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One-Pot Synthesis of 7*H*-Dibenzo[*b*,*d*]azepin-7-one by Heterogeneous Flash Vacuum Pyrolysis with MCM-41 Catalysts

Elizabeth L. Moyano,*,† Paola L. Lucero,† Griselda A. Eimer,‡ Eduardo R. Herrero,‡ and Gloria I. Yranzo*,†

INFIQC, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, Córdoba 5016, Argentina, and Centro de Investigación y Tecnología Química (CITeQ), Universidad Tecnológica Nacional, Facultad Regional Córdoba, Córdoba, Argentina

lauramoy@mail.fcq.unc.edu.ar

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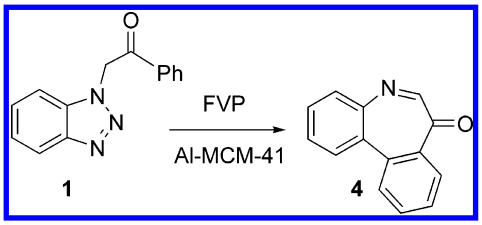
ABSTRACT



Homogeneous and heterogeneous flash vacuum pyrolysis (fvp) reactions of 2-(1*H*-1,2,3-benzotriazol-1-yl)phenylethanone (1) are reported. Heterogeneous reactions were carried out with Al-MCM-41 catalysts, mesoporous molecular sieves of the type M41S. In both cases, 7*H*-dibenzo[*b*,*d*]azepin-7-one (4) was the major product; however, in the catalytic reactions, yields and selectivity were very high. A mechanism for this reaction is also discussed.

Gas-phase thermolysis is a synthetic method of great preparative use in organic chemistry. A special form of thermolysis, the flash vacuum pyrolysis (fvp), has found wide application in the preparation of thermolabile compounds, in the isolation of reactive species, and in the mechanistic study of thermal reactions. It is also an important synthetic methodology in which one or more key steps have been performed in gas-phase thermolysis. The fvp technique is characterized by several features: (a) the process is carried out without solvents; (b) the substance to be pyrolyzed remains in the hot zone for a considerably short time or contact time ($\sim 10^{-2}-10^{-3}$ s); (c) the pyrolyzate is immediately cooled to cryogenic temperatures (−200 °C) after passage through the hot zone; and (d) the system is evacuated to ca. 10^{-2} Torr by a high-capacity pump.

Fvp reactions are particularly good for intramolecular processes, some of which do not take place under other thermal conditions.

The application of the fvp process to the study of thermal behavior of heterocyclic compounds has been widely investigated. 1-Substituted-1-*H*-benzotriazoles, in particular, afford 1,3-diradical intermediates which can interact with aromatic or unsaturated substituents to give cyclic and rearranged products.[1,2] In this work we report the fvp reactions of the acetylbenzotriazole **1** as a synthetic route to prepare the fused 1,3-azepinone **4** (azatropone) in a simple way. Dibenzoazepinones like **4** show interesting pharmacological properties; however, the synthesis of this class of compounds has not been well developed.[3]

† Ciudad Universitaria.
‡ Facultad Regional Córdoba.

(1) Brown, R. F. C. *Pyrolytic Methods in Organic Chemistry*; Wasserman, H. H., Ed.; Academic Press, New York, 1980.
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Fvp reaction conditions showed that this process should be performed at high temperatures and a mixture of products was always observed. We decided to study the possibility of lowering the energy of activation and increasing the selectivity without changing the type of reaction, and therefore we chose to use MCM-41 mesoporous molecular sieves as solid catalysts. Heterogeneous fvp systems using catalytic materials have potential applications than can provide new general synthetic methodologies. In our group we have already studied fvp reactions using zeolites and hydrotalcites as catalytic materials in the pyrolysis of NH-pyrazoles[4] and azolyl-malonamates[5] and this work is the first report of MCM-catalyzed systems. In this case we compare the fvp reactions of benzotriazole **1** in homogeneous system[6] (without catalyst) and heterogeneous system using Al-MCM-41 (Si/Al: 20) as the solid catalyst.[7]

When homogeneous fvp experiments of 2-(1*H*-1,2,3-benzotriazol-1-yl)phenylethanone[8] (**1**) were performed between 400 and 500 °C, the products mainly identified in the solid crude were 7*H*-dibenzo[*b*,*d*]azepin-7-one (**4**), phenanthridine (**5**), and 2-phenyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**12**) (Table 1, Schemes 1 and 2).

