ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2012, *57*(11), 965-970

THERMAL DECOMPOSITION OF ANNELATED 1,5-TETRAZOLES WITH MONO- AND DIBENZOCYCLOALKANE SKELETON OVER HZSM-5 ZEOLITE IN FLOW-VACUUM CONDITIONS

Marius PELMUS,[a] Angela POPESCU,[a] Beatrice-Anamaria TEODORU,[a] Daniela ISTRATI,[a,*] Constantin DRAGHICI,[b] Dan MIHAIESCU[a] and Florin BADEA[a]

[a] Organic Chemistry Department, Politehnica University of Bucharest, 313 Splaiul Independentei, 060042 Bucharest, Roumania
[b] C.D. Nenitzescu Institute of Organic Chemistry, Roumanian Academy, 202B Splaiul Independentei, 060023 Bucharest, Roumania

Received April 23, 2012

Monobenzo- and dibenzoannelated tetrazoloazocines **1** – **3** were thermally decomposed over HZSM-5 zeolite as catalyst, between 250 – 350 ºC, in flow-vacuum conditions: 0.1 – 0.2 Torr, inert atmosphere (argon, flow rate 4 mL min^{-1}) and glass tube. The reactions products were analyzed by GC/MS, separated by liquid chromatography and characterized by spectral methods: IR, ^{1}H-, ^{13}C- NMR, MS data. The main reaction products of **1** and **2** were the corresponding ring contracted N-cyanoderivatives (a new one, **7** and respectively **8**) whereas the tetrazole **3** with central unsaturated ring affords 6*H*-indolo[2,3-*b*]quinoline (**9**). Ionic mechanisms explaining the formation of obtained reaction products are discussed in comparison with the same transformations over quartz as catalyst, in radical conditions, between 400 – 550 ºC.

INTRODUCTION

The chemistry of tetrazoles is a very investigated domain[1-5] because the tetrazole ring has interesting properties and various areas of applications: medicine, agriculture, explosives, photography, corrosion inhibition, etc.

The recent researches were focused over the replacement of carboxylic group with tetrazole ring in notorious drugs.[6,7]

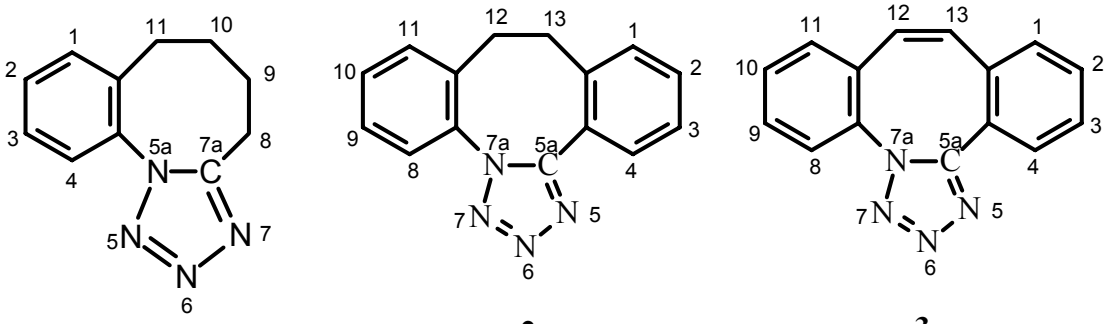
Banciu and coworkers[8] studied for the first time the flow-vacuum pyrolyses of some dibenzocycloalkane derivatives over zeolites as catalysts in order to compare their thermal behavior in ionic conditions *versus* radical ones.

We decided to investigate the thermal decomposition of some tetrazoloazocines (**1** – **3**) in flow-vacuum pyrolysis conditions to establish the influence of HZSM-5 zeolite as catalyst over the products distribution in comparison with thermal decomposition over quartz.

In previous papers were presented the **1** – **3** synthesis[9a,b] and thermal behavior[9b] of tetrazoloazocines (**2, 3** and **3**-substituted with t-butyl[9c] as marker) in flow-vacuum pyrolyses (FVP) over quartz as catalyst at temperatures between 400 – 550 ºC. The products distribution was explained by radical mechanisms of the thermal decomposition.

