The Thermal Decomposition of N,N-Succinoyl-N′-nitrosohydrazides

T. Koenig and L. Lam

Department of Chemistry, University of Oregon, Eugene, Oregon 97403

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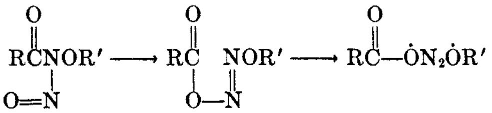
The decomposition of two N-nitroso-N-succinimidylamides have been investigated. The rearrangements of these nitrosoamides are relatively slow requiring temperatures of about 80° for appreciable reaction rate. The decomposition products are the isocyanates which would be expected from ionic cleavage of the triazene rearrangement product. Radical decomposition of the triazene appears to be ruled out since little carbon dioxide is formed with either the acetyl or phenylacetyl compound.

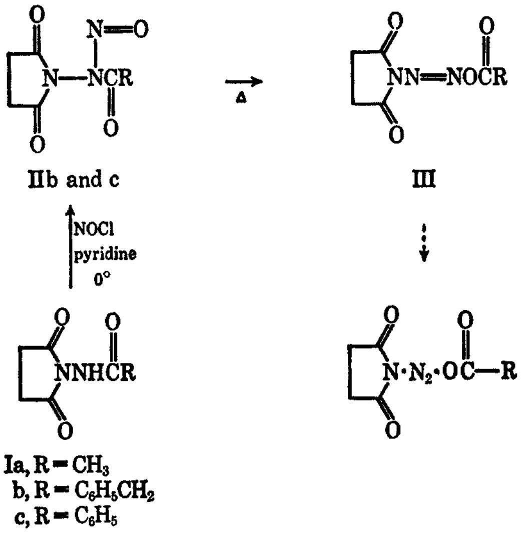
Recent studies[1] of the rearrangement and decomposition of N-nitrosohydroxylamine derivatives have indicated that these compounds can be used to generate acyloxy–alkoxy radical pairs under mild conditions.



$$\mathrm{R\overset{\overset{O}{\|}}{C}\underset{\underset{O=N}{|}}{N}OR'} \longrightarrow \mathrm{R\overset{\overset{O}{\|}}{\underset{\underset{O-}{|}}{C}}\ \underset{\underset{N}{\|}}{N}OR'} \longrightarrow \mathrm{R\overset{\overset{O}{\|}}{C}-\dot{O}N_2\dot{O}R'}$$

Because of our[2] interest in the chemistry of nitrogen radicals, we hoped that an analogous sequence might prove useful in the generation of acyloxy–aza radical pairs. We therefore have investigated two nitrosohydrazides (IIb and IIc) which might have been expected to give acyloxy–succinimidyl radical pairs (Scheme I).

Scheme I



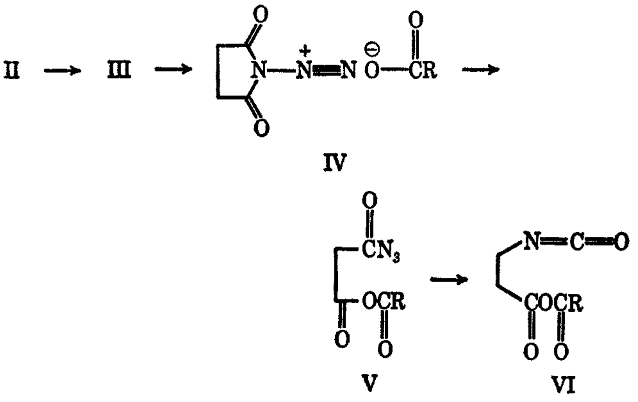
Results and Discussion

The starting hydrazides (I) were obtained from N-aminosuccinimide[3] and the appropriate acid chloride or anhydride. Nitrosation of the acetyl compound (Ia) was accomplished using nitrosyl chloride and pyridine at 0°. The nitroso compound (IIa) was obtained, in this case, as a crystalline solid. Its infrared spectrum showed the expected broad band around 1570 cm^{-1} for the N-nitroso group. Its nmr spectrum in deuteriochloroform consisted of two singlets at δ 2.92 (three protons) and 2.96 (four protons). The chemical shifts of these protons are highly solvent dependent, being separated by 0.25 ppm in benzene solution.

