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Flash vacuum pyrolysis (F.V.P.) of 1,2,4-benzotriazine derivatives

Zsuzsanna Riedl,[a] György Hajós,[a,*] Walter J. Peláez,[b] Ioulia T. Gafarova,[b]
Elizabeth L. Moyano[b] and Gloria I. Yranzo[b]

[a]Chemical Research Center, Institute of Chemistry, Hungarian Academy of Sciences, Pusztaszeri út 59-67, H-1025 Budapest, Hungary
[b]INFIQC—Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria,
5000 Córdoba, Argentina

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Abstract—Flash vacuum pyrolysis of 3-methylsulfanyl-1,2,4-benzotriazine *N*-oxide, 3-methylsulfanyl-1,2,4-benzotriazine, and 3-phenyl-1,2,4-benzotriazine are described. The *N*-oxide derivative underwent deoxygenation between 500 and 600°C, whereas at higher temperatures both methylsulfanyl compounds, besides yielding the same products, also gave benzimidazole formed by an independent mechanism. Transformation of these derivatives between 600 and 750°C led to formation of a complex reaction mixture indicating the radical nature of the processes. The phenyl substituted derivative was studied between 575 and 650°C and afforded benzonitrile and traces of biphenylene. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Flash vacuum pyrolysis (f.v.p.) is both a very useful technique to study reaction mechanisms and a powerful tool for synthetic purposes. One of the most interesting advantages of this technique is the lack of solvent, which facilitates the work up of the reaction mixture and allows the isolation of kinetically controlled products. Several excellent reviews concerning f.v.p. have appeared,[1] a world-wide known book was written by Brown[2] and, more recently, a book concerning synthetic gas phase reactions has also been published.[3]

In the course of our f.v.p. studies, we focused our interest on heterocycles bearing N–N double bonds due to their ability to lose nitrogen, thus generating reactive intermediates. Such reactions have been described for pyrazoles,[4] thiadiazoles,[5] triazoles,[6] and tetrazoles,[7] all of them containing five-membered rings. Concerning six-membered rings and, particularly, triazines (the object of the present study) some reports on f.v.p. reactions of 1,2,3-triazines have been published, and, to the best of our knowledge, only two studies discussed the behavior of 1,2,4-benzotriazines. Rees et al.[8] carried out flash vacuum pyrolysis reactions of some 1,2,3- and 1,2,4-benzotriazines in their attempts to find benzazete. They found benzazete as well as other products such as biphenylene and benzonitrile in reactions of 1,2,3-benzotriazines. Furthermore, they concluded, that 1,2,4-triazines do not afford benzazete and that the reaction temperature needed in order to observe transformation is higher than that used for the 1,2,3-isomer. Besides, Seybold mentioned in his review some unpublished results on f.v.p. of some 1,2,4-benzotriazines affording biphenylene (by dimerization of 1,2-dehydrobenzene) and a nitrile.[5] There is another report on f.v.p. of 1,2,3-triazines where the authors inform that these compounds also afforded benzonitrile (in phenyl substituted compounds) and substituted acetylenes.[9] More recently, Werstiuk et al. carried out f.v.p. reactions of some 1,2,3-benzotriazines and confirmed the formation of benzazete by photoelectron spectroscopy.[10]

Concerning the reactions of *N*-oxide compounds, there is a report on the f.v.p. of pyridazine *N*-oxides where the authors describe that at 750°C the starting material loses the oxygen function to afford pyridazine along with some nitriles.[11] In Rees's article, it is described that reactions of 1,2,3-benzotriazine *N*-oxide where they found some benzoxazoles, formed from a benzazete *N*-oxide intermediate.[8]

Since this literature survey reveals that pyrolysis of 1,2,4-benzotriazines has not been deeply explored, we decided to carry out a comparative study of reactions of 3-methylsulfanyl-1,2,4-benzotriazine *N*-oxide (**1**), 3-methylsulfanyl-1,2,4-benzotriazine (**2**), and 3-phenyl-1,2,4-benzotriazine (**3**) (Scheme 1).

F.v.p. reactions of compound **3** were studied by Rees et al.,[8] but as their interest was focused on 1,2,3-benzotriazines rather than on 1,2,4-benzotriazines, reinvestigation of the transformation of this compound seemed of interest.

