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Flash Vacuum Pyrolysis of Aromatic Oximes

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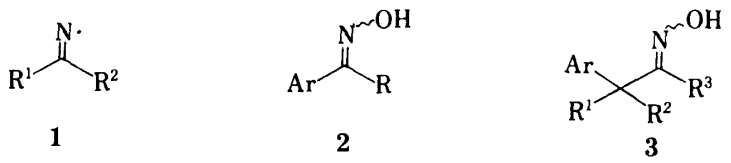
Flash vacuum pyrolysis (FVP) of benzaldoximes and aryl ketoximes afforded nitriles and additional aromatic compounds which were presumably generated from intermediary iminyl radicals. The FVP also gave benzoxazoles, which were presumably formed from iminoxyl radicals. Benzyl ketoximes afforded indoles together with fragmentation products of the iminyl radicals.

Keyword——gas-phase pyrolysis; flash vacuum pyrolysis; FVP; flash thermolysis; oxime; iminyl radical; iminoxyl radical; substituted indole; benzoxazole; mass spectra

In the chemistry of gas-phase pyrolysis of organic compounds,[1] it is known that some azines[1,2a] and oximes[1,2b] are subject to fragmentation reactions, and recently it has been reported that some conjugated hydrazones[3] and oximes[4] undergo cyclization reactions. In related works, it has also been found that thermal decomposition of some oximes and azines in solution affords cyclization products,[5] as does photolysis of certain oximes in solution.[6] All these fragmentations and cyclizations can be rationalized in terms of the formation of intermediary iminyl radicals **1**.

As a part of our studies on flash vacuum pyrolysis (FVP) of organic compounds, we examined the FVP of aromatic oximes of types **2** and **3** (Chart 1) and found that cyclization reactions took place to give benzoxazoles and indoles, respectively.



1 **2** **3**

Chart 1

Oximes were pyrolyzed at approximately 800°C and 0.001—0.01 mmHg,[7] and calculated contact times were in the range of 2—30 ms (see "Experimental"). As expected on the basis of the intermediary iminyl radicals (**1**) generated by N–O bond fission of the starting materials, FVP of benzaldoxime (**2a**, Ar=Ph, R=H) afforded benzonitrile (91%) and a small amount of benzene (2%), and likewise, *o*-hydroxybenzaldoxime (**2b**, Ar=*o*-hydroxybenzonitrile (70%) and a trace of phenol (Chart 2).

Next, aryl ketoximes **2c**—**h** were pyrolyzed, and the results are summarized in Table I. Ketoximes **2c**—**h** gave benzonitrile and benzene without exception. In most cases, counterpart nitriles (RCN) and aromatic compounds (RH), and products of coupling reactions (toluene, biphenyl, bipyridyl) were also formed. These data are consistent with the formation and fragmentation of the intermediate radical **1** (Chart 2).

Nevertheless, the formation of benzene and toluene in the FVP of **2c** is rather unexpected, in view of the known character of the iminyl radical generated in FVP of acetophenone azine, where the formation of these compounds is rare.[2a]

A characteristic feature of FVP of **2c**—**h** is the formation of benzoxazoles (**4** and/or **5**). The formation of **5** from the corresponding **2c**—**h** can be explained by an intramolecular addition of the conjugation-stabilized iminoxyl radical **6**[8] to the aromatic ring (Chart 3).

Table I. FVP of Aryl Ketoximes

2[a]	R	Products (Yield %) PhCN	RH	RCN	PhH	4[b]	5	Other products (%)
2c	Methyl	71	[c]	[c]	4	—	12[d]	Toluene (3)[e]
2d	Phenyl	45	(29)	(45)	29	20	(20)	Biphenyl (22)
2e	*o*-Methylphenyl	14	17	2	24	12	Trace[f]	[e]
2f	*o*-Hydroxyphenyl	14	17	0	28	32	4[g]	[e]
2g	*o*-Aminophenyl	13	7	46	14	22	4[h]	Biphenyl (8)
2h	2-Pyridyl	77	20	4	9	—	11[i]	Bipyridyl (12)[e]