The phenylacetylnitroso compound (IIb) was too unstable to be isolated in solid form and it was handled only in solution. The conversion from Ib was poor and significant amounts of the starting hydrazide were obtained from the basic washings after the nitrosation step. Attempts at obtaining even solutions of the benzoyl nitroso compound (IIc) failed and starting hydrazide was always largely recovered from the aqueous washings. These observations probably reflect the relative ease with which the nitroso group is removed in this series of compounds by aqueous base.

In benzene solution the rearrangement of IIa is slow compared to the nitrosohydroxylamines.[1] Convenient reaction rates require temperatures of above 80°. At this temperature, the N-nitroso band at 1570 cm^{-1} in the infrared spectrum disappears with new bands appearing at 2290 and 2825 cm^{-1}. The nmr spectrum, under these conditions, shows a decrease in the succinimidyl singlet and the appearance of two new triplets at 2.73 and 3.63 ppm. Nitrogen evolution also occurs under these conditions. The spectral characteristics of the product mixture are indicative of an isocyanate product such as VI (Scheme II).

Scheme II



Evaporation of the solvent from the product mixture gave a thick oil which resisted attempted distillation. When this oil was treated with methanol, carbamates VII and VIII were isolated (Scheme III). There are also the expected products from V.

While crystalline IIb was not obtained, the spectra of solutions obtained from the nitrosation procedure with Ib indicated that the expected nitroso compound was present in reasonably pure form. Heating these solutions to 30° showed changes formally identical with those for IIa. The products isolated after the meth-

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[1] T. Koenig and M. Deinzer, *J. Amer. Chem. Soc.*, **88**, 4518 (1966); *ibid.*, **90**, 7014 (1968).

[2] T. Koenig and W. Brewer, *ibid.*, **86**, 2728 (1964).

[3] E. Hadaya, R. L. Hinman, V. Schomaker, S. Theodoropulos, and L. Kyle, *ibid.*, **89**, 4875 (1967). We are grateful to Dr. Hinman for making his procedure for the preparation of N-aminosuccinimide known to us prior to its publication.

SCHEME III

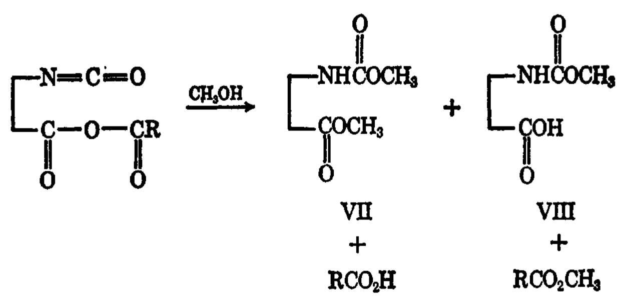


TABLE I

ISOLATED PRODUCTS FROM THE DECOMPOSITION OF II

Product	IIa	IIb
N_2	>0.94	1.00[a]
CO_2	<0.05	0.03
VII[b]	0.58	0.59
VIII[b]	0.33	0.35
RCO_2H[c]	c	0.42
RCO_2CH_3[c]	c	0.7

[a] Yields based on 100% nitrogen evolution. [b] After methanolysis. [c] Present but not determined quantitatively.

anol treatment were also formally identical. The yields of isolated products are summarized in Table I.

The fact that the carbon dioxide yield was not increased appreciably in the decomposition of IIb compared to IIa is a strong argument against the alternative formal possibility of radical cleavage of the triazene, followed by efficient cage collapse to give the anhydride azide (V). This statement is made because of the variety of evidence[4] which indicates that the radical cleavage of *t*-butyl perphenylacetate is a concented process. If this behavior is general for any X-O bond cleavage then quantitative carbon dioxide should be found in the phenylacetyl case no matter how efficient the cage recombination is proposed to be.