Keywords: flash vacuum pyrolysis; heterocycles; benzotriazines; radicals.
* Corresponding author; e-mail: ghajos@chemres.hu

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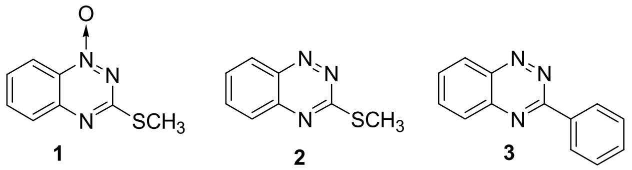


Scheme 1.

2. Results

2.1. F.v.p. reactions of 3-methylsulfanyl-1,2,4-benzotriazine *N*-oxide (1)

F.v.p. treatment of **1** was carried out between 575 and 650°C and the results are summarized in Table 1. Between 500 and 600°C the only reaction is N–O bond cleavage affording compound **2**, whereas at higher temperatures benzimidazole (**5**) as well as reaction products arising from f.v.p. of **2** were found as shown in Scheme 2.

Formation of **2** is clearly explained by loss of oxygen. This reaction was also described to occur in f.v.p. of some pyridazine *N*-oxides[11] and pyridine *N*-oxides.[12] An important difference between reactions of **1** and pyridazines *N*-oxides is, however, that these compounds are stable up to 650°C and oxygen loss is a competitive reaction with ring fragmentation and formation of products, whereas the N–O bond in 1,2,4-benzotriazine *N*-oxide (**1**) is less stable. At 600°C 32.5% of **1** remained unconverted and as the reaction temperature was raised, the reaction products deriving from **2** as well as compound **5** as a ring contraction product of a competitive reaction were detected. Compound **4** should be supposed as an intermediate in the pathway leading to **5**, similar to the case of formation of pyrrole (ring contraction) and pyridazine (deoxygenation) from pyridazine *N*-oxide.[11,12]

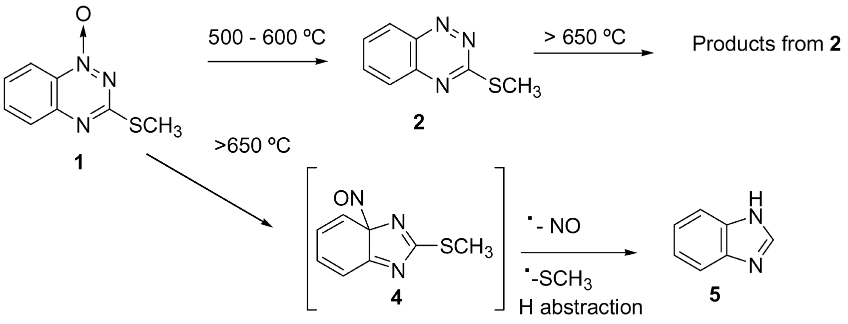
It should be noticed that 2-methylsulfanylbenzimidazole is the expected product. This C–S bond fission and formation of radicals was already described in f.v.p. reactions of some SPh compounds and in the cases where the S atom is bonded to an aromatic and to an alkyl group, the C_{Ar}–S is described as the stronger bond.[13] Formation of **5** requires loss of SCH_3, which may happen in one single step or two steps (if the S–CH_3 bond is the weaker one). Although it is not possible to decide which path is preferred, the fact that no 1*H*-benzimidazole-2-thiol (which would be an evidence of the presence of S radicals) was found may be considered as a support for the C_{Ar}–S bond breaking, which is usually not the weaker bond.

2.2. F.v.p. reactions of 3-methylsulphanyl-1,2,4-benzotriazine (2)

Reactions of **2** were studied between 650 and 750°C and the results are summarized in Table 2. Due to the fact that complex mixtures were obtained almost in the whole range of temperatures, the reaction mixtures were analyzed by GC/MS in each case.

