Molecular Rearrangements. XXVIII. Thermolysis and Photolysis of Some Hydroxamic Acid Derivatives

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Thermolysis and photolysis of benzohydroxamic acid and some of its derivatives have been investigated. Thermolysis of benzohydroxamic acid (BHA) either by heating in air or in a sealed tube gives NH_3, H_2O, CO, benzil, aniline, *o*- and *p*-aminophenols, phenoxazine, benzanilide, and benzoic acid. Whereas, thermolysis of *N*-(benzyloxy)benzamide (BBA) affords toluene, benzaldehyde, bibenzyl, stilbene, phenanthrene, acridine, and *o*- and *p*-aminodiphenylmethane in addition to the previous products. Analogous products were also obtained on pyrolysis of phenylacetohydroxamic acid. Photolysis of BHA and BBA in acetonitrile gives similar results to those of pyrolysis. A free-radical mechanism involving homolysis at different sites was postulated to account for the formation of such products.

Hydroxamic acids which have long been used for treatment of recurrent kidney stone formation were incriminated as potential carcinogens.[1)] The current concept is that the carcinogenic activity is further enhanced by *O*-esterification. The base-catalyzed rearrangement of hydroxamic acids to primary amines was first described by Lossen.[2)] Later, Tiemann[3)] reported the noncatalyzed Lossen rearrangement where he obtained aniline and CO_2 by the destructive distillation of benzohydroxamic acid. Moreover, refluxing of some hydroxamic acid derivatives in dimethyl sulfoxide as polar solvent was reported[4,5)] to proceed through an ionic mechanism, where *o*-(aroyloxy)arenecarboxanilides were obtained from *N*,*O*-diacyl-*N*-phenylhydroxylamine through heterolysis of the N–O bond. This prompted us to study the thermal and photostability characteristics of such class of compounds.

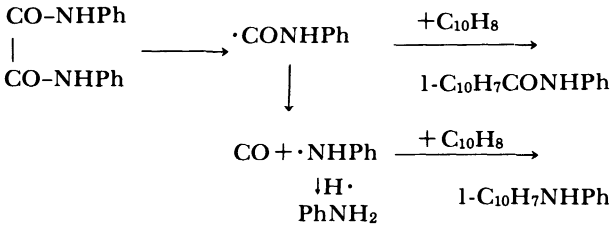
Thermolysis of benzohydroxamic acid (BHA) by heating in air at 240 °C for 30 min. leads to the formation of ammonia, water, carbon monoxide, benzil, aniline, *o*- and *p*-aminophenols, phenoxazine, benzanilide, benzoic acid, and ammonium benzoate (Table 1).

Similary, thermolysis of *N*-(benzyloxy)benzamide (BBA) under the same conditions gives the above mentioned products in addition to toluene, benzaldehyde, benzyl alcohol, bibenzyl, stilbene, phenanthrene, *o*- and *p*-aminodiphenylmethane, and acridine (Table 1).

Phenylacetohydroxamic acid (PAH) on similar treatment gives ammonia, toluene, benzaldehyde, bibenzyl, stilbene, phenanthrene, and *N*-benzylphenylacetamide (Table 2). When pyrolysis of PAH was affected by heating at 270 °C for 10 h in a sealed tube under nitrogen, the same products except benzaldehyde were also obtained, in addition to another unknown by-product with mp 147—148 °C; ν_{NH_2} at 3320 and 3120 cm^{-1} and $\nu_{C=O}$ at 1625 cm^{-1}, whereas its microanalysis result points to the formula $C_{12}H_{13}NO_2$.