The thermal behavior of tetrazoles in the flow-vacuum conditions over zeolites has not been investigated so far. We consider that it is useful to compare the FVP thermal behavior of tetrazoloazocines (**1 – 3**) over quartz *versus* HZSM-5 zeolite as catalyst at lower temperatures (250 – 350 ºC) and ionic conditions.

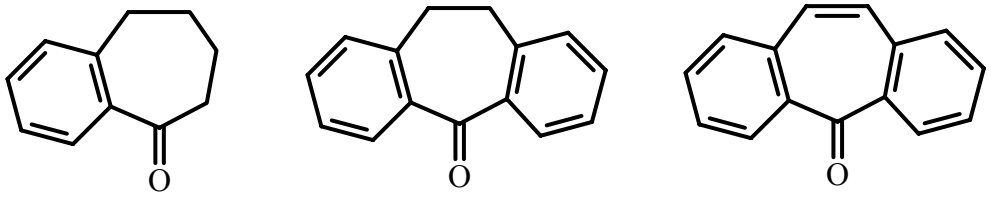
* Corresponding author: d_istrati@yahoo.com



1 **2** **3**

RESULTS AND DISCUSSION

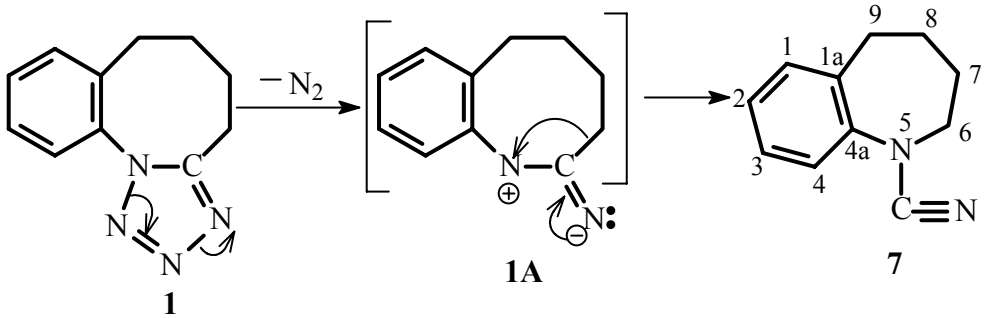
The synthesis of tetrazoloazocines **1 – 3** was performed using literature data[9a,b] by a reaction of the corresponding commercial ketones **4 – 6** with triazidochlorosilane generated *in situ* from silicon tetrachloride and sodium azide in anhydrous acetonitrile solution at room temperature and magnetic stirring (for about 35 hours).



4 **5** **6**

The spectral data (IR, ^{1}H-, ^{13}C-NMR and MS) confirmed the structure of tetrazoloazocines **1 – 3,** prepared for the first time by us using a modified mild method.[10]

By thermal decomposition of the 8,9,10,11-tetrahydrotetrazolo-benzo[*c*]azocine (**1**) over HZSM-5 zeolite in flow-vacuum conditions (0.20 Torr, inert atmosphere, argon, flow rate 4 mL min^{-1} in glass tube) at 350 ºC the 6,7,8,9-tetrahydro-benzo[*b*]azepine-5-carbonitrile (**7**) was obtained as main product (56 %) (Scheme 1):

