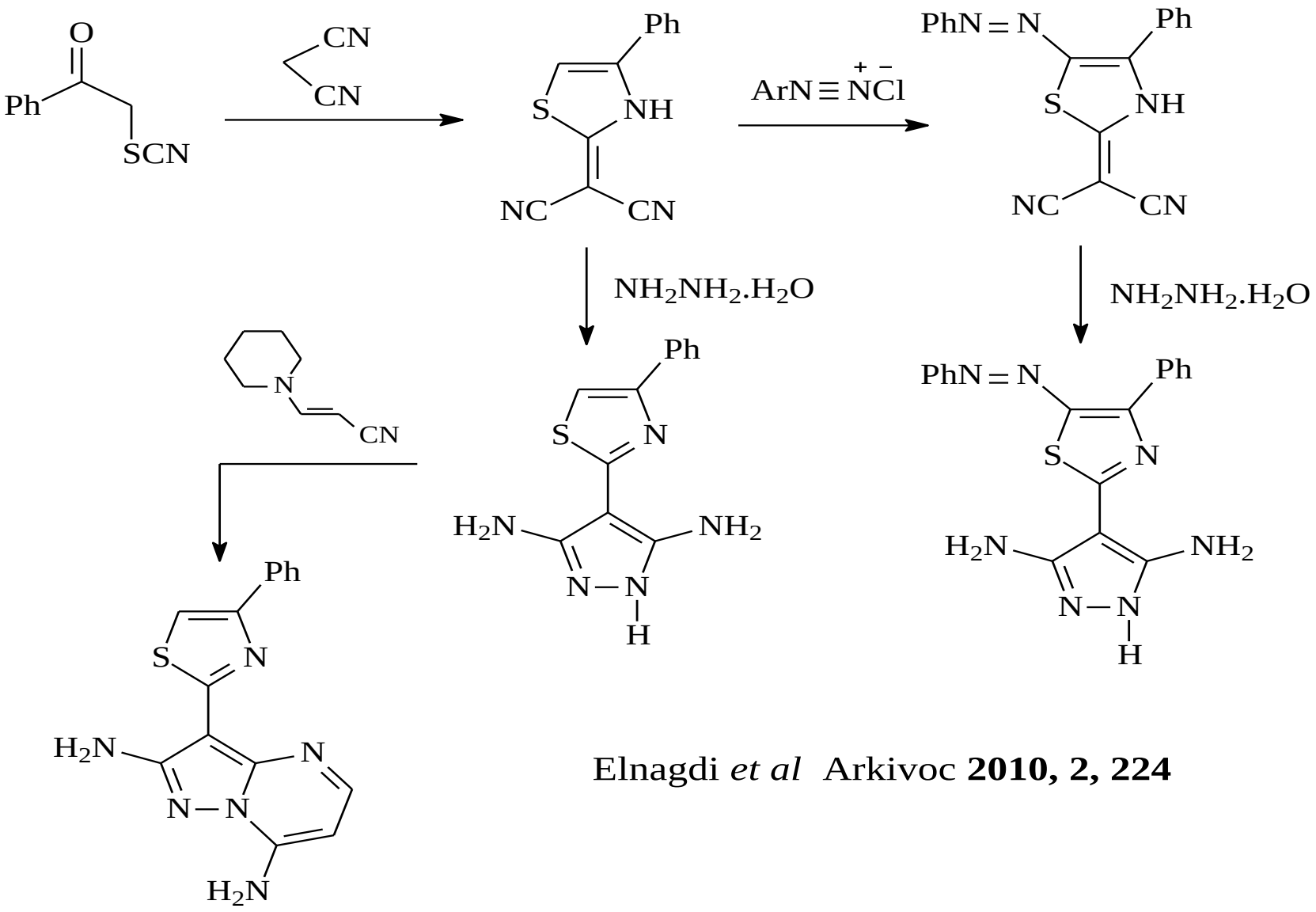
Elnagdi *et al* Molecules **2009, 14, 798**

- It was reported that



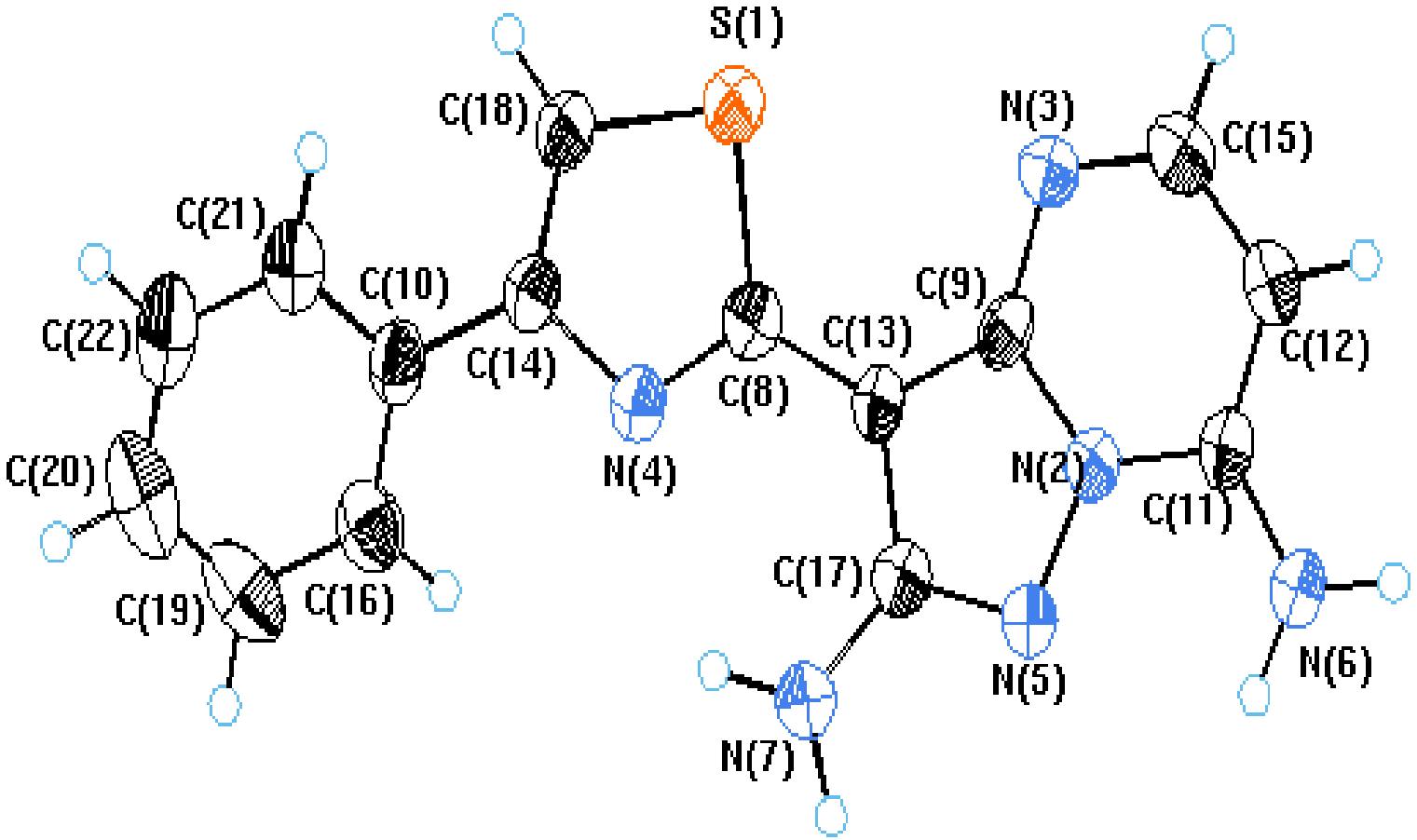
Abdelrazek *et al* Z. Naturforsch. B. **1986, 41b, 499**