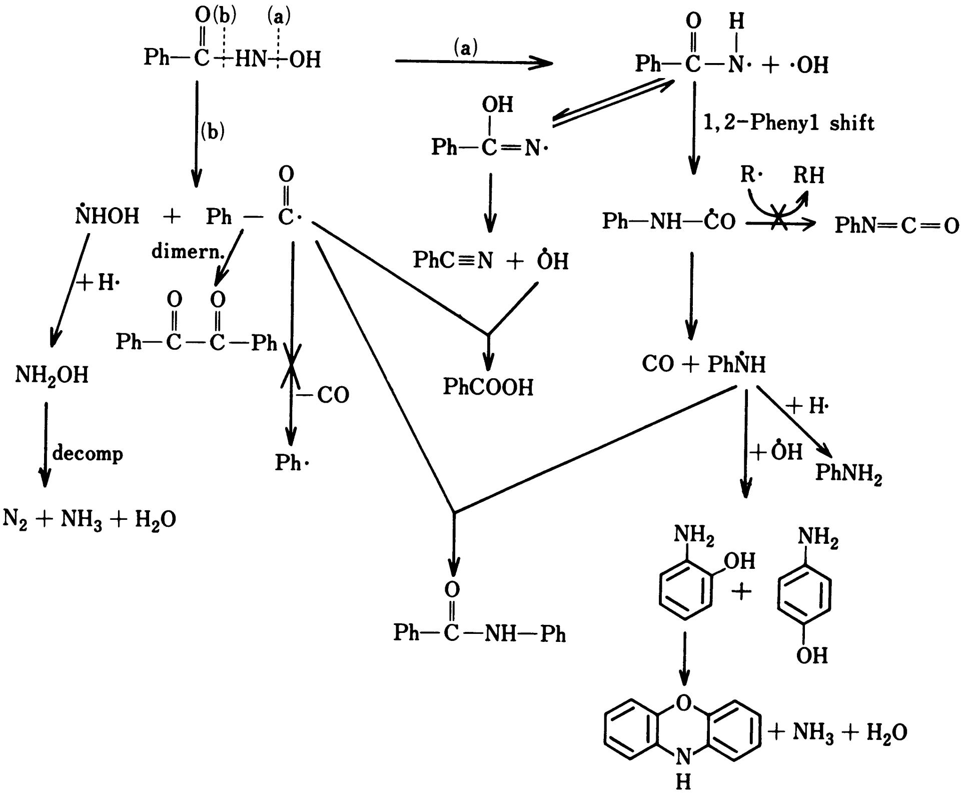
The formation of the identified products strongly points to a free radical mechanism starting by the preferential homolysis of the N–O bond of BHA (Scheme 1, route a) rather than C–N bond (route b) forming benzoylaminyl and hydroxyl free radicals on basis of bond energy values being of the order 48 and 70 kcal mol^{-1} respectively as observed by other workers.[5)] The benzoylaminyl radicals undergo rearrangement into *N*-phenylaminocarbonyl free radicals through a process of 1,2-phenyl shift involving a bridged radical intermediate. Subsequent decarbonylation of such radical leads to the formation of phenylaminyl radical which passes into aniline, *o*- and *p*- aminophenols, and phenoxazine as shown in Scheme 1.

Further evidence for the intermediate formation of *N*-phenylaminocarbonyl free radicals is the results obtained from pyrolysis of *N*,*N′*-diphenyloxamide in presence of naphthalene as solvent where substitution of the *N*-phenylaminocarbonyl radicals on the naphthalene nucleus occurs at position-1 forming 1-naphthanilide in addition to other fragmentation products of such radicals namely aniline, *N*-phenyl-1-naphthylamine, and carbon monoxide.



$$\begin{tikzcd} \begin{array}{l}CO\text{-}NHPh\\ |\\ CO\text{-}NHPh\end{array} \arrow[r] & \cdot CONHPh \arrow[r, "+C_{10}H_8"] \arrow[d] & 1\text{-}C_{10}H_7CONHPh \\ & CO+\cdot NHPh \arrow[r, "+C_{10}H_8"] \arrow[d, "H\cdot"] & 1\text{-}C_{10}H_7NHPh \\ & PhNH_2 & \end{tikzcd}$$

The observed low yield of *o*-aminophenol can be attributed to its incorporation in the formation of phenoxazine, ammonia and water. The formation of phenyl isocyanate was ruled out due to the absence of its condensation product with aniline, namely, *N*,*N′*-diphenylurea among the pyrolysis products. The probability of homolysis of the C–N bond (route b) into benzoyl and hydroxyaminyl radicals is worth considering to account for the formation of benzil, benzoic acid, and benzanilide as shown in Scheme 1. The benzoyl free radicals are involved in the formation of benzil, benzoic acid, and benzanilide



Scheme 1. Pyrolysis of BHA.