a) For some oximes, the *syn*-isomer, *anti*-isomer, and their mixture were pyrolyzed separately and comparatively, but the difference in the results was negligible (see "Experimental").
b) Colorless needles from pentane, mp 102—103°C; K. Nakagawa, H. Onoue, and J. Sugita, *Chem. Pharm. Bull.*, **12** 1135 (1964) and ref. in footnote *f*.
c) These products were not confirmed.
d) Pale yellow oil, bp 182°C/760 mmHg; C. J. Pouchert and J. R. Campbell (ed.), "The Aldrich Library of NMR," 1974; C. J. Pouchert (ed.), "The Aldrich Library of IR," 1975.
e) Biphenyl was not isolated in these runs, although it was presumed to be formed (probably in low yields).
f) 2-(*o*-Tolyl) benzoxazole, colorless needles from pentane mp 63—66°C, NMR δ 2.80 (3H, s, CH_3), 7.28—7.46 (5H, m), 7.57 (1H, dd, J=4, 6 Hz), 7.78 (1H, dd, J=2, 6 Hz), 8.17 (1H, dd, J=2, 6 Hz), IR (KBr) 1613 (s), 1550 (s), 1488 (s), 1450 cm^{-1} (s); R. Passerini, *J. Chem. Soc.*, **1954** 2256.
g) 2-(*o*-Hydroxyphenyl)benzoxazole, colorless needles from pentane, mp 122—122.5°C, NMR δ 6.89—7.74 (7H, m), 7.98 (1H, dd, J=2, 6 Hz), 11.45 (1H, br s), IR (KBr) 3050 (m) 1623 (s), 1585 (s), 1480 (s), 1450 (s), 1405 cm^{-1} (s), see ref. in footnote *b*.
h) 2-(*o*-Aminophenyl)benzoxazole, colorless plates from pentane, mp 105—105.5°C, NMR δ 5.87 (2H, brs), 6.66—6.89 (2H, m), 7.17—7.37 (3H, m), 7.44—7.73 (2H, m), 8.06 (1H, dd, J=2, 6 Hz), IR (KBr) 3440 (m), 3330 (m), 1620 (s), 1537 (s), 1493 (s), 1449 cm^{-1} (s); T. H. Haskel, F. E. Peterson, D. Watson N. R. Plessas, and T. Culbertson, *J. Med. Chem.*, **13**, 697 (1970), see ref. in footnote *b*.
i) 2-(2-Pyridyl)benzoxazole, colorless prisms from hexane, mp 107—107.5°C, NMR δ 7.34—7.53 (3H, m), 7.62—7.99 (3H, m), 8.38 (1H, d, J=8 Hz), 8.83 (1H, dd, J=1, 5 Hz), IR (KBr) 1581 (s), 1550 (s), 1450 (s), 1437 cm^{-1} (s); T. R. Harkins, J. L. Walter, O. E. Harris, and H. Freiser, *J. Am. Chem. Soc.*, **78**, 260 (1956).