In Fact

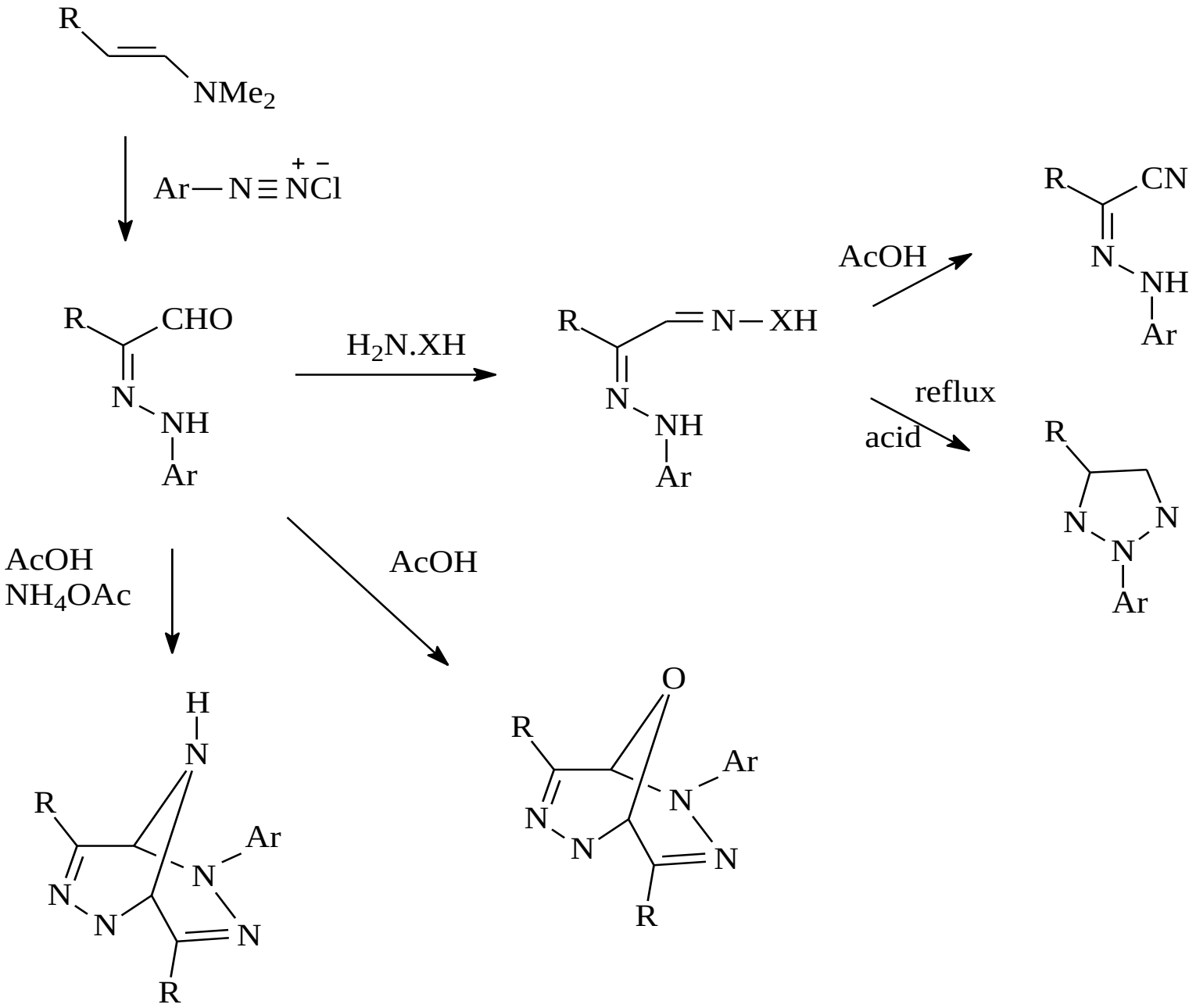


Elnagdi *et al* Arkivoc **2010, 2, 224**

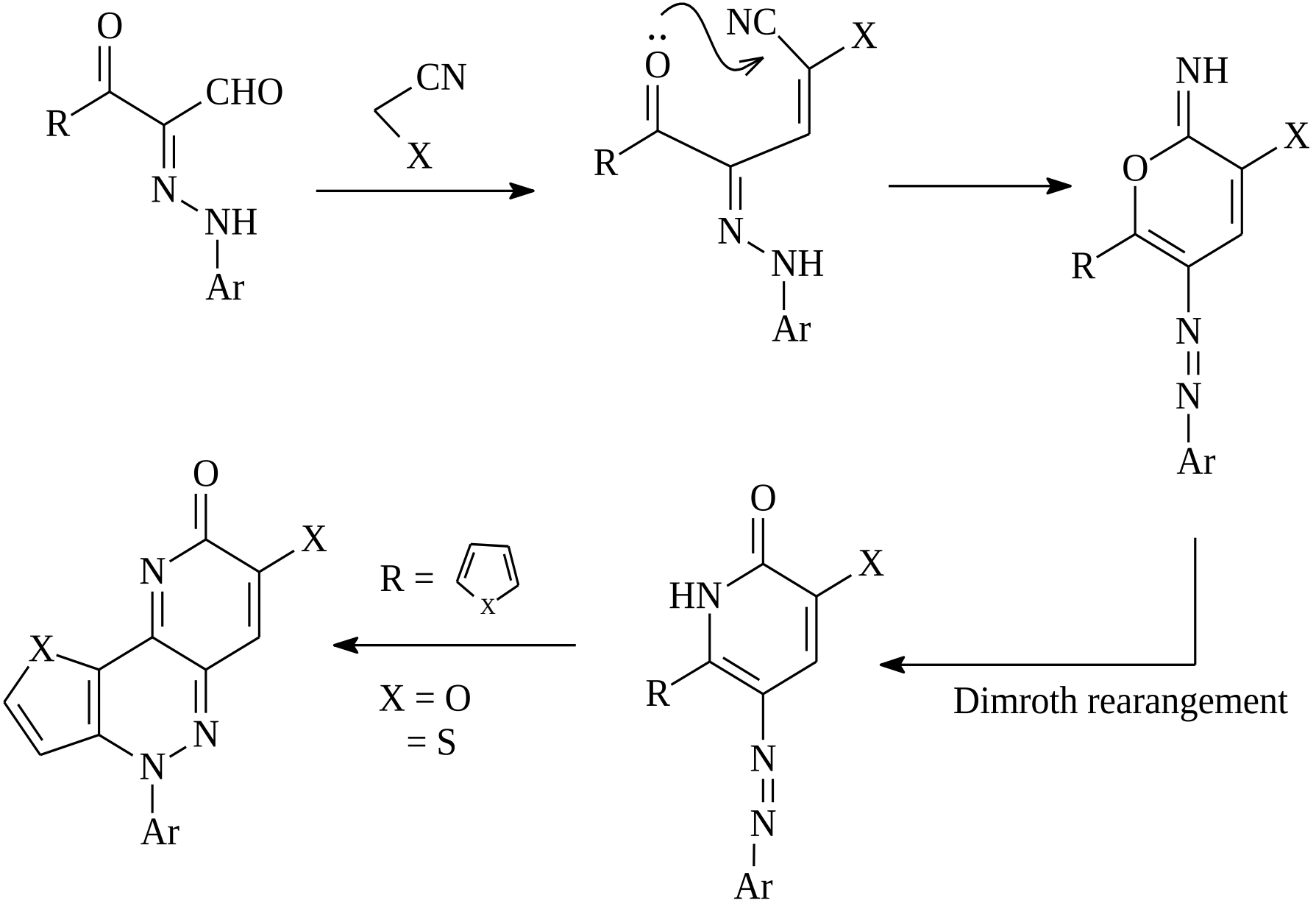
Structure elucidated by X-Ray


S(1)
C(18)
N(3)
C(15)
C(21)
C(10)
C(9)
C(22)
C(14)
C(13)
C(12)
C(8)
C(20)
N(4)
N(2)
C(11)
C(17)
C(19)
C(16)
N(5)
N(6)
N(7)

- In 1997 we published synthesis of 2-arylhydrazonals in an expected reaction sequence and started exploring its synthetic potentials and through this activity we have observed several unexpected results that are summarized below.