through processes of dimerization or coupling with hydroxyl or phenylaminyl radicals respectively. On the other hand, the hydroxyaminyl radicals undergo H-abstraction forming hydroxylamine, which ultimately decomposes into ammonia and water.⁶⁾

Thermolysis of BBA is suggested to proceed through homolysis of the N–O bond (route a; Scheme 2) forming benzyloxyl and benzoylaminyl radical pairs. The benzyloxyl radical are the precursor of benzaldehyde and benzyl alcohol through a disproportionation process, whereas the benzoylaminyl radical is transformed into benzonitrile. Other fates of benzoylaminyl radicals such as fragmentation into phenyl radicals and isocyanic acid, which ultimately undergoes hydrolysis by water to give ammonia and carbon dioxide, were ruled out due to the absence of CO_2 and biphenyl among the products.

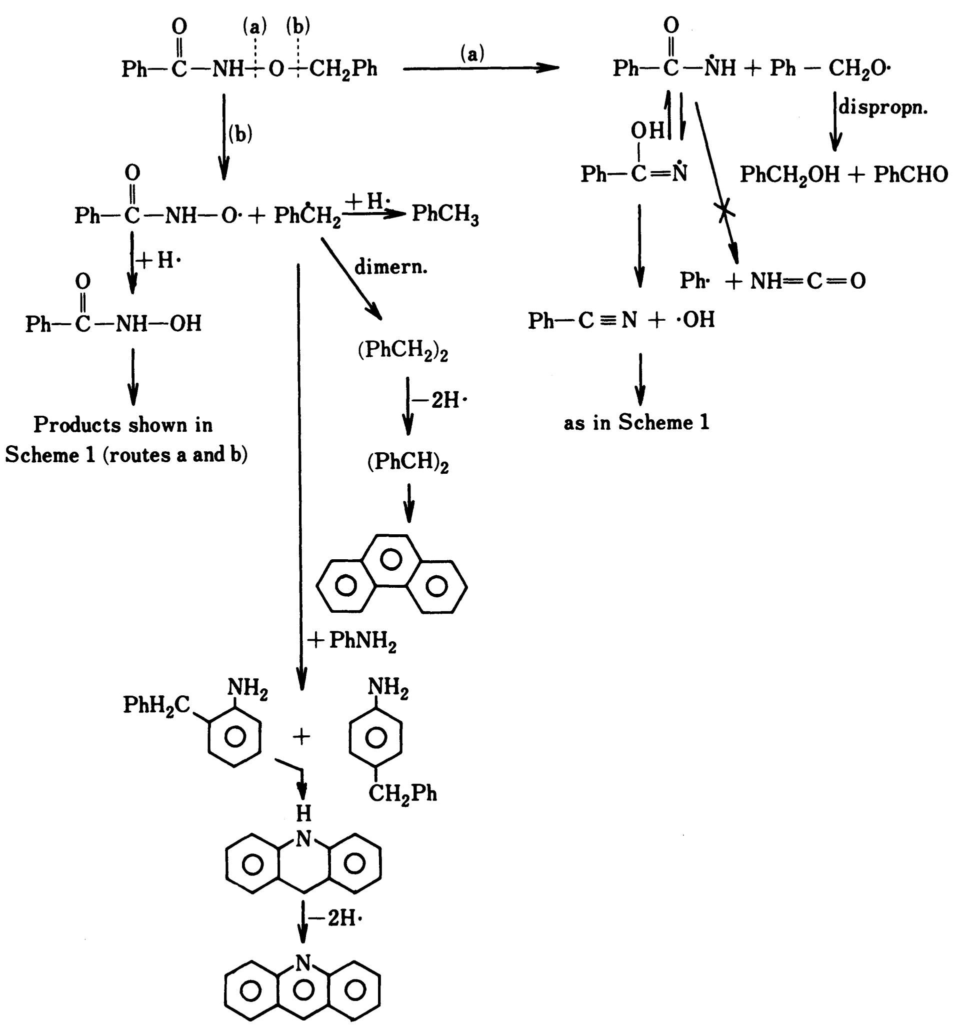
However, formation of products derived from benzyl radicals necessitates another pathway, involving homolysis of the benzyl–O bond (route b, Scheme 2) forming benzyl and benzohydroxamoyl radical pairs. The benzyl radicals are involved in the formation of toluene, bibenzyl, stilbene, and phenanthrene through processes of H-abstraction and/or dimerization, followed by dehydrogenation and cyclization respectively.