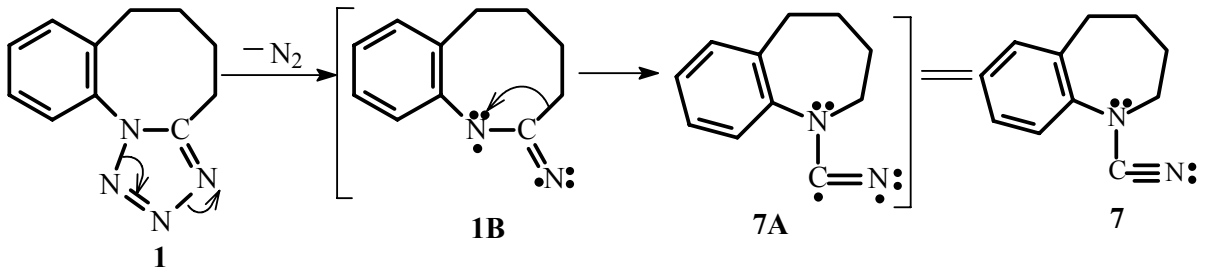


1 **1A** **7**

Scheme 1

Elimination of the nitrogen molecule in order to form a positive charge at the nitrogen atom located in the benzylic position is facilitated by electron donating ability of the neighboring benzene nucleus. The ring contraction is relieved by formation of the cyano group's triple bond.

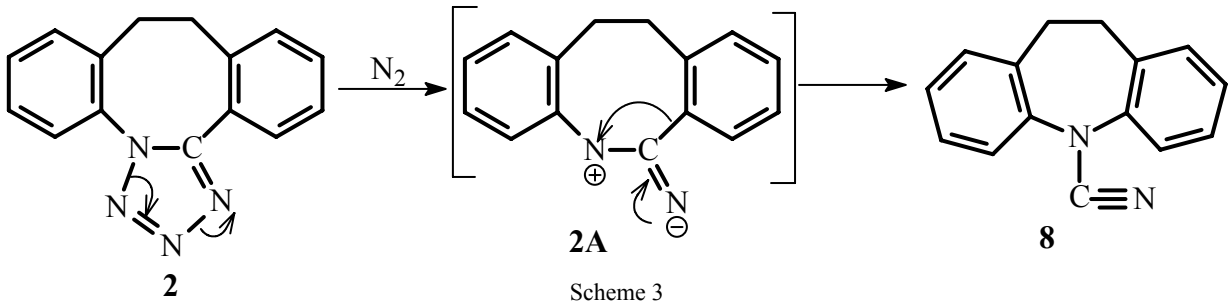
The flow-vacuum pyrolysis of monobenzo-tetrazoloazocine **1** afforded the same N-cyano-derivative **7** as main reaction product at 550 ºC, when the starting material was totally decomposed. In this case a radical mechanism is suggested in Scheme 2:



Scheme 2

The tetrazole ring is thermally decomposed with removal of nitrogen molecule and formation of nitrene **1B**. Ring contraction of this unstable intermediate affords N-cyanoderivative **7** as main product of the pyrolysis reaction. At lower temperatures (250 – 350 ºC) the starting material was partially untransformed (~ 20 % – 9.5 %), while at higher temperature (550 ºC) over quartz it was totally transformed in N-cyanoderivative **7.**

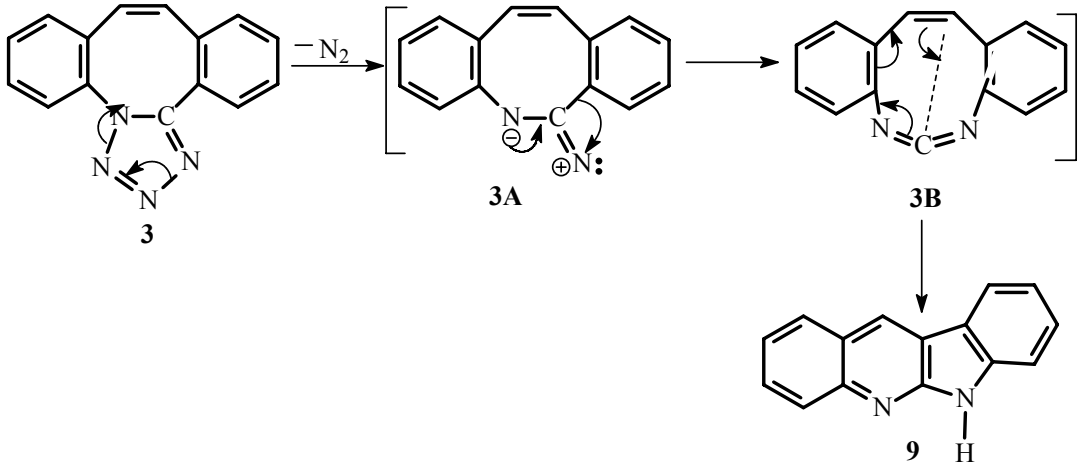
12,13-Dihydro-tetrazolo[1,5-a]dibenzo[*c,g*]azocine (**2**) has a similar thermal behavior with monobenzo-tetrazoloazocine **1** in flow-vacuum conditions over HZSM-5 when the corresponding N-cyanoderivative **8** (Scheme 3) was obtained as the main product:



Scheme 3

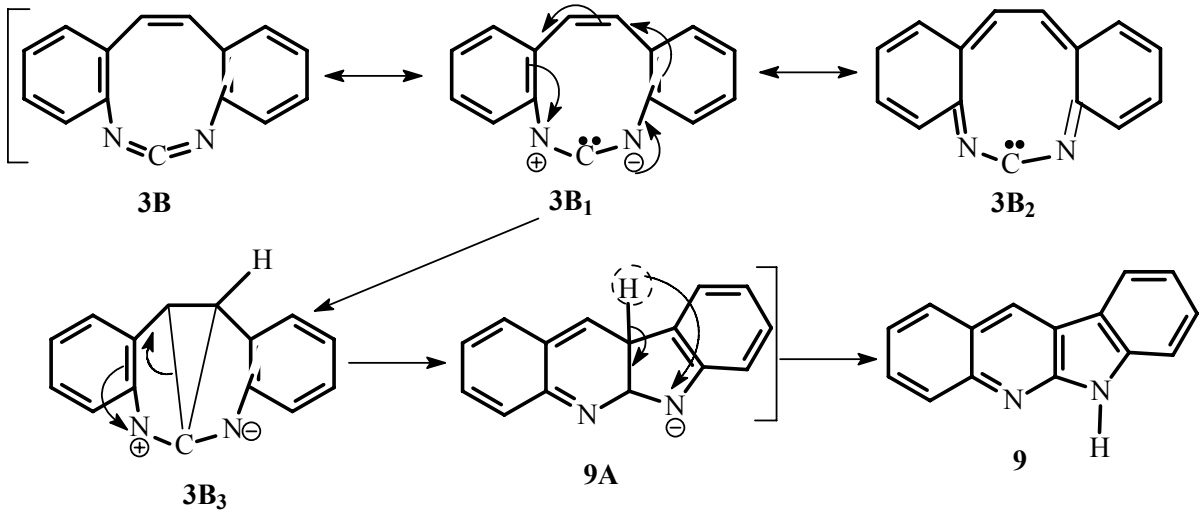
The same product was obtained with radical conditions in flow-vacuum pyrolysis of tetrazoloazocine **2** over quartz, between 400 ºC and 550 ºC.[9b]

Tetrazolo[1,5-a]dibenzo[c,g]azocine (**3**) was totally transformed at 350 ºC over zeolite HZSM-5 when two products are formed in amounts higher than 1 % compound **9 (**80.7 %) being the main product. The proposed mechanism of this transformation is presented in Schemes 4 and 5. In the first step, the elimination of a nitrogen molecule is facilitated by the electron attractive effect of the double bond from the median cycle:



Scheme 4

In the intermediate zwitterion **3A,** the negative charge on benzylic nitrogen allows formation of carbodiimide **3B** as unstable intermediate. The last reaction step is related to a rearrangement of the carbodiimide **3B** in 6*H*-indolo[2,3-*b*]quinoline (**9**) (Scheme 5):