Table 1. F.v.p. reactions of **1**

T (°C)	% **1**	% **2**	% **5**	% **6**	% **8**	% **9**	% **15**	% **21**	% **24**
400	100	0	–	–	–	–	–	–	–
500	95.1	4.9	–	–	–	–	–	–	–
550	76.5	23.5	–	–	–	–	–	–	–
600	32.5	67.5	–	–	–	–	–	–	–
750	–	–	12.8	2.0	36.3	3.8	5.0	5.8	3.4

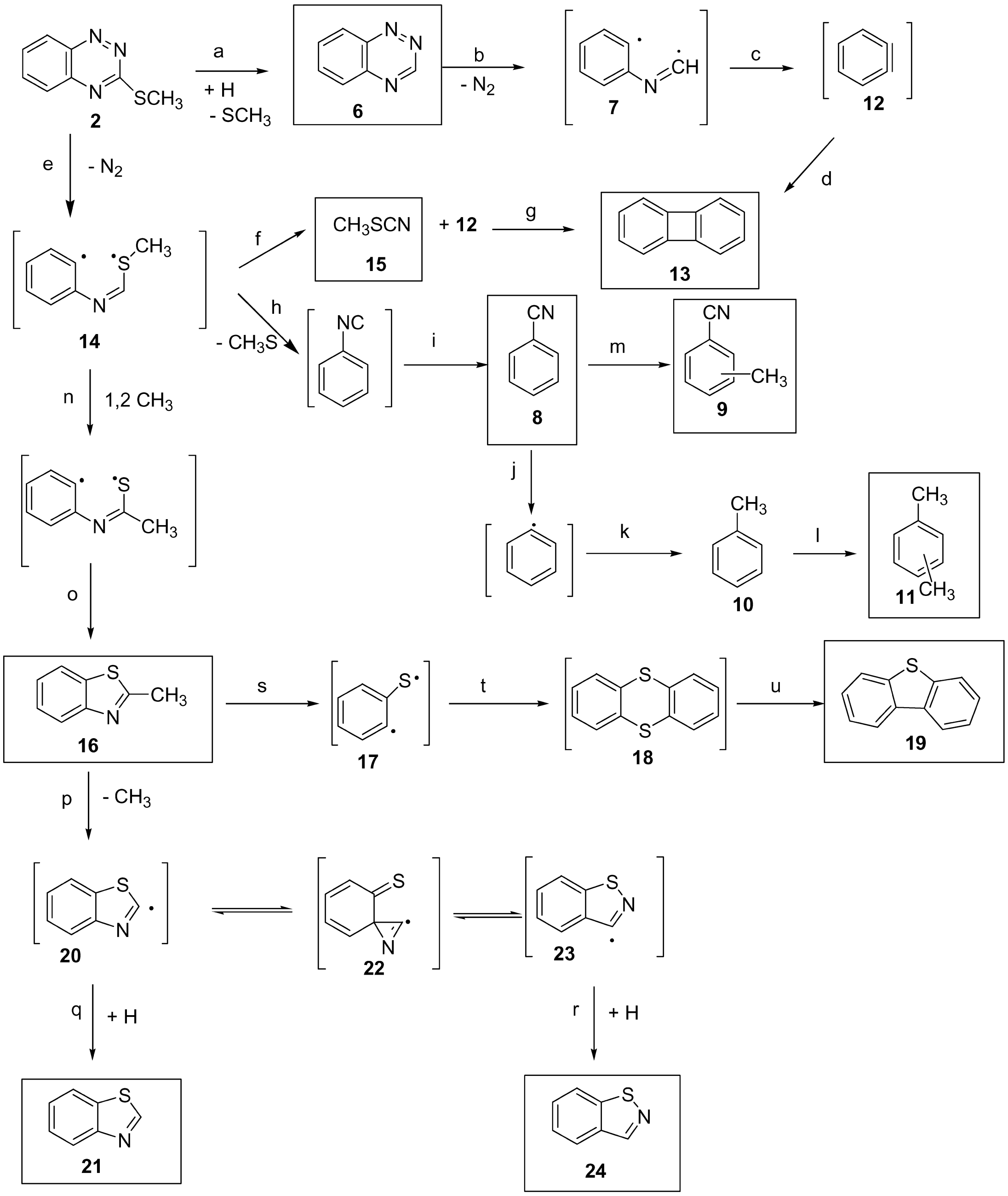


Scheme 2.