The formation of *o*- and *p*-aminodiphenylmethanes can be assumed to take place through attack of benzyl radicals on aniline formed in the reaction medium. Radical oxidative cyclization of some *o*-aminodiphenylmethane will ultimately lead to the formation of acridine.⁷⁾ A result which explains the low yield of *o*-aminodiphenylmethane as compared with its *p*-isomer. On the other hand, benzohydroxamoyl free radicals abstract hydrogen to form benzohydroxamic acid which passes into the products identified in Scheme 1, namely; benzil, benzoic acid, benzanilide, aniline, *o*- and *p*-aminophenols, phenoxazine, carbon monoxide, ammonia, and water.

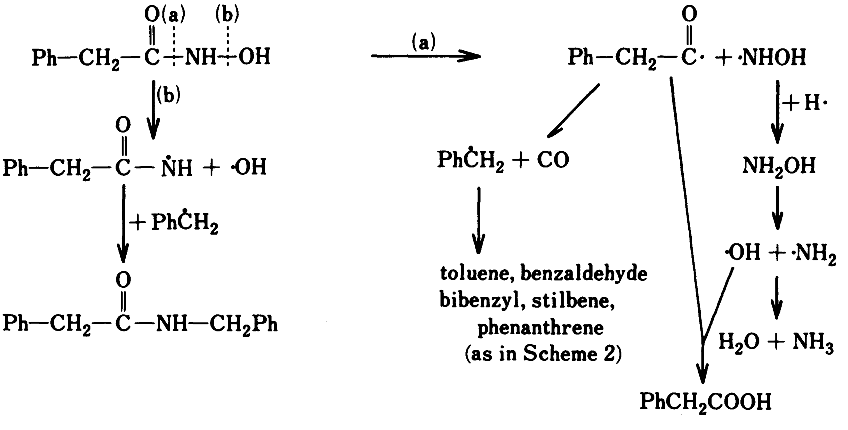
The products formed from pyrolysis of PAH by refluxing imply the homolysis of the $-\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{N}}-$ bond (route a), forming phenylacetyl and hydroxyaminyl radical paris (Scheme 3).

The phenylacetyl radicals decarbonylate⁸⁾ mainly into benzyl free radicals which are considered as the precursor of toluene, benzaldehyde, bibenzyl, stilbene, and phenanthrene as shown previously, whereas some of the phenylacetyl radicals form phenylacetic acid on coupling with hydroxyl free radicals which are considered as intermediates in the decomposition of hydroxylamine.⁶⁾

The formation of benzaldehyde can be reasonably assumed to be through atmospheric oxidation of benzyl radicals since absence of air on heating PAH in a sealed tube in nitrogen atmosphere does not give benzaldehyde among the products. The formation of *N*-benzylphenylacetamide necessitates homolysis of

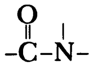


Scheme 2. Pyrolysis of BBA.



Scheme 3. Pyrolysis of PHA.

the N-OH bond (route b) forming hydroxyl and phenylacetylaminyl radicals. The latter subsequently couples with the benzyl radical. The normal fate of hydroxyaminyl free radicals is the formation of hydroxylamine as shown in case of BHA.

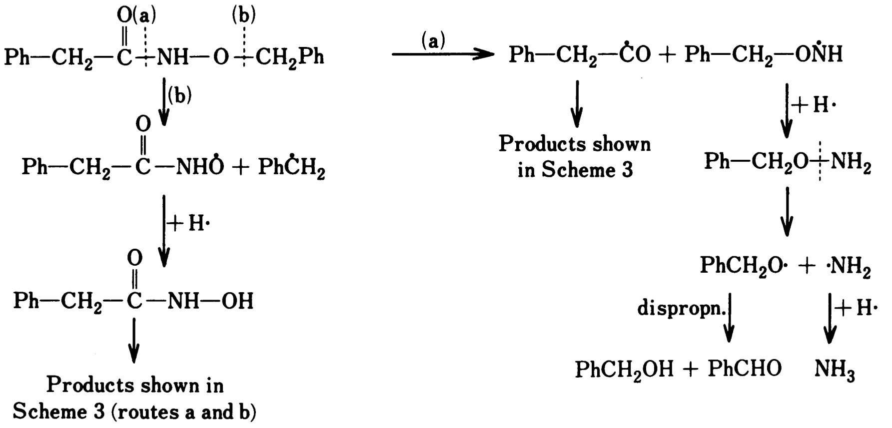
N-(Benzyloxy)phenylacetamide (BPAA) on pyrolysis by reflux in air gives the same products in addition to benzyl alcohol and benzaldehyde which are suggested to be formed through homolysis of the  $-\overset{\overset{O}{\|}}{C}-\overset{|}{N}-$ bond forming phenylacetyl and benzyloxyaminyl free radicals.