Scheme 5

The carbodiimide **3B** is mesomeric with two carbene structures: **3B$_1$** and **3B$_2$**. The addition of the carbene structure to the central double bond affords the cyclopropane derivative **3B$_3$** followed by the skeleton rearrangement with the main reaction product **9** formation. The carbodiimide as an intermediate in the radical mechanism of flow-vacuum pyrolyses of tetrazoles was proved by its isolation at low temperatures.[11]

The indoloquinoline skeleton was identified in the alkaloid structures which are contained in the *Cryptolepis sanguinolenta* roots. The *Cryptolepis* roots extracts have been used to treat some diseases as malaria,[12] respiratory infections[13] and arthritis.[14]

EXPERIMENTAL

Apparatus for physical analyses

Melting points were determined on a Boetius Kruss Optronic apparatus and are uncorrected. IR spectra were obtained on a FTIR Thermoelectron 6700 with micro ATR smart performer. The NMR spectra were registered on a Varian Gemini 300 apparatus at 300 MHz (^{1}H) and 75 MHz (^{13}C) using TMS as internal standard. The GC/MS analyses were performed on an Agilent 6890 gas-chromatograph with split/splitless injector, coupled with an Agilent 5975B mass-spectrometer provided with quadrupole. A DB5-MS capillary column Agilent 19091s-433 (length 30m; 0.25 mm diameter, 7.04 psi initial pressure) was used. The analysis conditions were: injector temperature, 250 ºC; split ratio, 30:1, carrier gas, hydrogen (1.2 mL min^{-1} flow rate); temperature of transfer-line 250 ºC, electron ionization 70 eV, mass range 46 – 550 u.a.m. The main characteristics of the HZSM-5 zeolite (catalyst) are presented in Table 1.

Synthesis of the tetrazoloazocines 1 – 3

The 8,9,10,11-tetrahydrotetrazolo-benzo[*c*]azocine (**1**),[9a] 12,13-dihydrotetrazolo[1,5-*a*]dibenzo[*c,g*]azocine (**2**)[9b] and tetrazolo[1,5-*a*]dibenzo[*c,g*]azocine (**3**)[9b] were obtained from the corresponding commercial ketones (**4 – 6**) with triazido-chlorosilane generated *in situ* from silicon tetrachloride and sodium azide, at 25 – 35 ºC in anhydrous acetonitrile. The spectral data for these compounds were similar to those reported in literature.

Thermal decomposition of the tetrazoloazocines 1 – 3

General procedure

The thermal decompositions were performed in flow-vacuum conditions with the previously described apparatus.[15]

Table 1

Characteristics of the zeolite catalyst (acid zeolite)

Zeolite catalyst	Molar ratio SiO_2/ Al_2O_3	Atomic ratio Si/Al	Langmuir specific surface $m^2 g^{-1}$	Volume of pores $cm^3 g^{-1}$
HZSM-5	20	40	485	0.16

The pyrolysis glass tube (60 cm length, 10 mm inner diameter) was filled with HZSM-5 acid zeolite on 10 cm length and heated with cylindrical Nabertherm P330 vertical electric oven provided with temperature indicator and programmer. The vacuum (0.1 – 0.2 Torr) was continuously measured with a Varian 801 vacuum gauge. The tetrazoloazocine sample (35 mg) was sublimed under inert atmosphere (argon, flow rate 4 mL min^{-1}) in the pyrolysis tube. The reaction products accumulated at the cooled end of the glass pyrolysis tube were dissolved in dichloromethane, the solvent was evaporated and the residue was analyzed by GC/MS. The temperature interval of thermal decompositions was between 250 – 350 ºC in order *to avoid or reduce the radical conditions*. Analytical pyrolyses at optimal temperature (when the starting tetrazoloazocine was totally or almost decomposed) were followed by preparative runs. The reaction products were separated by liquid chromatography and their structures confirmed by IR, ^{1}H- and ^{13}C-NMR spectroscopy including specific experiments.