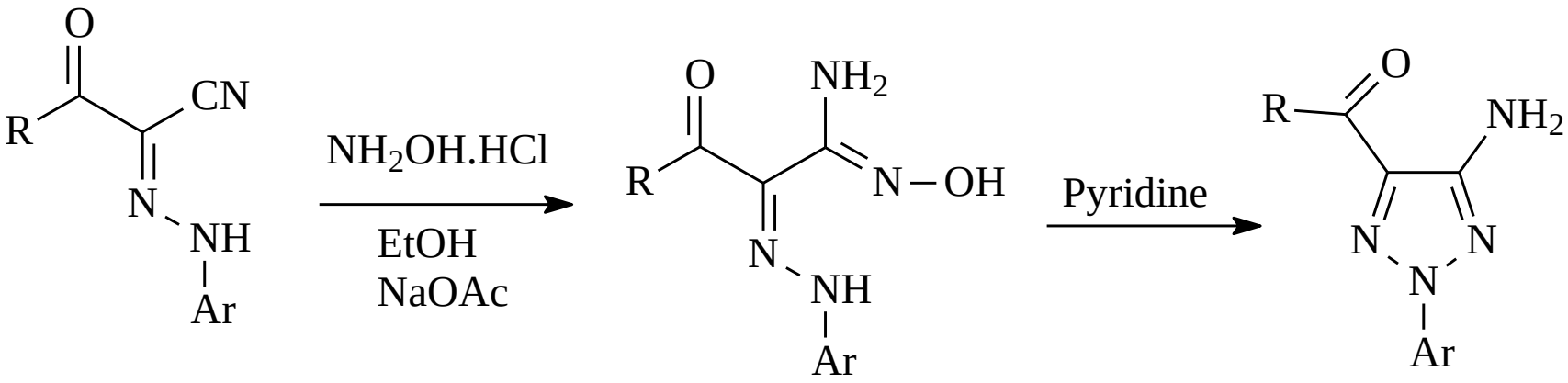


Elnagdi *et al* Z. Naturforsh, **(2000, 55(12), 1211**

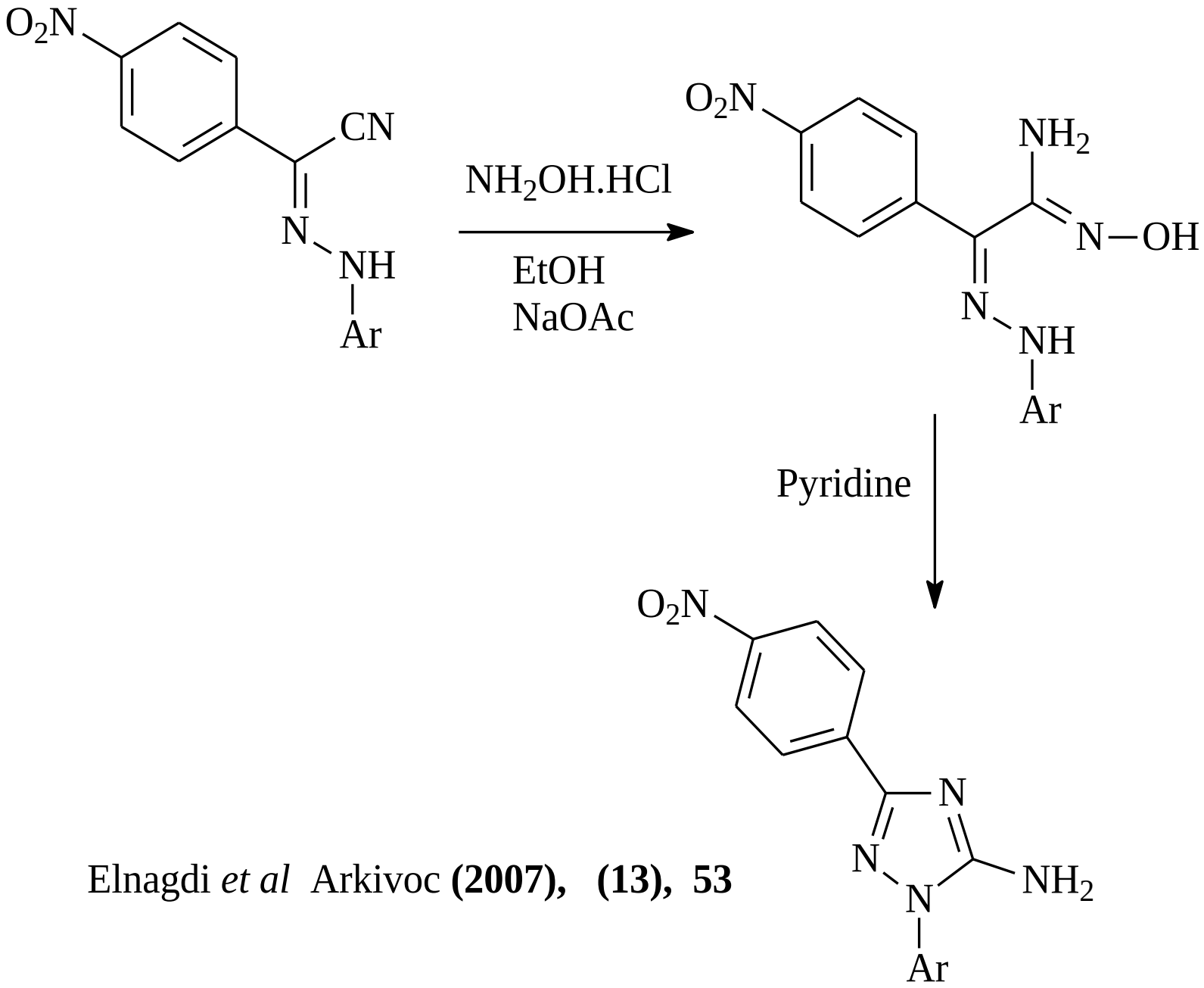


paper in preparation