The normal fate of phenylacetyl free radicals was discussed previously (Scheme 3), whereas the benzyloxyaminyl radical abstracts hydrogen to form *O*-benzylhydroxylamine which subsequently undergoes homolysis of the N-O bond as shown in (Scheme 4). This was further confirmed by the results obtained from pyrolysis of *O*-benzylhydroxylamine where NH_3, H_2O, benzyl alcohol, and benzaldehyde were identified among the products.

Photolysis of BHA and BBA in acetonitrile solution at 280 nm at 25 °C affords analogous products to those obtained on pyrolysis. Hence it is reasonable to assume that the photolysis of these hydroxamic acid derivatives involves the homolytic cleavage of the N-O bond in the excited state forming aroylamino and alkyloxyl free radicals, which either react within the solvent cage affording the rearrangement products or escape out of the cage to give the fragmentation products so identified.

Experimental

All melting points are uncorrected. The IR spectroscopic



Scheme 4. Pyrolysis of BPAA.

Table 1. Thermolysis Products of Benzohydroxamic Acid and Its *O*-Benzyl Derivatives in Gram (%)

Expt. No.[a]			1	2
Expt. conditions			Reflux in air (30 min)	Reflux in air (5 h)
Products in gram (%)	Bp θ_b/°C/5 mmHg[p]	Mp θ_m/°C		
Ammonia			Evolved	Evolved
Carbon monoxide			Evolved	Evolved
Water			Drops	Drops
Toluene[b]			—	0.3(3.0)
Benzaldehyde[c]	45—55		—	0.7(7.0)
Benzyl alcohol[d]	60—70			0.8(8.0)
Bibenzyl[e]	108—122	52—53	—	0.4(4.0)
trans-Stilbene[f]	140—148	124	—	0.3(3.0)
Benzil[g]		95	0.2(2.0)	Trace*
Aniline[h]	62—75		3.2(32)	1.5(15)
o- and *p*-Aminodiphenyl methanes[i]	162—170		—	0.9(9.0)
Acridine[j]	192—200	107—110	—	0.2(2.0)
Phenoxazine[k]		153—155	0.4(4.0)	Trace
Benzanilide[l]		160—163	1.1(11)	1.5(15)
o- and *p*-Aminophenols[m]			1.5(15)	0.8(8.0)**
Benzoic acid[n]		120—122	1.4(14)	0.2(2.0)
Phenanthrene[o]		100	—	0.7(7.0)
Residue			1.1(11)	0.8(8.0)

a) Experiment 1 using benzohydroxamic acid and 2 using *N*-(benzyloxy)benzamide. b) 2,4-Dinitro derivative mixture mp 72 °C. c) Benzaldehyde estimated in the mixture by DNP formation mp 230—232 °C. d) n_D^{20}, 1.5395; 3,5-dinitrobenzoate mp 113 °C. e) Mixture mp 52 °C, 4,4′-dinitro derivative mixture mp 179—180 °C. f) Mixture mp 124 °C. g) Mixture mp 96 °C.* Identified by preparative TLC using pet. ether (60—80°C)–acetone (5:1) v/v as eluent, *trans*-stilbene $R_f=0.66$, benzil $R_f=0.9$. h) n_D^{20}, 1.5836; acetyl derivative mixture mp=113—114 °C. i) Separated by column chromatography on silica gel (100—150 mesh) using benzene as eluent, *o*-isomer 0.2 g, acetyl derivative mmp 135°C and *p*-isomer 0.6 g, picrate mmp 179 °C. j) Mixture mp 111 °C. k) Mixture mp 152—153 °C. l) Mixture mp 161—163 °C. m) Separated by column chromatography silica gel (100—150 mesh) using benzene–ether (4:1) v/v as eluent, *o*-isomer 0.2 g, mmp 174 °C and *p*-isomer 1.2 g mmp 186 °C in case of benzohydroxamic acid; 0.15 g of *o*-isomer, 0.5 g of *o*-isomer in case of *O*-benzyl derivative**, *N*-benzyl derivative mmp 167 °C, 153—154 °C respectively. n) Mixture mp 120 °C. o) Mixture mp 100 °C; picrate derivative mp and mmp 143 °C. p) 1 mmHg=133.322 Pa.

