Application of the Nitrosoamide Reaction to Hydrazones

Richard H. McGirk,* Clifford R. Cyr, William D. Ellis, and Emil H. White

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

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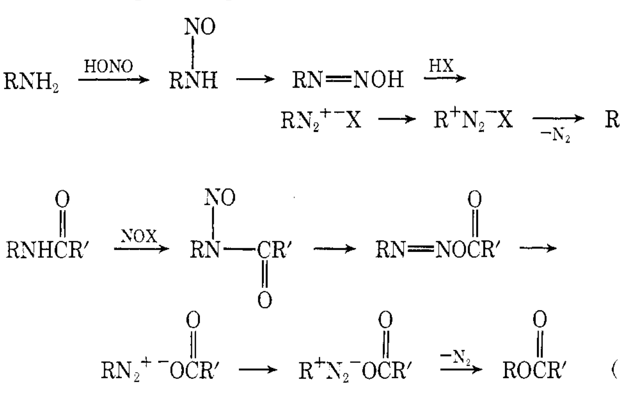
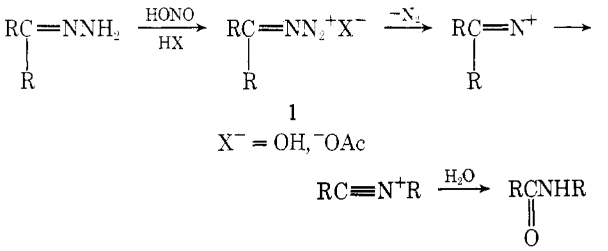
Nitrosation of the *N*-acetylhydrazones of benzophenone, acetophenone, cyclohexanone, and heptaldehyde affords the corresponding 1-acetoxy-1-azido compounds, ketones (or aldehydes), and acetyl azide as the principal products. The unstable *N*-nitrosoamide is undoubtedly formed in the first step of the reaction; a rearrangement to a diazo ester and migration of the carboxylate group complete the process. Minor products of the reaction appear to stem from nitrosation at the imine nitrogen.

The nitrous acid and the nitrosoamide methods for the deamination of aliphatic amines proceed *via* similar intermediates (eq 1).[1] Reports that the reaction of nitrous acid with hydrazones gave a Beckmann type rearrangement (eq 2)[2] suggested to us that the nitrosoamide method of deamination could be applied to the reaction with advantage, in view of the greater choice of counterion and solvent available with this method. We now report that nitrosation of *N*-acetylhydrazones does not lead to a Beckmann type rearrangement *via* loss of nitrogen from an intermediate iminodiazonium ion such as **1** (X = $^-$OAc); instead, ion recombination occurs to give 1-acetoxy-1-azidoalkanes.



$$RNH_2 \xrightarrow{HONO} R\overset{NO}{N}H \longrightarrow RN{=}NOH \xrightarrow{HX} RN_2{}^{+}\,{}^{-}X \longrightarrow R^+N_2{}^-X \xrightarrow[-N_2]{} RX$$

$$RNH\overset{O}{\overset{\|}{C}}R' \xrightarrow{NOX} R\overset{NO}{N}{-}\underset{O}{\underset{\|}{C}}R' \longrightarrow RN{=}NO\overset{O}{\overset{\|}{C}}R' \longrightarrow RN_2{}^{+}\,{}^{-}O\overset{O}{\overset{\|}{C}}R' \longrightarrow R^+N_2{}^-O\overset{O}{\overset{\|}{C}}R' \xrightarrow{-N_2} RO\overset{O}{\overset{\|}{C}}R' \qquad (1)$$



$$\underset{R}{RC}{=}NNH_2 \xrightarrow[HX]{HONO} \underset{R}{RC}{=}NN_2{}^+X^- \xrightarrow{-N_2} \underset{R}{RC}{=}N^+ \longrightarrow$$

$$\mathbf{1} \qquad X^- = OH, {}^-OAc$$

$$RC{\equiv}N^+R \xrightarrow{H_2O} R\underset{O}{\underset{\|}{C}}NHR \qquad (2)$$

Results and Discussion

N-Acetylhydrazones **2** were prepared by reaction of an aldehyde or ketone with acetylhydrazine. These hydrazones were nitrosated with nitrosyl chloride or dinitrogen tetroxide at −5° in the presence of solid sodium acetate (Chart I). The principal products were identified as the 1-acetoxy-1-azidoalkanes **6**[3] and the corresponding ketone or aldehyde; in some instances, acetyl azide was also detected. The yields of these products are given in Table I.