- Similarly reactions of arylhydrazononitriles

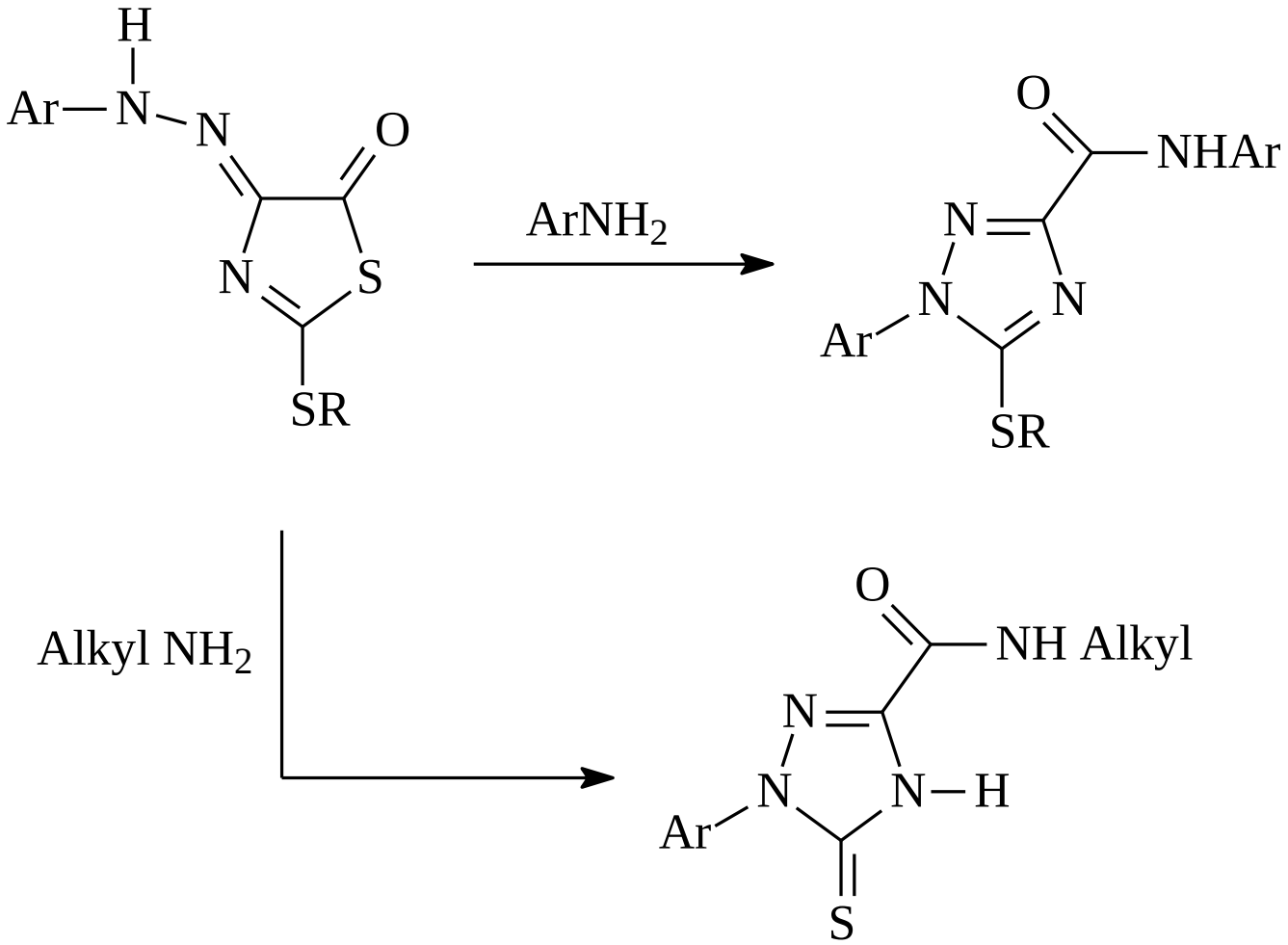


Elnagdi *et al* J.O.C. **1975, 40(18), 2604**

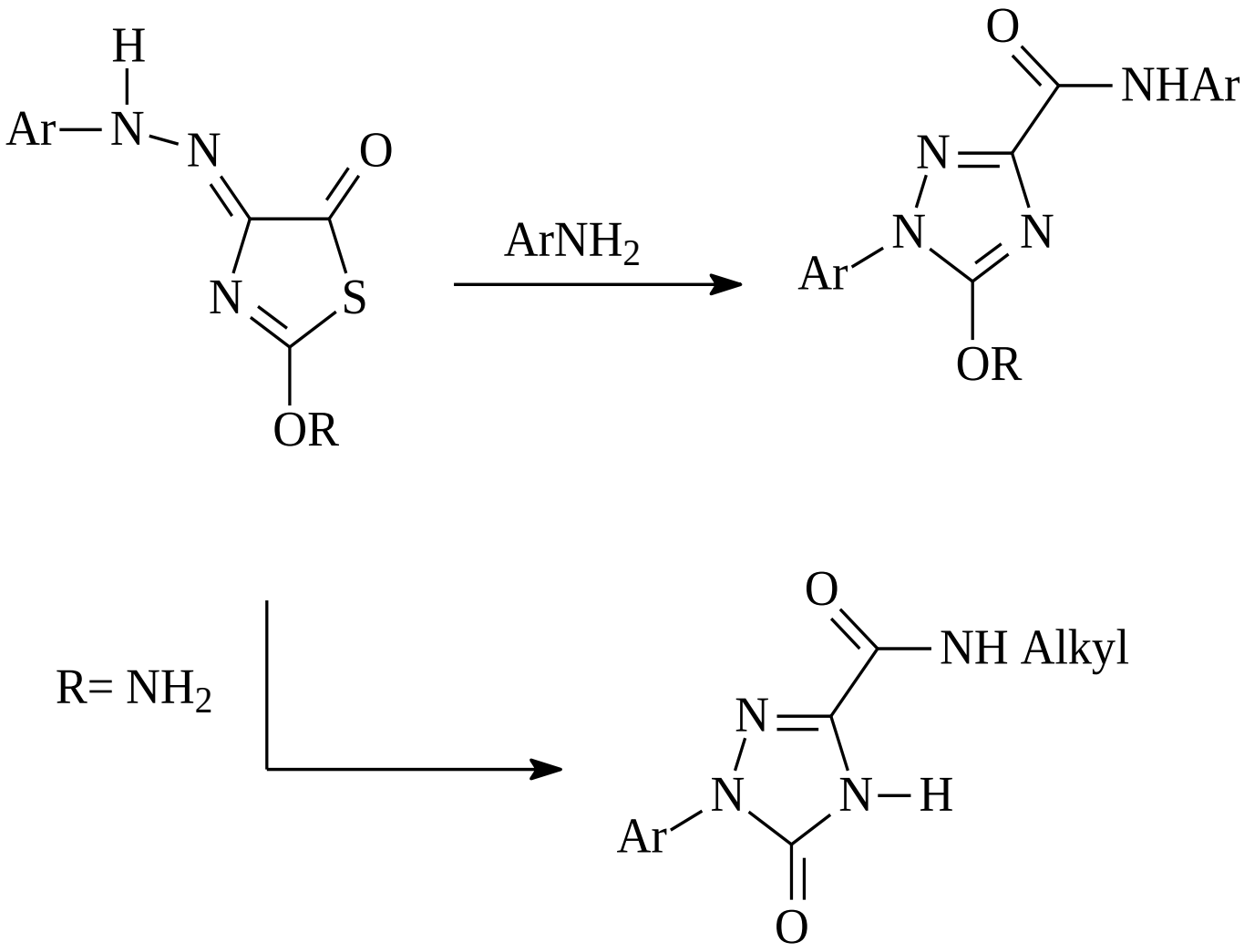