A brief examination of the kinetics of nitrogen evolution was carried out. The results are summarized in Figure 1. The nitrogen evolution shows a good first-order dependence after the first 10 min. The form of the figure can be fit by the solution to a simple three-component kinetic system

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

The solution for this system in terms of the usual first-order rate law (for $k_2 \rightarrow k_1$) is

$$\ln\left(\frac{1}{1-\alpha}\right) = k_1t + \ln\left(1 - \frac{k_1}{k_2}\right) - \ln\left[1 - \frac{k_1}{k_2}\, e^{-(k_2-k_1)t}\right]$$

where α is fraction reaction and k_1 and k_2 are rate constants in the conversion of A into B and B into C, respectively. The leftmost member of the expression drops rapidly to zero and the function soon becomes linear in time as observed. Extrapolation of the linear part of the curve, to the positive time of zero reaction, gives a measure of k_2/k_1 which is 16.5. The slope of the linear part of the expression gives k_1 which is 6×10^{-3} min^{-1}. Thus k_2 must be of the order of 1×10^{-1} min^{-1} (all at refluxing benzene temperature).

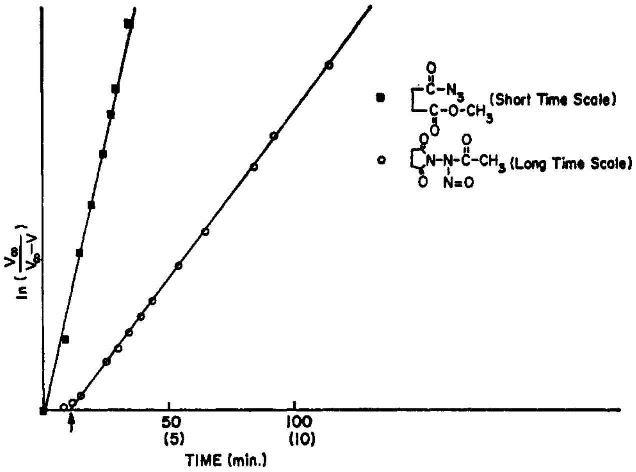
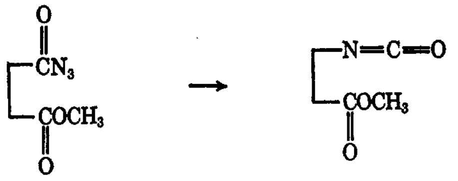


Figure 1.—Rates of nitrogen formation.

Scheme II actually involves more than three components but the system can degenerate to a formal three-component system if the neglected steps are sufficiently rapid. The kinetically important intermediate (B) could be either the triazene or the azide. A control to test for the possibility of the azide as the kinetically important intermediate was carried out. This was the measurement of the kinetics of nitrogen evolution of the closely related methyl azidosuccinate (IX). The rate plot for this reaction is also shown in



IX

Figure 1. The observed rate constant is 2.3×10^{-1} min^{-1} which is close to that for the unknown (B). The formal kinetic sheme may thus be identical with Scheme II if the conversion of the triazene into the azide is sufficiently rapid to make it a kinetically unimportant intermediate. We cannot rule out other formal mechanisms leading from nitroso compounds II to azide VI which do not involve triazene (III). However, by analogy with the general behavior of nitrosoamides,[5] the triazene is certainly expected to intervene. It is also possible that the triazene is in fact B in the formal kinetic scheme. This could be so if its conversion into the isocyanate did not involve the azide. The isocyanate could arise directly from the nitrenium acylate ion pair which would be formed by loss of nitrogen from IV. This possibility seems less attractive at the present time.

The present study is, to our knowledge, the first to deal with the decomposition of nitrosohydrazides and the remaining ambiguities in this sequence will hopefully be resolved when more cases have been examined. The greater stability of these compounds toward rearrangement, compared to nitrosoamides and nitrosohydroxylamines, is a puzzling question. We are presently pursuing investigations of other members of this series of compounds with the hope of gaining a clearer understanding of their behavior.

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(4) P. D. Bartlett and R. R. Hiatt, *ibid.*, **80**, 1398 (1958); T. Koenig and W. D. Brewer, *Tetrahedron Lett.*, 2773 (1965); R. Neuman and J. Behar, *J. Amer. Chem. Soc.*, **89**, 4549 (1967).