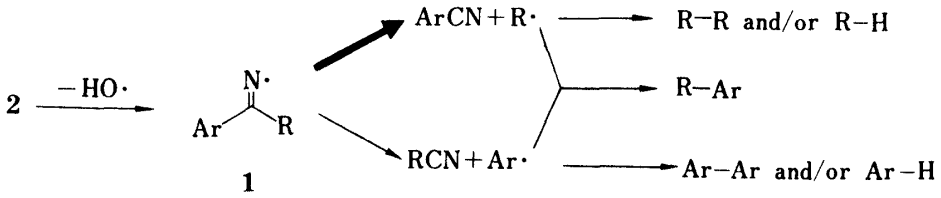


Chart 2

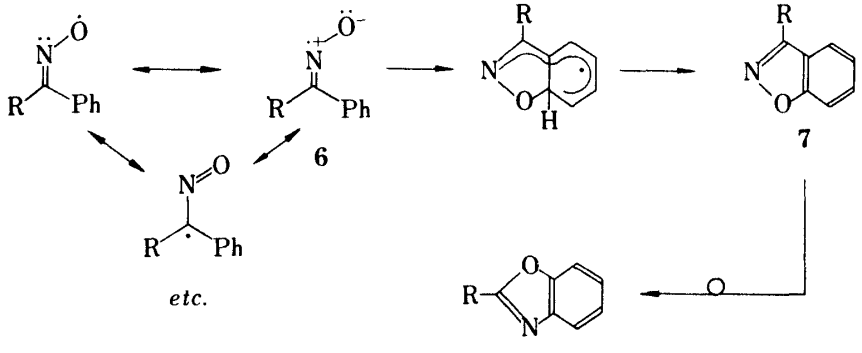


Chart 3

Isomerization of 1,2-benzisoxazole(**7**, R=Ph) to **4**, in FVP, is known.[1,9] The cyclization, however, is rather unusual in terms of the reactivity of common iminoxyl radicals generated by oxidation of oximes in solution, where the radicals tend to dimerize.[8,10]

The formation of 2-phenylbenzisoxazole **4** from **2e, f, g** is quite striking; **4** might be derived *via* loss of a substituent group (methyl, hydroxy, or amino group) on the benzene ring of the starting materials.

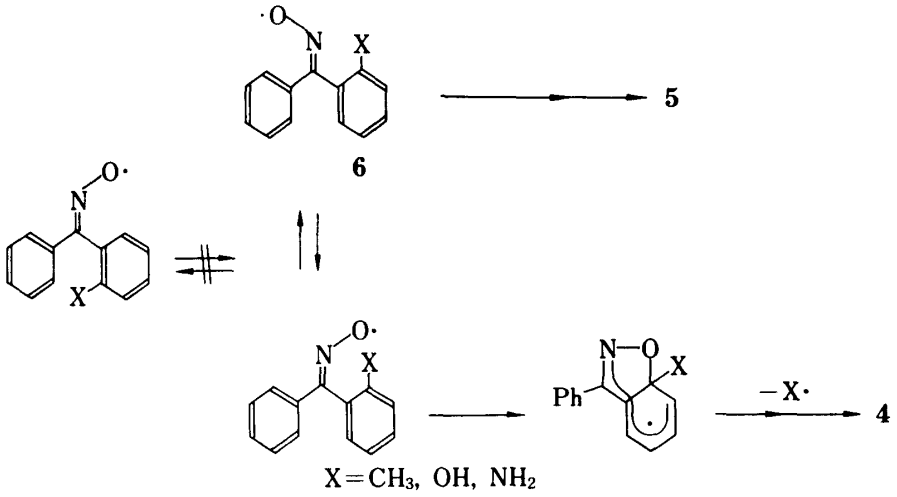


Chart 4

As for the orientation of cyclization, the preferential formation of **4** and/or **5** rather than that of 4-substituted 2-phenylbenzoxazoles from **2e, f, g** can be explained by consideration of the steric repulsion between the phenyl group and the substituent group X, and of the conformational geometry of the radical **6** (Chart 4).

Relationships between thermal behavior and mass spectral behavior have often been discussed, and the similarity of the FVP and electron-impact behaviors has been pointed out in some cases.[1] Some mass spectral data for **2d—g** are listed in Table II.

Table II. EI Mass Spectra of Aryl Ketoximes

		Ions (%)						
2	X	M^+	$[M-H]^+$	$[M-X]^+$	$[M-CO-H]^+$	$[M-CO-X]^+$	$[M-OH]^+$	Base *m/e*
2d	H	100	15.6		11.4		96.5	197 (M^+)
2e	CH_3	37.2	11.1	20.8	v.w.[a]	v.w.	100	195 ($[M-OH]^+$)
2f	OH	55.4	2.2	35.0	v.w.	12.5	35.0	195 ($[M-H_2O]^+$)
2g	NH_2	100	9.7	17.4	v.w.	7.2	53.2	212 (M^+)

a) v.w. less than 1.0%

The fragmentation courses, $2^{+\cdot}\rightarrow$**8**$\rightarrow$**9** and **8**$\rightarrow$**10**$\rightarrow$**11** are well established for the EI mass spectrum of benzophenone oxime **2d**.[11] It is noteworthy that the cyclization orientations of these oximes in FVP are analogous to their mass spectral behavior; namely, not only are the intensities of $[M-X]^+$ (which are assignable to the ion **9A**) stronger than those of $[M-H]^+$ (assigned to **9B** and/or **9C**)[11] in the mass spectra of **2e, f, g**, but also the ions $[M-CO-X]^+$ (assigned to **11A**) precede the ions $[M-CO-H]^+$ (**11B** and/or **11C**)[11] in the mass spectra of **2f** and **2g**.