Elnagdi *et al* Arkivoc **(2007), (13), 53**

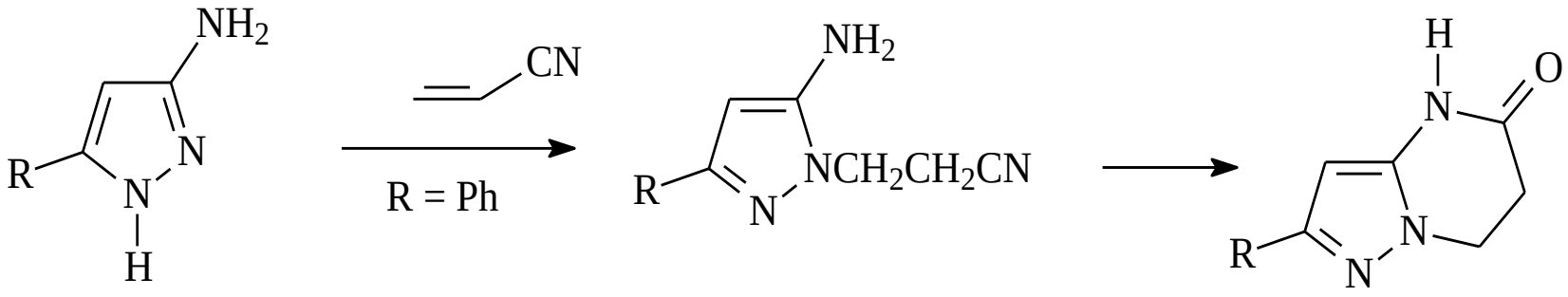
- Some of our observed unexpected results are also given below