(5) R. Huisgen and G. Horeld, *Ann.*, **562**, 137 (1944); R. Huisgen and L. Krause, *ibid.*, **574**, 157 (1951).

Experimental Section

Infrared spectra were obtained using a Beckman IR-5 spectrophotometer. Nuclear magnetic resonance spectra were recorded relative to tetramethylsilane, used as an internal standard, with a Varian A-60 spectrometer. Quantitative analyses using glpc were with an Aerograph HyFy Model 600D using known compounds to obtain calibration curves. Benzene was dried by distillation from sodium. N-Aminosuccinimide was prepared by the method of Hinman.[3]

N,N-Succinoylhydrazides.—The hydrazides were prepared from crude N-aminosuccinimide. Acetyl compound Ia was obtained by dissolving the amine in acetic acid followed by the addition of excess acetic anhydride and warming for 1 hr on a steam bath. The acetic acid and excess acetic anhydride were evaporated and the residue was recrystallized from ethanol. A white solid resulted, mp 157–158°, in 50% yield.

Anal. Calcd for $C_6H_8N_2O_3$: C, 46.15; H, 5.17; N, 17.94. Found: C, 46.30; H, 5.18; N, 17.76.

The nmr spectrum, in pyridine, showed two singlets at δ 2.12 and 2.77 in a 3:4 ratio.

Phenylacetyl compound Ib was obtained from crude N-aminosuccinimide and phenylacetyl chloride in methylene chloride with 1 equiv of pyridine added. The acid chloride was added slowly for 1.5 hr to the amine at room temperature. The resulting solution was washed with water and dried and the solvent removed. The resulting solid was recrystallized from chloroform to give a crystalline material, mp 157.5–159°, in 50% yield.

Anal. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.84; H, 5.20; N, 12.25.

The nmr spectrum of this material in deuteriochloroform showed three apparent singlets at δ 7.32, 3.72 and 2.75 in intensity ratio 5:2:4.

Benzoyl compound Ic was prepared in from N-aminosuccinimide and benzoyl chloride in acetonitrile with pyridine added. In this case the solvent was evaporated and the entire residue shaken with water, diluted acid and again with water. The solid remaining was dried in a vacuum desiccator and recrystallized from acetonitrile to give a crystalline product, mp 218–219°.

Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.41; H, 4.43; N, 12.71.

The nmr spectrum of this compound in acetonitrile showed benzoyl multiplets at δ 7.67 and 7.92 and a singlet at 2.86 ppm.

Nitrosation.—Acetylhydrazide Ia (15.6 g, 0.10 mol) was ground into a fine powder and suspended in 300 ml of chloroform with 1 equiv of pyridine added. This suspension was cooled to 0° in an ice bath and nitrosyl chloride (8 g, 0.12 mol) dissolved in 100 ml of chloroform was added dropwise to the cold suspension over a 2-hr period. The solid disappeared during the addition and the resulting solution was washed with ice water and dried over magnesium sulfate. The chloroform was evaporated at 0° leaving 12.5 g (68% crude yield) of a yellow solid. This material was recrystallized from petroleum ether (bp 60–90°) giving a yellow crystalline solid, mp 112° dec. The infrared spectrum of this material in chloroform showed broad $N-N=O$ absorption at 1570 cm^{-1} and a broad carbonyl band at 1760 cm^{-1}. No NH absorption was apparent. The nmr spectrum of this material in benzene solution showed singlets at δ 1.81 and 2.21 while in deuteriochloroform they appeared at δ 2.92 and 2.96. A sample, sent for combustion analysis, *exploded* enroute.