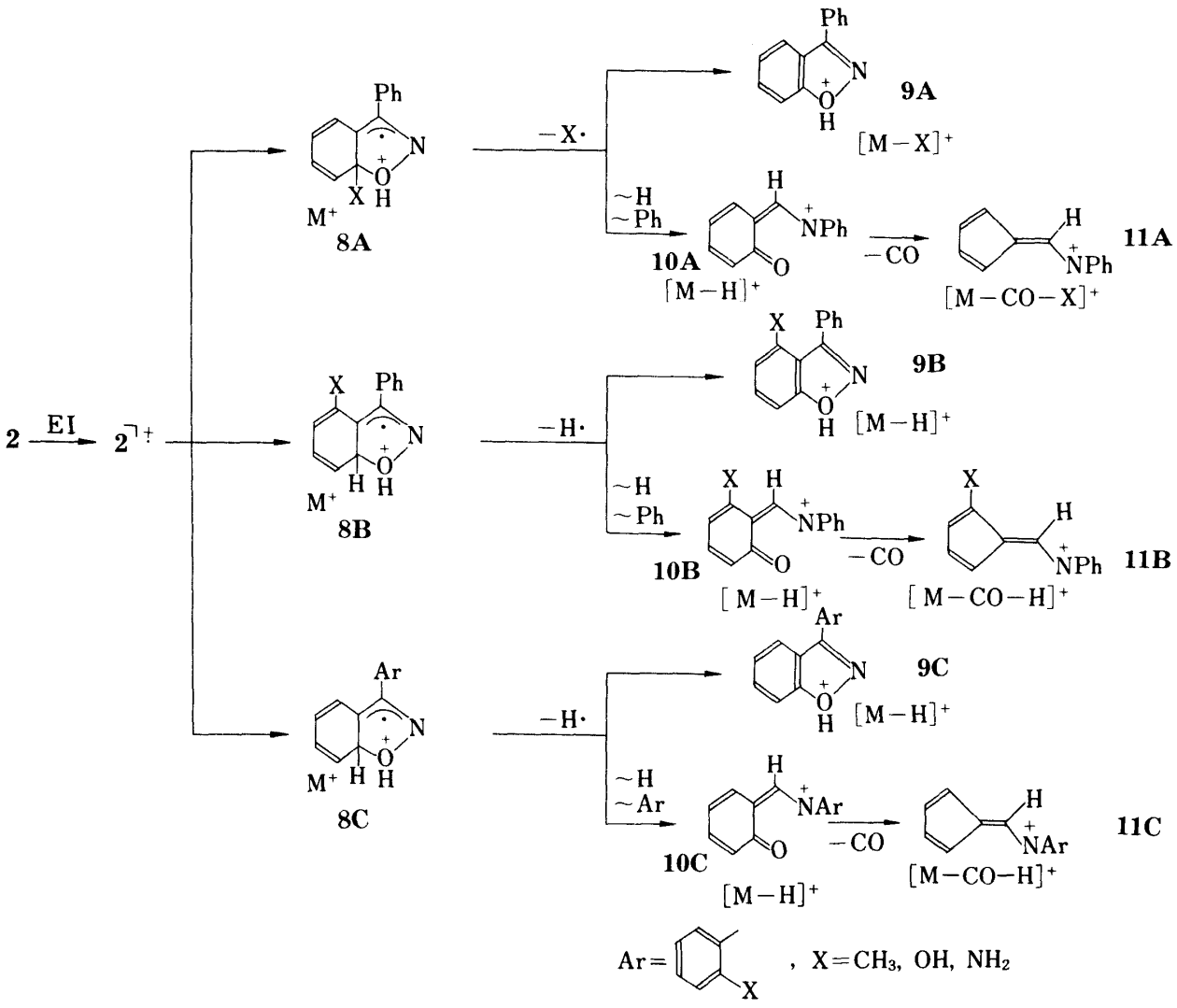


Chart 5

The question of whether the iminoxyl radicals were derived from thermal dissociation of the O–H bond of the oximes, or through intermolecular hydrogen abstraction from the O–H group of the oximes still remains unresolved in the present FVP study.
Further, the formation of *o*-methylbenzonitrile (2% from **2e**), *o*-hydroxybenzonitrile (0% from **2f**), and picolinonitrile (4% from **2h**) compared with the predominant formation of benzonitrile and *o*-aminobenzonitrile (46% from **2g**) cannot be explained from the present data.