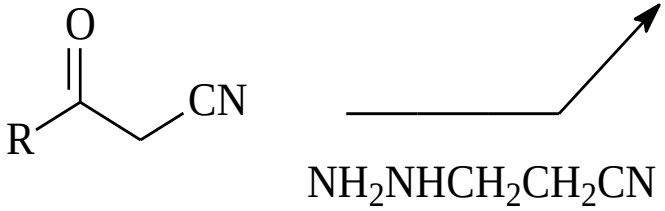


Elnagdi *et al* Liebigs Annalen der Chemie **(1971), 748 79**

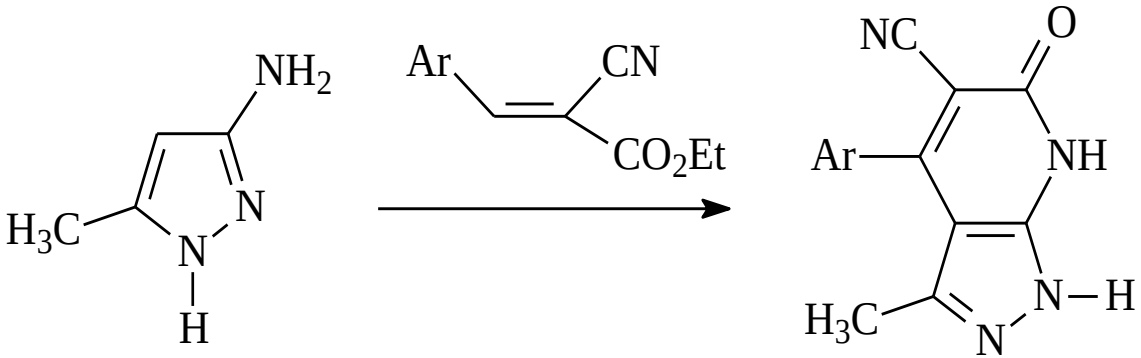


Liebigs Ann, Chem. **1971,748 70**



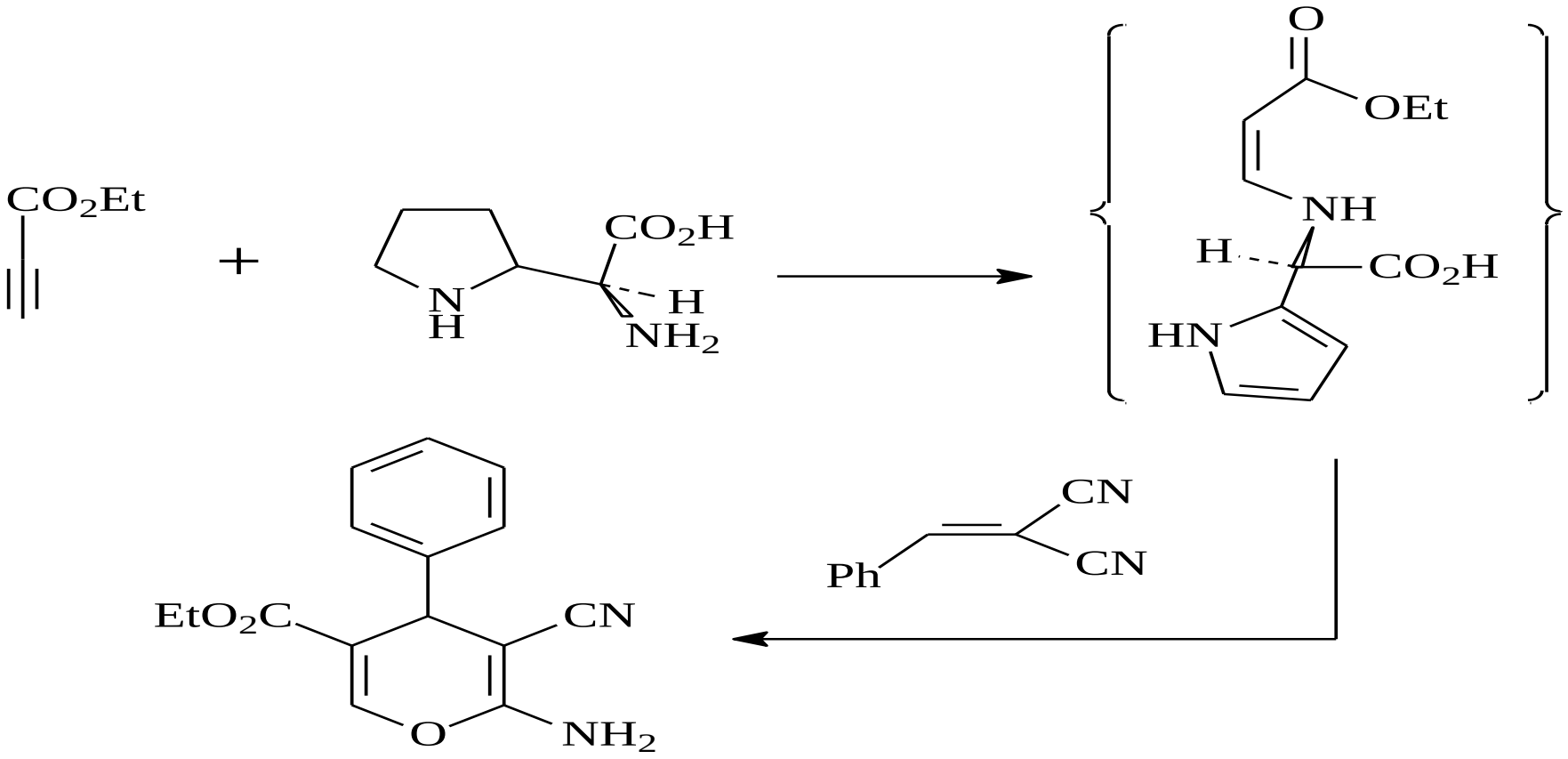


Elnagdi *et al* Tetrahedron **(1974), 30(16), 279**