Table 2. F.v.p. reactions of **2**

T (°C)	% **2**	% **6**	% **8**	% **9**	% **10**	% **11**	% **13**	% **15**	% **16**	% **19**	% **21**	% **24**
650	47.8	4.7	21.9	3.1	3.5	–	–	6.9	3.9	0.5	0.9	1.2
680	19.1	8.2	32.8	7.9	3.0	1.5	1.1	8.9	10.7	–	1.2	1.4
700	1.3	9.5	38.0	5.6	8.9	1.3	–	13.5	4.4	1.5	3.7	0.5
750	–	8.4	26.3	6.3	23.1	3.2	–	12.8	–	–	13.5	–

Some minor amounts of condensed aromatics were detected but not quantified.



Scheme 3.

Work up of the reaction mixture by column chromatography resulted in isolation of 2-methylbenzothiazole (**16**) and dibenzothiophene (**19**), but GC/MS analysis showed that the major product was always benzonitrile (**8**). Other products detected were benzotriazine (**6**), benzothiazole (**21**), benzisothiazole (**24**), toluene (**10**), xylene (**11**), methylthiocyanate (**15**), tolunitrile (**9**) and biphenylene (**13**) (Scheme 3).

2.3. F.v.p. reactions of 3-phenylbenzotriazine (3)

Reactions were studied between 575 and 650°C and the results are summarized in Table 3.

As mentioned before, this compound was briefly studied by Rees et al.[8a] as part of their attempt to obtain benzazete from benzotriazines. These authors reported that biphenylene (**13**) was the only product (obtained in 40% yield) obtained at 870°C, at much higher temperature than used by us. Furthermore, there is no comment of appearance of **8** in this publication, which is the obvious expected product if benzyne (**12**) is formed affording **13** by dimerization. In our reactions, **8** is the major product (see Table 3) and we found only traces of **13**. Compound **8** may be formed from diradical **25** as shown in Scheme 4. We found no evidence for the formation of a phenylbenzazete which would be accompanied by appearance of red color.[8a]

3. Discussion

Comparison of the results here described suggests that in f.v.p. of **1** and **2**, radical chain reactions occur (many

Table 3. F.v.p. reactions of **3**

T (°C)	% **3**	% **8**
575	79.4	20.6
600	45.5	54.5
625[a]	27.5	72.5
650[b]	<5	>95

Quantified as relative amounts of **3** and **8**.

[a] Compound **13** was detected but not quantified.

[b] At this temperature small amounts of naphthalene were found as well as of **13**.

products are formed which contrasts with that of **3**). This seems to be strongly supported by formation of bibenzyl when toluene was used as carrier gas. There are two main routes to explain the different products found in reactions of **2**, which are depicted in Scheme 3 (structures of products detected in the reaction mixture are framed). One of these ways is loss of SCH_3 and H abstraction to afford **6** (route *a*) which affords benzyne (**12**) and biphenylene (**13**) as described by Rees et al.[8] (routes *b*,*c*,*d*). As in reactions of **1**, it was not possible to distinguish how SCH_3 groups are lost (one or two steps) and no 2-methylsulfanylbenzimidazole was found in the reaction mixture.

Route *e* is the expected nitrogen extrusion reaction with formation of diradical **14**. This diradical can afford three different reactions:

(i) Formation of **12** (subsequently **13**) and **15** (routes *f*,*g*).

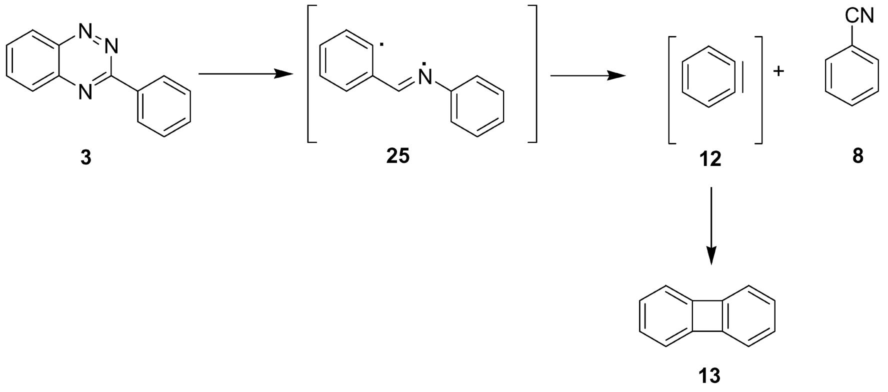
(ii) Formation of isonitrile and rearrangement to **8** (routes *h*,*i*), which is a well known reaction of isonitriles.[14] Formation of tolunitrile (**9**), toluene (**10**), and xylene (**11**) can be interpreted by radical processes generally known from earlier f.v.p. studies: a benzene radical formed from **8** can react with a methyl radical to afford **10** (routes *j*,*k*), and **11** can be obtained by reaction with another methyl radical (route *l*). Furthermore, **8** can also react with a methyl radical to give **9** (route *m*). To check this hypothesis, some **8** was subjected to f.v.p. at 650° (the upper limit in reactions of **1**) and at 750° (the upper limit in reactions of **2**). In reactions at 650°, **8** remained unchanged while at 750° some products—e.g. benzene—were found in the NMR and GC/MS experiences. The presence of benzene reveals formation of phenyl radicals under these experimental conditions. In reactions of **8** with toluene as carrier gas, bibenzyl was found and, surprisingly, **9** showing that methyl radicals were also formed from toluene.