Next, pyrolysis of oximes of type **3** was carried out, with the results shown in Table III. Predominant formation of bibenzyl and toluene in FVP of phenylacetaldoxime (**3a**) and benzyl phenyl ketoxime (**3b**) suggests the facile formation of the stable benzyl radical by fragmentation of the intermediate iminyl radical **12** (Chart 6).

The nature of the products of pyrolysis of (2-pyridyl)acetone (**3e**) suggests not only the formation of the 2-picolyl radical **13e** from **12e** but also considerable stability of **13e**. Further, pyridine, 2-picoline, 2-ethylpyridine, 2-vinylpyridine and 1,2-bis(2-pyridyl)ethane are common products in FVP of 2-picoline *N*-oxide, in which formation of the radical **13e** has been assumed.[12] Similarly, the results in FVP of (2-thienyl)acetone oxime suggest the participation of the (2-thienyl) methyl radical (**13g**). Benzyl alcohol in FVP of **3a** and **3b** would be

Table III. FVP of Aldoxime and Ketoximes

3[a]	Ar	R^1	R^2	R^3	Products (Yield %) ArH	ArMe	ArEt	$ArCH=CH_2$	$(ArCH_2)_2$	R^3CN	14	Other products (%)[b]
3a	Ph	H	H	H	3	39	4	Trace	32	[c]	9	[d]
3b	Ph	H	H	Ph	10	18	Trace	3	20	68	22[e]	[f]
3c	Ph	Me	H	Ph	13	—	6	71	—	59	4[g]	
3d	Ph	Me	Me	Ph	18	Trace	Trace	7	—	93	—	[h]
3e	2-Pyridyl	H	H	Me	18	32	11	5	32[i]	[c]	[j]	
3f[k]	2-Furyl	H	H	Me	—	2	—	—	—	Quant.	—	
3g	2-Thienyl	H	H	Me	10	15	—	—	19[l]	Quant.	—	

a) See footnote *a* of Table I.
b) Only isolated products are noted.
c) These compounds were not confirmed.
d) Phenylacetonitrile (3%) and benzyl alcohol (5%).
e) 2-Phenylindole, colorless needles from hexane, mp 187—188°C; see refs. in footnote *d* of Table I.
f) 2-Benzylbenzoxazole[m] (trace), benzyl alcohol (5%), and phenylacetonitrile (2%).
g) 3-Methyl-2-phenylindole, colorless needles, mp 89—91°C, C. E. Blades and A.L. Wilds, *J. Org. Chem.*, **21**, 1013 (1956); H.M. Kissman, D.W. Farnsworth, and B. Witkop, *J. Am. Chem. Soc.*, **74**, 3948 (1952).
h) 2-Phenylpropene (80%).
i) 1,2-Bis(2-pyridyl)ethane, mp 50—51°C; see ref. 12.
j) 2-Methylpyrrolo[3,2-*b*]pyridine[n] (**14e**, 4%) and 2-methylpyrazolo[1,5-*a*]pyridine[o] (**15**, 3%).
k) FVP of **3f** was carried out at 650°C and 800°C; acetonitrile was the major component of a complicated product mixture in both cases.
l) 1,2-Bis(2-thienyl)ethane, colorless prisms from pentane, mp 66—67°C, NMR δ 3.16 (4H, s, CH_2-CH_2), 6.68—7.11 (6H, m); R. Gaertner, *J. Am. Chem. Soc.*, **73**, 3934 (1951).
m) Colorless oil (bp 150—160°C/ 4 mmHg), IR (Neat) 1610 (s), 1567 (s), 1453 (s), 1240 (s), NMR δ 4.23 (2H, s), 7.12—7.41 (8H, m), 7.59 (1H, dd, J=2, 7 Hz); G. I. Braz, G. V. Mayasnikova, and A.Y. Yakubovich, V.P. Bazov, I.E. Kardash, and A.N. Pravednikov, *Khim. Geterotsikl. Soedin.*, **1967**, 215.
n) Colorless prisms from benzene-$(isopr)_2O$, mp 192—193°C, NMR δ 2.50 (3H,s, CH_3), 6.42 (1H, s, 3-H), 7.01 (1H, dd, J=4, 5 Hz, 6-H), 7.55 (1H, dd, J=1, 5 Hz, 7-H), 8.36 (1H, dd, J=1, 4 Hz, 5-H), 9.04 (1H, br s, NH); G.R. Clemo and G.A. Swan, *J. Chem. Soc.*, **1948**, 198.
o) Pale yellow oil, picrate mp 137—138°C, IR ($CHCl_3$) 2970 (s), 2930 (s), 1633 (s), 1523 (s), 1490 (m), 1428 (m), 1335 (s), 1253 (s), 1143 cm^{-1} (m), UV (EtOH) 225, 229, 283 nm; Y. Tamura, A. Yamakami, and M. Ikeda, *Yakugaku Zasshi*, **91**, 1154 (1971).