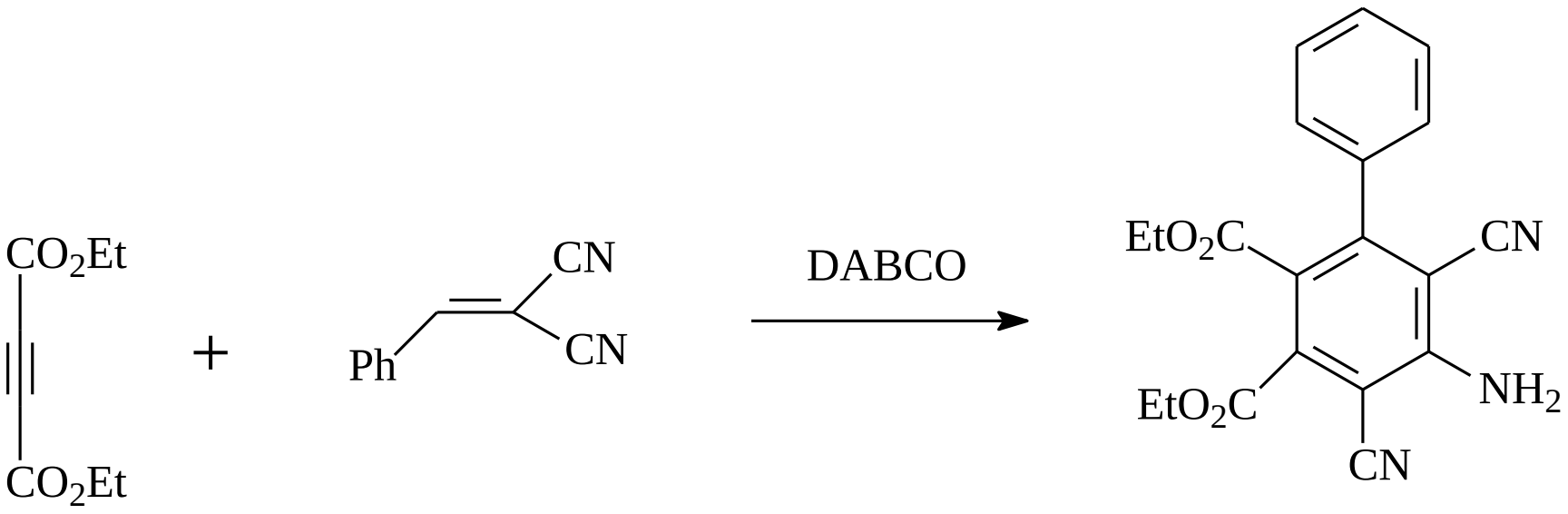
Elnagdi *et al* J. Chem. Res., **(1997), (1), 4**

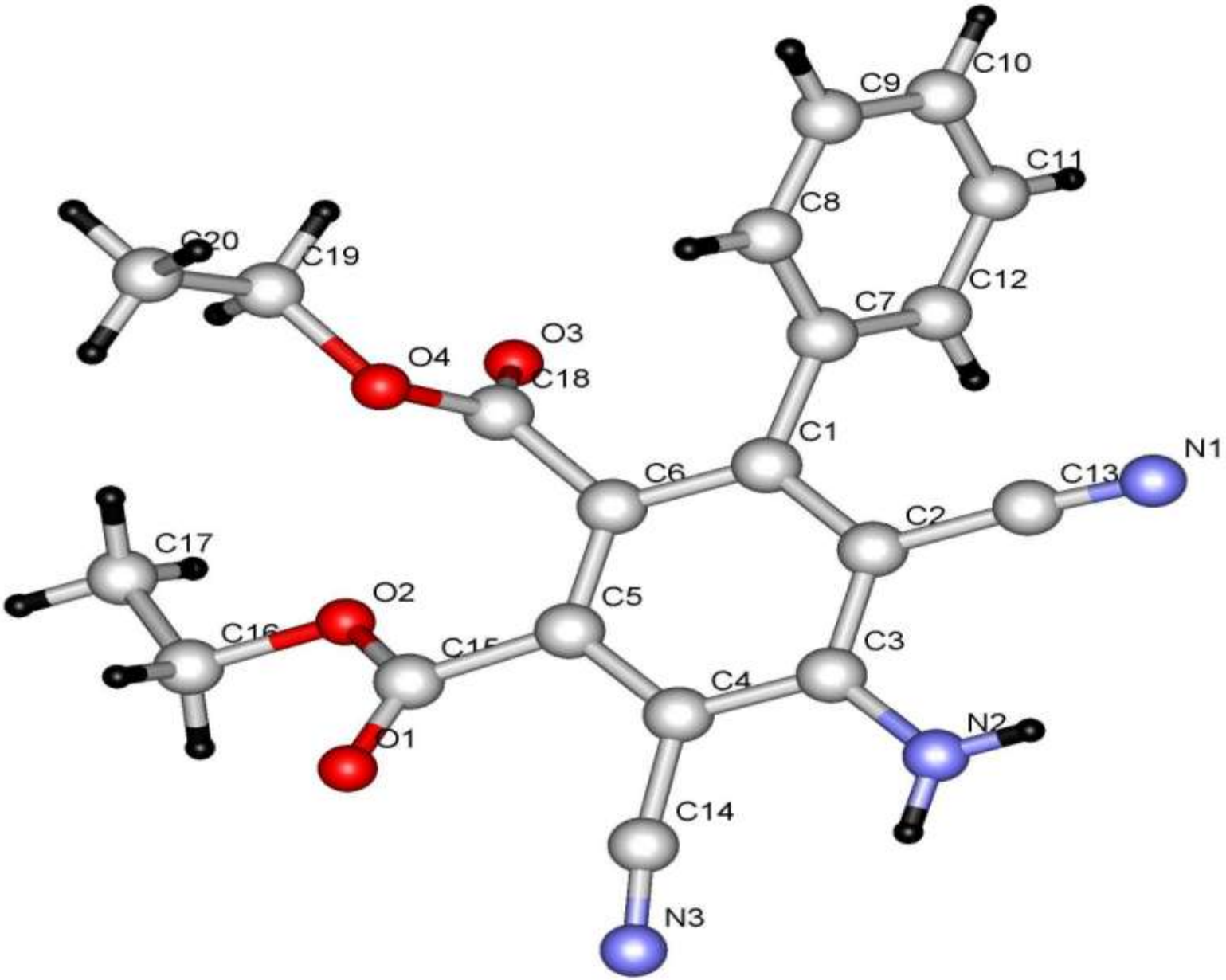
- Just last month we could develop a novel synthesis of pyrans and hexasubstituted benzenes and we are now exploring the potential of these reactions.