Thermal decomposition of the 8,9,10,11-tetrahydrotetrazolo-benzo[c]azocine (1)

A sample of tetrazole **1** was pyrolyzed at 350 ºC over HZSM-5 zeolite under argon atmosphere (argon, 4 mL min^{-1}) at 0.20 Torr. The reaction product was dissolved in dichloromethane, the solvent was evaporated and the solid residue (26.7 mg; 88.7 %) was obtained. The GC/MS analysis indicated a main component (56 %) with M = 172. This product was separated and purified by recrystallization from methanol and the spectral data indicated as structure the 6,7,8,9-tetrahydro-benzo[*b*]azepine-5-carbonitrile (**7**)**,** m.p. 108 – 110 ºC.

IR spectrum (CH_2Cl_2; cm^{-1}): 758m; 1458m; 1496m; 1680w; 2112.6 vs (CN); 2931.5m.

^{1}H-NMR spectrum ($CDCl_3$; δ, ppm): 1.78 (m, 2H^7); 1.88 (m, 2H^8); 2.91 (t, 6.9, 2H^9); 3.56 (t, 6.0, 2H^6); 6.98 (dd, 7.5,1.4, H^4); 7.03 (td, 7.5,1.4, H^2); 7.12 (dd, 7.5, 1.7, H^1); 7.16 (td, 7.5, 1.7, H^3).

^{13}C-NMR spectrum ($CDCl_3$; δ, ppm): 25,94 (C^7 or C^8); 26.07 (C^7 or C^8); 32.62 (C^9); 49.30(C^6); 124.73 (C^4); 125.04(C^2); 127.65 (C^3); 130.76(C^1); 138.17(CN); 139.27 (C^{1a}); 146.50 (C^{4a}).

Mass spectrum (*m/e*; relative abundance %): 39 (59); 41 (18.5); 50 (23); 51 (35); 63 (26); 65 (16); 77 (35); 89 (45); 90 (29); 91 (20); 103 (37); 115 (24); 116 (39); 117 (61); 130 (37); 131 (22); 143 (24); 144 (78); 145 (12); 171 (100, PB); 172 (M, 25);173 (M+1, 2).

Thermal decomposition of the 12,13-dihydro-tetrazolo[1,5-a]dibenzo[c,g]azocine (2)

A sample of tetrazole **2** was pyrolyzed over HZSM-5 zeolite, at 350 ºC, under argon atmosphere (4 mL min^{-1}) at 0.18 Torr. The reaction product, a light yellow solid, was dissolved in dichloromethane, the solvent was evaporated and the solid residue (26mg; 75 %) was analyzed by GC/MS. Two important components: C_1 = 9.9 %, M = 208 and C_2 = 84.7 %, M = 220 were observed. The main product was purified by recrystallization from ethanol and the spectral data proved to correspond to 10,11-dihydro-5H-dibenzo[*b,f*]azepine-5-carbonitrile (**8**) (lit.[9] 98.5 %), m.p. 140-141 ºC.

Thermal decomposition of the tetrazolo[1,5-a]dibenzo[c,g]azocine (3)

A sample of tetrazole **3** was pyrolyzed over HZSM-5 zeolite, at 350 ºC, under argon atmosphere (4 mL min^{-1}) at 0.20 Torr. The reaction product, an insoluble yellowish solid, was scratched and washed from the pyrolysis glass tube with dichloromethane. After solvent evaporation, GC/MS analysis indicated 6*H*-indolo[2,3-*b*]quinoline (**9**) as main product (80.7 %), presenting the same spectral data with the previously described.[9b]

CONCLUSIONS

In this work we have studied for the first time the thermal behavior of three mono- and dibenzoannelated tetrazoloazocines in flow-vacuum conditions over HZSM-5 zeolite as catalyst. The reaction product **7** (6,7,8,9-tetrahydro-benzo[b]azepine-5-carbonitrile) is a new compound and it was characterized by spectral methods (IR, ^{1}H- and ^{13}C-NMR, MS).

We have proposed the ionic mechanism pathways that explain the thermal decomposition products. A comparison of the ionic mechanisms of two benzoannelated tetrazoloazocines (**2**, **3**) with the radical ones described in literature[9b] for thermal decomposition in flow-vacuum pyrolyses, between 400-550 ºC, over quartz, is discussed.