analysis were carried out on a Pye-Unicam IR spectrophotometer, Model Sp. 200 G. GLC was carried out using a Pye-Unicam gas chromatograph series 104, with dual flame ionization detector, Model 24 and the column used was 20% SE 30 on Chromosorb W (35—80 mesh) at temperature 185 °C using nitrogen as carrier gas. Molecular weight determination of some reaction products was carried out by mass spectrophotometer, Model A.E.I.M.S. 902. Ultraviolet irradiation was carried out using Mallinkrodt 150 W mercury discharge lamp and the solutions were contained in open topped Pyrex beakers. ^{1}H NMR spectrum for some reaction products were obtained using EM-390 90 MHz NMR spectrometer.

Thermolysis of Arene-, Arylalkanehydroxamic Acids and *O*-Benzyl Derivatives: The arene- and arylalkanehydroxamic acid (10 g) was heated on an oil bath (bath temp 240 °C) for 30 min where frothing takes place or in a sealed tube under nitrogen atmosphere. The carbon monoxide evolved was detected by platinum chloride test paper. The ammonia gas evolved was detected by HCl. The products were separated into neutral, basic, phenolic and acidic components as in a previous work.[7] The separated products were subjected to further separation into their constituents by column chromatography and identified by TLC and GLC or by comparison of their infrared spectra with those of authentic samples.

The *O*-benzyl derivatives of these hydroxamic acids were pyrolyzed by refluxing for 5 h in air whereby ammonia and carbon monoxide were evolved and detected by chemical means. The pyrolysate was separated and detected as described before. The results are given in Tables 1 and 2.

Photolysis of Benzohydroxamic Acid and *O*-Benzyl Derivatives: A solution of BHA or BBA (1 g) in dry acetone (50 ml) was irradiated at room temperature (25 °C) for 20 h. The photolysate was separated as indicated in a previous work[9] into amine, acid and neutral products and analyzed by GLC as compared with authentic samples using nitrobenzene as internal standard. The results are summarized in Table 3.

Pyrolysis of *O*-Benzylhydroxylamine: *O*-Benzylhydroxylamine (10 g) was refluxed for 10 h. The ammonia evolved was detected by chemical means. The dark brown viscous product was subjected to fractional distillation under reduced pressure whereby the following products were obtained:

Product	Bp θ_b/°C /100 mmHg	gram(%)
NH_3	Evolved	—
Benzaldehyde	68	3.0(30)
Benzyl alcohol	85	3.15(31.5)
Unchanged hydroxylamine		2.80(28)

Pyrolysis of *N,N'*-Diphenyloxamide: A mixture of *N,N'*-diphenyloxamide (10 g) and naphthalene (20 g) was refluxed for 3 h whereby CO was evolved and detected by turning platinum chloride test paper grey. The dark brown viscous product obtained was subjected to distillation under reduced pressure where excess naphthalene (16 g) come over

Table 3. Photolysis Products of Benzohydroxamic Acid and Its *O*-Benzyl Derivatives

	BHA	BBA
Products, in gram (%)		
NH_3, CO gas	Exist	Exist
Benzaldehyde	—	0.15(15)
Bibenzyl	—	0.10(10)
Benzanilide	0.32(32)	0.25(25)
Benzoic acid	0.2(20)	0.15(15)
BHA	0.23(23)	0.10(10)
Unknown solid[a]	0.10(10)	0.08(8.0)
Ammonium benzoate	Trace	Trace

a) Unknown mp 119—120 °C. Analysis C, 69.78; H, 6.15; N, 11.53. ν band at 3350, 3150, $\rangle$C=, at 1695, 1615 cm^{-1}.