Structure could be evidenced by X-ray. Also

C8
C9
C10
C7
C11
C6
N1
C12
C5
O2
C13
C4
C14
C3
N2
O1
C15
O3
C2
C1


CO2Et
CO2Et
+
Ph
CN
CN
DABCO
EtO2C
CN
EtO2C
NH2
CN


C9
C10
C11
C8
C12
C7
C20
C19
O4
O3
C18
C1
N1
C6
C13
C2
C17
O2
C5
C16
C15
C3
C4
N2
O1
C14
N3

- By the end I do want only to indicate that in 50 year of work mostly in Egypt and Kuwait I could publish 437 papers with more than 250 co-Authors and have now about 6000 citations.

No doubt that I am enjoying working in Kuwait in perhaps one of the best equipped chemistry institutes in the middle east and generous funding on middle eastern standards. But the situation in Egypt was quite different. I have already indicated that in my poster in Amman and indicated that I have worked in Egypt under very difficult conditions.

- I have never got governmental funding as funds were directed only to those connected to the system. Surely I was not one of them. However I could self finance my activity through coordination with several multinational chemical industries. The international organization for chemistry in development founded by J. Fred and the Alexander Von Humboldt foundation that granted us on more than eleven occupations research grants, travel all awards and also some equipments. Moreover invited ten of my former students to do research in Germany. Of course I got help from several German professors. Their help should be acknowledged.
- I have also enjoyed cooperation with prof Katritzki's team in my chapters in Advances in heterocyclic chem. And in comprehensive heterocyclic chem. II and III

- Prof. K. Hafner; Technish Hoch Schule Dermstadt
- Prof. H. Wambroff; Univ of Bonn
- Prof. M Regetz; Univ of Kaisers Luten
- Prof. K. Hartkie in Marbourg
- Prof. E. Fanganel in Halle
- And Prof. H. Meier in Mains

- I Have also cooperate with several British scientists, Norwegian and Japanese ones through finance of their scientific institutes.
- Most effective cooperation with B.J. Wakefield of Univ. of Salford, K. Undheim of University of Oslo and Prof M. Ohta of Tokyo institute of Technology
- I hope that after our “revolution” things will change and funds will be oriented to the productive otherwise continued emigration of the capable persons will continue and only those very inefficient will stay at home. The result we all know.

- Finally there is no research without money. I am thus indebted to Kuwait University for generous funding through 14 research projects financed by Kuwait Univ. R. A.

I am also indebted to Saudi Arabia Authorities for Financing activity of Prof. Dr. K. Al-Zaidi and her students. University of Alebo (Syria) has also supported work of two students.

The support I got from the AvH foundation; the IOCD, Royal Norwegian council for scientific and industrial research; university of Utah and Japan commission for UNESCO is highly appreciated.

Acknowledgment

I am great full to my research assistants

1. **Dr. M. A. Khalik**; Associate prof. at Kuwait institute for technical studies
2. **Dr**. **I. A. Shafi**; Lecture of chemistry in Cairo Univ. and former AvH fellow
3. **Dr. H. Fakhry**; research Fellow in University of Oslo

4. **Dr**. **M. Alapasery**; Associated prof of chemistry at NRC
5. **Dr. S. Riyad;** lecture of chemistry in Saudi Arabia
6. **Dr. K. Khalil**; lecture of chemistry at Cairo University
7. **Dr**. **H. Ibrahim**; Lecture of chemistry at University of Fayyom
8. **Moustafa Sherief Moustafa;** Research assistant at Kuwait University

- I am equally indebted to my colleges who shared me planning research projects and running them to successful ends.
- **Prof. N. Al-Awadi** Kuwait University
- **Dr. B. Al-Saleh** Kuwait University
- **Dr. S. Al-Mousawi** Kuwait University
- **Dr. S. Makhseed** Kuwait University
- **Dr. H. Behbhany** Kuwait University
- **Prof. Dr. N. Al-Galal** Kuwait University

- **Dr. H. Al-Mater** Kuwait University
- **Prof. Dr. K. Al-Zaidi** Saudi Arabia
- **Dr. M. A. Alsheikh** Saudi Arabia
- **Dr. M. Toma** Syria
- **Prof K. U. Sadek** University of Menia, Egypt
- **O. Zaki** South Valley University ; Egypt

Tank You

M. H. ELNAGDI