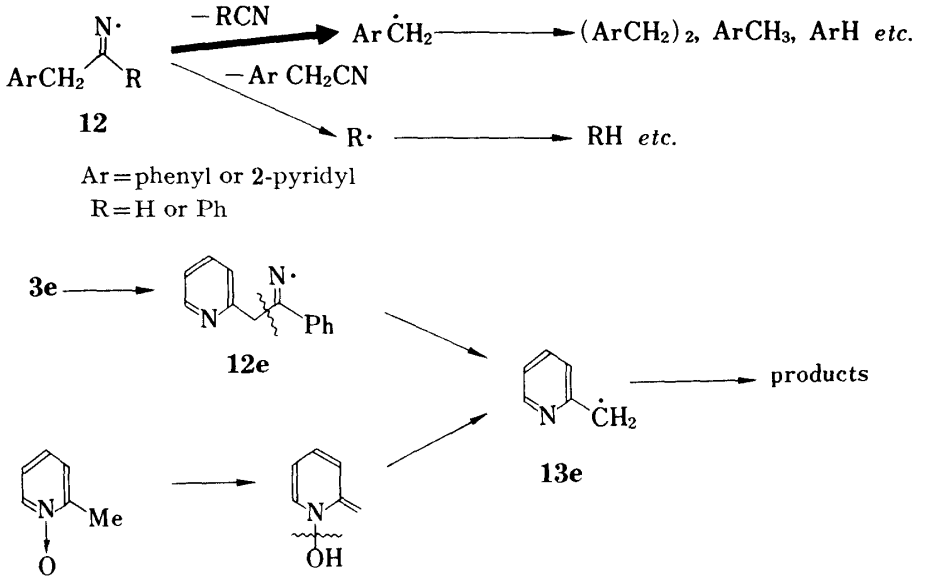
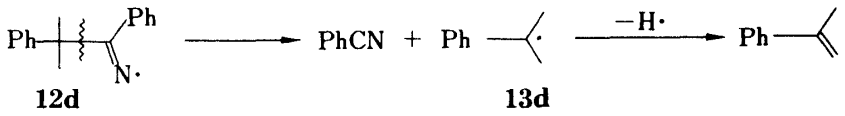


Chart 6

produced *via* coupling between a hydroxyl radical and benzyl radical. Predominant formation of 2-phenylpropene and benzonitrile in pyrolysis of the dimethyl derivative **3d** indicates the presence of the intermediary radical (**13d**) which could be generated from **12d** (Chart 7).



12d 13d

Chart 7

The most characteristic feature of FVP of **3** is the formation of indoles (**14**) and a pyrazolopyridine (**15**) from the oximes **3a**—**c** and **e** where R^2=H. These compounds are presumed to be formed from **12** through intramolecular addition of the radical (**12**) or of the enaminyl radical (**16**) to the aromatic ring (Chart 8).