When an identical experiment was attempted with Ib, rapid decomposition of the nitrosation product occurred while the chloroform was being evaporated. Large amounts of brown gas (probably nitric oxide) were given off during this process. The chloroform solution obtained directly from the nitrosation procedure after aqueous the wash and drying steps showed the infrared characteristics expected of the nitrosoamide (1570 and 1760 cm^{-1}, NH absent). When benzene was used as a solvent in the nitrosation procedure, the solution obtained after the aqueous washes and drying steps showed a nmr spectrum consisting of two singlets at δ 4.22 and 1.80 ppm (besides the solvent peak). Acidification of the aqueous bicarbonate washings gave significant amounts of starting hydrazide. The benzene solutions obtained in this way were used directly in the decomposition product studies. All attempts at nitrosation of benzoylhydrazide Ic resulted in recovery of starting material after aqueous washing.

Decomposition Products.—IIa (4.40 g, 23.8 mmol) was dissolved in 50 ml of dried benzene and added to a break-seal flask. The solution was degassed by several freeze–thaw cycles and sealed off under high vacuum. The flask was transferred to a constant-temperature bath at 80° for 14 hr. The gaseous products were determined on a calibrated vacuum line. The gas yield was 23.5 mmol (98.6%). The mass spectrum of this gas mixture indicated it contained nitrogen (>96%) and carbon dioxide (<4%) and a trace of nitrous oxide. The benzene was removed *in vacuo* leaving a residual oil (3.14 g) which show strong bands in the infrared spectrum at 2290, 1825, and 1740 cm^{-1}. The residue was dissolved in methanol and refluxed overnight. Upon distillation, a small amount of methyl acetate was isolated and identified by its infrared spectrum. After most of the methanol had been removed, bulb-to-bulb distillation under high vacuum gave some acetic acid in the distillate. The remaining residue was dissolved in chloroform, extracted with cold bicarbonate solution, and dried over calcium chloride and the chloroform evaporated. The resulting residue showed infrared and nmr spectra identical with those of authentic methyl β-carbomethoxyamidoproprioate (VII). The yield of this product was determined by glpc using a 5 ft × $^1/_8$ in. column packed with 5% SE-30 on Chromosorb P.

Acidification of the aqueous washings and evaporation of the water gave an oily residue. This material was extracted with chloroform and identified as β-(N-carbomethoxyamido)proprionic acid (VIII) by comparison with an authentic sample. The yield was 1.13 g (7.68 mmol, 33%).

The procedure for the decomposition of IIb was identical except that the benzene solution was used directly from the nitrosation procedure without isolution of the nitrosohydrazide in solid form. The gaseous products amounted to 4.90 mmol of which 3% was carbon dioxide and the remainder nitrogen. The yield of VII after the methanolysis step was determined directly by glpc. Methyl phenylacetate was also detected and determined directly in this way. The yield of phenylacetic acid was determined by acidification of the basic extract of the methanolysis residue. At this point the phenylacetic acid precipitates while VIII remains in the aqueous solution. The yields of the two acids were by weight.

Methyl β-Carbomethoxyamidopropionate.—The half methyl ester of succinic acid was converted into the acid chloride and this was stirred with sodium azide in benzene overnight. Attempts to isolate this azide lead to an *explosion*. Heating the benzene solution obtained after filtration of the sodium chloride caused nitrogen evolution. When the nitrogen ceased to evolve, the benzene was evaporated and the residue treated with methanol. Distillation of this material gave the product [bp 80° (0.48 mm)] in 70% yield from the acid chloride. This distillate solidified on standing, mp 33–34° (lit.[6] mp 33–35°). A portion of this ester was hydrolyzed with 1 equiv of base to give the corresponding acid (VIII).

Kinetic Studies.—A flask fitted with a turnable side arm and a condenser connected to a gas buret was charged with benzene. The benzene was brought to reflux equilibrium and the gas buret leveled. The solid nitrosoamide was added by turning the side arm. The volume of gas evolved *vs.* time was noted. The procedure for decomposition of the azide was identical except that the azide was added in benzene solution as rapidly as possible.

Registry No.—Ia, 18542-73-9; Ib, 18542-74-0; Ic, 18542-75-1; IIa, 18542-72-8; IX, 18542-76-2.

Acknowledgment.—We are grateful to the National Science Foundation for the support of this work.

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(6) F. Langfield and J. Steiglity, *Amer. Chem. J.*, **15**, 504 (1893).