Acknowledgements: This research work was financially supported by the Ministry of Education and Research of Roumania, Grant 1557, 2009-2011. The authors thank to professor Ioan Calinescu (Faculty of Applied Chemistry and Materials Science) for a HZSM 5 zeolite sample.

REFERENCES

1. a) G. I. Yranzo, J. Elguero, R. Flammang and C. Wentrup, *Eur. J. Org. Chem*., **2001**, 2209; b) C. Wentrup, R. Flammang, *J. Phys. Org. Chem*., **1998**, *11*, 350; c) R.N. Bulter, in C.W. Ress and E.F.V. Scriven, Editors, "Comprehensive Heterocyclic Chemistry", vol. 4, Pergamon, Oxford, UK, 1996, 791-838;
2. R.J. Herr, *Bioorg. Med. Chem*., **2002**, *10*, 3379.
3. a) D. Varadaraji, S. S. Suban, V. R. Ramasamy and K.Kubendiran, *Org. Commun.,* **2010**, *3*, 45-46. b) P.R. Wyde, S. Laquerre, S.N. Chetty, B.E. Gilbert, T. J. Nitz, D.C. Pevear, *Antiviral Research.*, **2005**, *68*, 18.
4. W. Han, X. Jiang, Z. Hu, Z.R. Wasserman and C.P. Decicco, *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 3487.
5. V.V. Dhayabaran, I. Sharmila Lydia, J. Princy Merlin and P. Srirenganayaki, *Ionics*, **2004**, *10*, 123.
6. J.B. Taylor and D.J. Triggle, "Comprehensive Medicinal Chemistry", Vol. 2: Strategy and Drug Research, Elsevier, 2006.
7. K. Pegklidou, C. Koukoulitsa, I. Nicolaou and V. J. Demopoulos, *Bioorg. & Med. Chem*., **2010**, *18*, 2107.
8. a) M.D. Banciu, O. Cira, A. Petride, A. Banciu and C. Draghici, *J. Anal. and Appl. Pyrol.*, **1997**, *42*, 177; b) M.D. Banciu, O. Cira, A. Petride and A. Banciu, *Rev. Roum. Chim.,* **1997**, *42*, 1093.

9. a) M.D. Banciu, C. Draghici, A.Popescu, A. Banciu and A. Simion, *Rev. Roum. Chim.*, **1998***, 43*, 649. b) M.D. Banciu, A. Popescu, A. Simion, C. Draghici, C. Mangra, D. Mihaiescu and M. Pocol, *J. Anal. Appl. Pyrolysis*, **1999**, *48,* 129 ; c) A. Popescu, A. Lari, A. Banciu, C. Draghici, D. Ciuculescu, D. Istrati and M.D. Banciu, *Rev. Roum. Chim.,* **2006**, *51*, 345.
10. A.A.S. El-Ahl, S.S. Elmorsy, H. Soliman and F.A. Amer, *Tetrahedron Lett*, **1995**, *36*, 7337.
11. a) C. Wentrup, C. Thetaz, E. Tagliaferi, H. Linderner, B. Kitschke, H.-W. Winter and H.P. Reisenauer, *Angew. Chem.* **1980**, *92*, 556; b) C. Wentrup and H.-W. Winter, *J. Amer. Chem. Soc.*, **1980**, *102*, 6161.
12. A. Ansah, A. Khan and N.J. Gooderham, *Toxicology*, **2005**, *208*, 141.
13. S. Gibbons, F. Fallah and C.W. Wright, *Phytother. Research.*, **2003**, *17*, 434.
14. P. Laupattarakasem, P.J. Houghton, J.R. Hoult and A. Itharat, *J. Ethnopharmacol.*, **2003**, *85*, 207.
15. M.D. Banciu, E. Olteanu, C. Draghici, A. Petride and M. Danila, *J. Anal. Appl. Pyrolysis*, **1996**, *37*, 151.