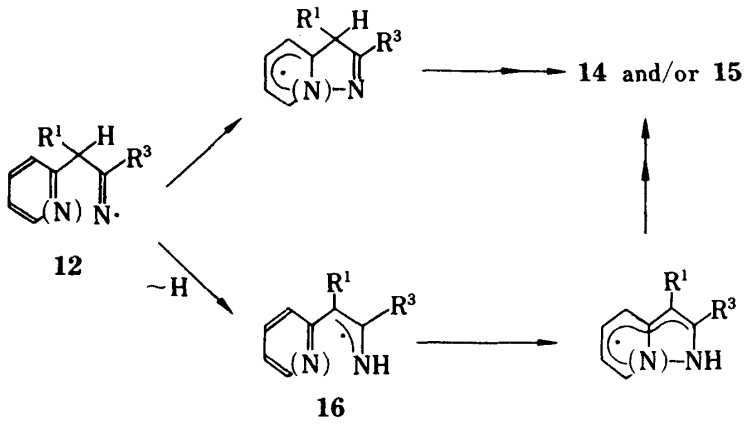


Chart 8

Although the formation of iminoxyl radicals (**6**) and cyclization to benzoxazoles (**5**) were expected to occur, their participation was very minor in these cases (thus, only a trace of 2-benzylbenzoxazole was obtained in FVP of **3b**).

The formation of benzyl phenyl ketiminyl radical (**12b**) in solution has been reported,[13] but the character of the radical in the present reaction appreciably differed from the reported behavior of **12b**, as neither benzene nor 2-phenylindole was produced from **12b** in the solution reaction.

Finally, the poor production of the furan derivative in FVP of **12f** might be due to instability of the furan derivatives to heat and further pyrolytic fragmentations.

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded on a JASCO A-102, ultraviolet (UV) spectra on a Hitachi 340, and NMR on a JEOL FX-100 (δ from TMS, in $CDCl_3$). Vapor phase chromatography (VPC) was carried out using a Shimadzu GC-4B instrument with a column (210 cm × 2 mm) packed with 2% OV-17 or 2% SE-30 on Chromosolv-W at appropriate pressure (N_2) and temperature. Mass spectra were measured on a JEOL JMS-D300 mass spectrometer (ionization was carried out at 70 eV). Physical data for some products are shown in the tables.

Materials——Oximes (**2** and **3**) were obtained from the corresponding ketones according to the usual method for oxime synthesis. In several cases, separation of *syn*- and *anti*-isomers was feasible and in these cases, pure *syn*-isomer, pure *anti*-isomer, and *syn-anti* mixture were pyrolyzed separately and comparatively. The difference among the results of these separate pyrolyses was insignificant. Thus, the present data take no account of the contents of the *syn*- and *anti*-forms of the oximes.

Pyrolysis Method——FVP were carried out at 800°C and 0.001—0.01 mmHg using an apparatus described in our previous papers.[12] Calculated approximate contact times were in the range of 0.002—0.03 s, depending upon the pressure and the sublimation time of the oximes.[7] Products were collected in traps cooled with liq. N_2 and the collected mixture was separated into a residual portion and a distillable one (bp $\leq$80°C/0.1

mmHg). The former was subjected to alumina or silica column chromatography and eluted with hexane–ether. The latter was subjected to VPC for the identification and estimation of the volatile products. Some volatile products were identified by using a VPC-MS (JEOL JMS-D300) system without isolation.

References and Notes

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7) Carrier gas was not employed. The influences of pressure and contact time in the ranges shown were slight, although variation of the reaction temperature seriously affected the yields of the products.
8) For example, see J.L. Brokenshire, G.D. Mendenhall, and K.U. Ingold, *J. Am. Chem. Soc.*, **93**, 5278 (1971); J.R. Thomas, *ibid.*, **86**, 1446 (1964); H. Lemaire and A. Rassat, *Tetrahedron Lett.*, **1964**, 2245; and ref. 9.
9) Almost quantitative isomerization of **7** (R=Ph) to **4** (**5**) was observed in our run under these conditions, see also J.D. Pérez, G.I. Yranzo, and D.A. Wunderlin, *J. Org. Chem.*, **47**, 982 (1982).
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