(iii) Diradical **14** can undergo a [1,2] CH_3 shift (route *n*) and then a subsequent ring closure affords 2-methylbenzothiazole (**16**) (route *o*). From **16**, radicals **17**, **20**, and **22** may be formed (routes *s*,*p*). There are some reports of C_{Ar}–CH_3 bond fission, for example in reactions of 2-methylpyridine *N*-oxide where pyridine is formed in 23% yield.[13b] This reaction is obviously due to the presence of radicals in the system: this study concluded that H atom is first abstracted by another radical to give ($Ar-CH_2^{\cdot}$) and, subsequently, ($Ar^{\cdot}$) is formed. Along this series of equilibria, **21** is formed (route *q*), whereas **23** is precursor of **24** (route *r*), both transformations imply H abstraction reaction. Formation of **19** can be explained by formation of diradical **17** (route *s*) which can dimerize to the supposed intermediate **18** (route *t*),[15] which is known to lose S (route *u*) to give **19**.[13a]

With the attempt to complete these studies, f.v.p. treatment of 3-phenyl-1,2,4-benzotriazine (**3**) was repeated.[8] The only reaction products were **8** and **13**, which reveals that the parallel reactions present in reactions of **1** and **2** were due to the presence of the SCH_3 group (radical chain reactions, and formation of benzisonitrile) and they are not formed from the 1,2,4-benzotriazine ring itself. The 1,2,4-benzotriazine ring under f.v.p. conditions affords, in turn, a diradical by nitrogen loss and not a radical chain reaction, similar to the reactions of 1,2,3-benzotriazines cited above.[8] The absence of the radical chain reaction in the case of **3** is obviously a consequence of the stronger C–phenyl bond compared to the C–S bond, also supported by the finding that compounds **9**–**11** were not detected among the products.

4. Conclusion

In this systematic study of f.v.p. reactions of 1,2,4-benzotriazines, no experimental evidence of benzazete was found and formation of the reaction products has been interpreted by different mechanisms. This result reveals that the behavior of 1,2,4-benzotroazines and 1,2,3-benzotriazines under f.v.p. conditions are basically different. The *N*-oxide 1,2,4-benzotriazine afforded either O loss followed by a series of radical reactions, or underwent



Scheme 4.

some transformations retaining the O atom and simultaneous nitrogen extrusion. Although benzonitrile is one of the products in all reactions, it is not formed by the same mechanism in all of the studied compounds. It was also demonstrated that benzonitrile can react at temperatures over 700°C affording phenyl radical.

5. Experimental

5.1. General

Reactions were carried out in a vycor glass f.v.p. equipment using a Thermolyne 21100 tube furnace with a temperature controller device. Oxygen free dry nitrogen or a mixture of nitrogen/toluene was used as carrier gas. Samples to be pyrolyzed were 30–50 mg. Contact times were around 10^{-2} s and pressures of 0.2–0.1 Torr were measured with a McLeod manometer. Products were trapped at the liquid air temperature, extracted with solvent and submitted to different analyses or separation techniques. Gas chromatography/mass spectrometry (GC/MS) analyses were performed in a Perkin–Elmer Q-Mass 910 spectrometer equipped with an SE-30 column, using Helium as eluent gas at a flow rate of 1 mL/min and a heating rate of 40°C for 5 min and 40–280°C for 35–40 min. Mass spectra were obtained in the electron impact mode (EI) using 70 eV as ionization energy. ^{1}H NMR and ^{13}C NMR spectra were carried out in $CDCl_3$ in a Bruker 200 FT spectrometer (at 200 MHz). Chemical shifts are reported in parts per million (ppm) downfield from TMS. Column and thin layer chromatography were performed on silica gel. Recovery of material was >90% in all in f.v.p. experiments.