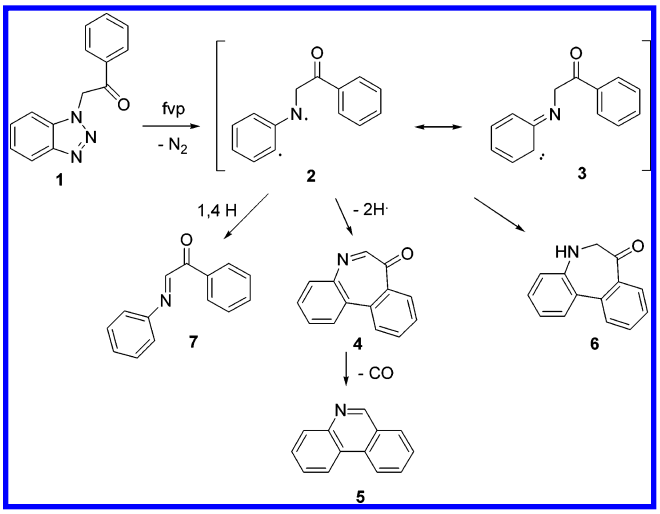
Table 1. Results of the Homogeneous Fvp Experiments

temp (°C)	% **1**	% **4**	% **5**	% **12**	% other
400	48	29	2	12	9[a]
450	24	36	5	10	25[a]
500	0	30	15	15	40[b]

[a] Minor products: 1,2-dihydrodibenzo[*b*,*d*]azepin-7-one (**6**), 1-phenyl-2-(phenylimino)ethanone (**7**), 2-phenylbenzoxazole (**13**), benzonitrile, and biphenylene (**14**). [b] Minor products: **7**, **13**, benzonitrile, and biphenylene (**14**).

The formation of the major product **4** is explained by hydrogen loss from the intermediate **2** resulting from nitrogen extrusion form **1** and followed by intramolecular cyclization (Scheme 1). As the temperature was raised, the decarbonylation reaction of azepinone **4** was favored to afford the aromatic ring phenanthridine (**5**). Between 400 and 450 °C the azepinone **6** was detected by GC/MS as a minor product. This compound can be formed from the diradical **2** by cyclization followed by 1,5-hydrogen shift or from carbene **3** by C−H insertion followed by 1,3-H migration.

Scheme 1. Mechanism Proposed for Fvp Reactions of Benzotriazole **1**



As in other reactions of alkylbenzotriazoles,[9] the *N*-phenylimine **7** was obtained by 1,4-hydrogen transfer in the intermediate **2**. However, in this case the imine did not undergo electrocyclization reaction to give 2-phenyl-1,4-benzoxazine as was observed in the reaction of allylbenzotriazoles.[10]

2-Phenyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**12**) was detected at all temperatures, and an explanation for this observation is given in Scheme 2. Benzotriazole **1** can undergo an acyl migration to give the zwitterionic specie **8**, which eliminates diazomethane (detected in the volatile fractions by GC/MS) to afford diradical **9**. Rearrangement of this intermediate could afford **10**, a hybrid of oxazirene, acylnitrene, and nitrile oxide.[11] The coupling reaction of **10** with diradical **11** could result in the formation of benzoxazinone **12**. It is known that oxazirenes collapse with many species to give more stable structures.[12] Compound **12** could also be formed by a [2+3] cycloaddition of 1*H*-cyclopropabenzen-1-one **16** with the nitrile oxide, as proposed in the formation of other benzoxazinones.[13] Benzocyclopropenone **16** was not detected in the reaction crude; however, this key intermediate, in equilibrium with diradical **11** under reaction conditions, can arise from ring fragmentations in azepinones **4** and **6**. In a control experiment, the fvp reaction of the pure azepinone **4** at 450 °C gave small quantities of products such as benzonitrile and biphenylene (**14**) supporting the presence of **11**. Benzonitrile could be formed by rearrangement of the isonitrile fragment generated in the ring fragmentation, while biphen-

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(4) (a) Moyano, E. L.; Yranzo, G. I. *J. Org. Chem.* **2001**, *66*, 2943. (b) Moyano, E. L.; del Arco, M.; Rives, V.; Yranzo, G. I. *J. Org. Chem.* **2002**, *67*, 8147.

(5) Peláez, W. J.; Gafarova, I. T.; Yranzo, G. I. *ARKIVOC* **2003**, *10*, 262.

(6) Reactions were carried out in vycor glass fvp equipment with use of a GAYNOR PRDH temperature controller and a Thermolyne 21100 tube furnace. Oxygen free dry nitrogen was used as the carrier gas. Samples to be pyrolyzed were 30−50 mg. Contact times were around 10^{-2} s with pressures of 0.2 to 0.1 Torr . Products were trapped at the liquid air temperature, extracted with solvent, and submitted to different analyses or separation techniques.