Table 2. Thermolysis Products of Phenylacetohydroxamic Acid and Its *O*-Benzyl Derivatives in Gram (%)

Expt. No.[a]			1	2	3
Expt. conditions			Reflux in air (4 h)	Sealed tube at 270 °C (10 h)	Reflux in air (5 h)
Products in gram (%)	Bb θ_b/°C/5 mmHg	Mp θ_m/°C			
Ammonia			Evolved	Evolved	Evolved
Carbon monoxide			Evolved	Evolved	Evolved
Water			Drops	Drops	Drops
Toluene[b]	40—55		0.3(3.0)	0.8(8.0)	Trace
Benzaldehyde[c]			0.6(6.0)	—	2.1(21)
Benzyl alcohol[d]	60—70		—	—	0.9(9.0)
Bibenzyl[e]	110—125		1.2(12)	0.5(5.0)	0.8(8.0)
trans-Stilbene[f]	130—152		0.7(7.0)	0.3(3.0)	0.6(6.0)
Phenantherene[g]			0.5(5.0)	0.2(2.0)	Traces
N-Benzylphenylacetamide[h]		116—118	3.5(35)	3.1(31)	2.3(23)
Unknown solid[i]		147—148	—	2.6(26)	—
Phenylacetic acid[j]		77—78	0.2(2.0)	0.3(3.0)	Trace
Residue			1.4(14)	0.5(5.0)	1.5(15)

a) Experiments 1, 2 using phenylacetohydroxamic acid and 3 using *N*-(benzyloxy)phenylacetamide. b—g) As in footnote Table 1. h) Identified by mol. wt. determination (*m/z* 225), elemental analysis Calcd for $C_{15}H_{15}NO$: C, 80.00; H, 6.6, N, 6.2; Found: C, 79.88; H, 6.6; N, 6.3%, mixture mp and IR absorption spectrum are coincident with that of an authentic sample. i) Solid separated from (g) by column chromatography on silica gel (100—150 mesh) using pet. ether (60—80°) acetone (4:1 v/v) as eluent, analysis, C, 71.1; H, 6.4; N, 7.4%. j) Mixture mp 78 °C.

at first followed by aniline (2.5 g) bp 80 °C/10 mmHg and *N*-phenyl-1-naphthylamine (1.2 g), bp 200 °C/10 mmHg, which was triturated with pet. ether (40—60 °C) and crystallized from ligroine mp 62 °C. The residue was crystallized from ethanol to give 1-naphthanilide (3.2 g) mp and mixed mp 160—162 °C.

Reference Compounds: Benzohydroxamic acid,[10] crystals from ethanol, mp 129—130 °C.

N-(Benzyloxy)benzamide:[11] crystals from pet. ether (60—80 °C) mp 103—104 °C.

Phenylacetohydroxamic acid:[12] crystals from ethanol, mp 140—142 °C.

N-(Benzyloxy)phenylacetamide:[11] crystals from ethanol mp 71—72 °C.

trans-Stilbene:[13] crystals from ethanol, mp 123—4 °C.

Bibenzyl:[14] crystals from ethanol, mp 52 °C, 4,4′-dinitroderivatives, mp 180 °C.

Phenoxazine:[15] crystals from ethanol mp 152—154 °C.

o-Aminodiphenylmethane:[16] crystals from pet. ether (40—60 °C) mp 52 °C, *N*-acetyl derivative mp 135 °C.

p-Aminodiphenylmethane:[17] bp 165—167 °C/3 mmHg, crystals from pet. ether (40—60 °C) mp 34—36 °C, picrate, mp 179 °C.

N-Benzylphenylacetamide:[18] crystals from ethanol, mp 116—118 °C.

o-Benzylhydroxylamine:[19] bp 118—119 °C/30 mmHg; hydrochloride mp 238 °C.

N,N′-Diphenyloxamide:[20] crystals from benzene, mp 254 °C.

N,-Phenyl-1-naphthylamine:[21] crystals from ligroine mp 62 °C.

1-Naphthanilide:[22] crystals from ethanol, mp 160—161 °C.

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