5.1.1. F.v.p. reactions of 3-methylsulfanyl-1,2,4-benzotriazine *N*-oxide (1).[16,19] F.v.p. reactions were carried out between 400 and 750°C under pressures around 10^{-2} Torr and contact times 10^{-2} s, approximately; the mass balance was >90%. Between 500 and 600°C the only detected product was **2**. Reaction products were extracted from the cold trap with $CDCl_3$ and submitted to ^{1}H NMR. Results depicted in Table 1 were calculated as relative amounts using ^{1}H NMR. Products of reactions carried out at higher temperatures were dissolved in acetone and submitted to GC/MS analysis. Products were identified by their MS spectrum by comparison with those reported in the NIST database.[17] To check the presence of radicals, a mixture of nitrogen/toluene vapors was used as carrier gas. Reaction products were analyzed by TLC and GC/MS using authentic bibenzyl sample to detect the presence on bibenzyl in the reaction mixture.

5.1.2. F.v.p. reactions of 3-methylsulfanyl-1,2,4-benzotriazine (2).[16] F.v.p. reactions were carried out under the following conditions: temperature between 400 and 750°C, pressure: 10^{-2} Torr, and contact time 10^{-2} s, approximately. The mass balance was >70%. Between 650 and 750°C reaction products were extracted from the cold trap with acetone and submitted to column chromatography and GC/MS. Results depicted in Table 2 were calculated as relative amounts. Column chromatography was performed over silica gel with hexane–chloroform (1:1) as an eluent. In order to carry out this separation, products of several reactions carried out a 750°C were collected and evaporated (thus, no volatile products were present in the mixture). The only isolated products with this procedure were **16** and **19** identified by comparison of their ^{1}H NMR and MS spectra with those previously reported;[18] MS: **16**: $M^+=149$ (EPA MS number 4603), **19**: $M^+=184$ (EPA MS number 133303). The identity of **8** was established by comparing the ^{1}H NMR signals and the mass spectrum with those of a commercial sample, $M^+=103$ (EPA MS number 60870); **6**: MS=131; **21**: $M^+=135$ (EPA MS number 249193); **24**: $M^+=135$ (isomer of **21** with identical MS); **9**: $M^+=117$ (EPA MS numbers 118648, 118646, 2005, three isomers); **15**: $M^+=73$ (EPA MS number 118611), ^{1}H NMR: δ: 2.69;[18] **10**: $M^+=92$ (EPA MS number 61211); **11**: $M^+=106$ (EPA MS number 1349, 228010, 150812, three isomers); **13**: $M^+=152$ (EPA MS number 118587).

5.1.3. F.v.p. reactions of 3-phenyl-1,2,4-benzotriazine (3).[20] F.v.p. reactions of **3** were performed between 575 and 650°C, pressures around 10^{-2} Torr and contact times around 10^{-2} s; the mass balance was >90%. After the reactions were completed, the reaction products were extracted from the cold trap either with acetone for GC/MS or with $CDCl_3$ for NMR analysis. Results depicted in Table 3 were calculated as relative amounts obtained by GC/MS. The identity of **8** was established by comparing the ^{1}H NMR signals and the mass spectrum with those of the commercial sample, $M^+=103$ (EPA MS number 60870). Compound **13**: $M^+=152$ (EPA MS number 118587).

5.1.4. F.v.p. reactions of 8. Reactions of **8** were carried out to check its stability under the reaction conditions and the reaction mixtures were analyzed by ^{1}H NMR and GC/MS. In reactions carried out at 650°C only unchanged compound **8** was detected, whereas in reactions carried out at 750°C benzene and unchanged **8** were present. To check if this was a radical chain reaction, a mixture of nitrogen/toluene vapors was used as a carrier gas. The analysis of the reaction mixture afforded bibenzyl tolunitrile (**9**).

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