(7) In a typical run 0.50 g of fractured catalyst was placed along the reactor (30 cm length, 1 cm diameter) with use of ceramic wool fiber as an inert support. All catalysts were preactivated in air at 500 °C for 4 h before each reaction.

(8) Prepared by a reported procedure, see: Katritzky, A. R.; Wu, J. *Synthesis* **1994**, 597.

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(11) (a) Wentrup, C.; Bornemann, H. *Eur. J. Org. Chem.* **2005**, 4521. (b) Poppinger, D.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 7806.

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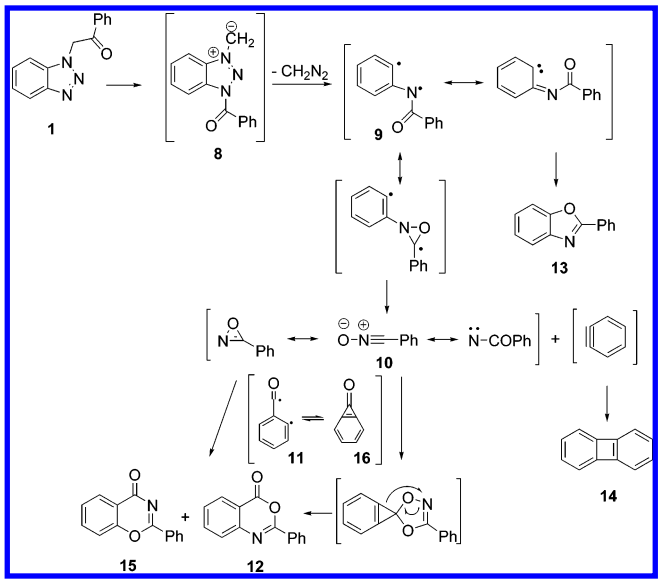
Scheme 2. Mechanism Proposed for the Formation of Benzoxazinone **12** and Benzoxazole **13** from **1**



ylene could be formed by dimerization of benzyne arising from decarbonylation reaction of diradical **11** and/or cyclopropenone **16**. Diradical **9** is also an intermediate in the reaction to obtain the benzoxazole (**13**) also found in the pyrolyzate, through the carbene structure. Alkyl and arylbenzoxazoles are typical products in the thermolysis of acylbenzotriazoles.[14]

When the fvp experiments were carried out in the presence of Al-MCM-41[15] (catalyst:substrate ratio equal to 25) the total conversion of **1** was achieved at 450 °C, which is 50 °C lower than the homogeneous system. In this case, the azepinone **4** was obtained in 87% yield (Table 2).

These results show that mesoporous solids Al-MCM-41 can be used as excellent catalysts in the thermal reaction of benzotriazole **1**. In addition to the enhanced yields toward azepinone **4**, the selectivity of this process is high giving less conversion of **1** to other products in contrast to homogeneous systems.

(14) (a) Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1988**, 98. (b) Druliner, J. D. *J. Am. Chem. Soc.* **1968**, *90*, 6879.

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Table 2. Results of the Fvp/Al-MCM-41 Experiments

temp (°C)	% **1**	% **4**	% **5**	% **12**	% other
350	17	6	7	6	64[a]
400	2	55	8	15	20[b]
450	0	87	10	2	1

[a] Minor products: 1,2-dihydrodibenzo[*b*,*d*]azepin-7-one (**6**), 1-phenyl-2-(phenylimino)ethanone (**7**), 2-phenylbenzoxazole (**13**), benzonitrile, and biphenylene (**14**). [b] Minor products: 1-phenyl-2-(phenylimino)ethanone (**7**), 2-phenylbenzoxazole (**13**), benzonitrile, and biphenylene (**14**).

The catalytic activity of Al-MCM-41 materials could be related to a high surface area,[16] to an ordered structure of mesopores[17] which allows the processing large organic molecules, and also to active sites: acidic and metal sites. An effective interaction of the gaseous substrate with different sites takes place, resulting in a decrease of the temperature for the process. The aluminum content is a significant factor determining catalytic activity, as was demonstrated when fvp reactions were carried out with pure Si-MCM-41. In this case, almost total conversion of benzotriazole **1** (7% left) was achieved at 350 °C; however, a complex mixture of products was obtained giving azepinone **4** in 14% yield.

These preliminary studies indicate that catalytic fvp experiments with Al-MCM-41 mesoporous molecular sieves constitute a novel method for the generation of dibenzoazepinone **4** from the readily accessible precursor **1**. These results point to the potential for the synthesis of azepinones, unavailable by conventional methodologies, and for a broader use of acetylbenzotriazoles.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Above 1400 m^2/g.

(17) Diameter between 1 and 10 nm.