The presence of the acetoxy azides was easily established from their characteristic ir spectra: a strong azide absorption at ~2120 cm^{-1} and a strong carbonyl absorption at 1750–1780 cm^{-1}. That the ketone or aldehyde and acetyl azide were also present was established by comparison of the ir and nmr spectra with those of the authentic compounds.

The structure of the acetoxy azides follows from the method of preparation, the physical data (Experimental Section), and the reactions. Attempts to prepare **6a** from benzophenone, acetyl chloride, and sodium azide (or from acetyl azide) were unsuccessful, leading only to the decomposition of the acetyl azide.

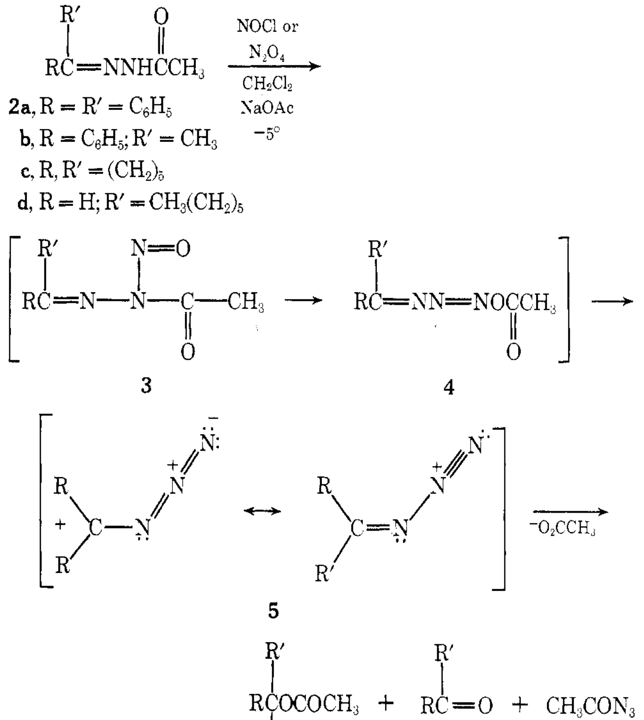
The acetoxy azides **6** were further characterized by their reactions. Chromatography of azide **6a** on silica gel led to decomposition; diazidodiphenylmethane[4] (39%), benzophenone (56%), and benzanilide (9%) were formed (eq 3). Treatment of **6a** with gaseous hydrogen chloride led to formation of benzophenone (65%) and benzanilide (15%). Prolonged treatment of **6a** with aqueous sodium carbonate caused a slow conversion to benzophenone.

Table I
Products from Nitrosation of Hydrazones 2[a]

Hydrazone	Products, %		
	Acetoxy azide **6**	Aldehyde or ketone **7**	Acetyl azide **8**
2a	70–86	5–13	
2b	33–63[b]	2–6	
2c	45	35	9–11
2d	20	23	14

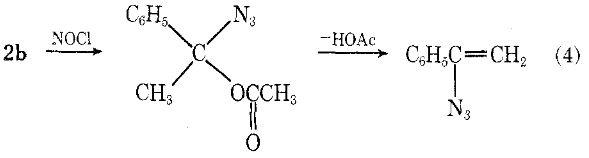
[a] Yields were determined by nmr using ethylene bromide as an internal standard. [b] Based on the final product α-azidostyrene.

Chart I



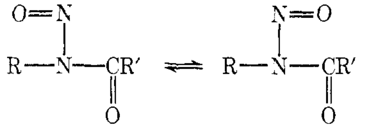
$$\mathbf{6a} \xrightarrow{H^-} \mathbf{7a} + \underset{\mathbf{9}}{(C_6H_5)_2C(N_3)_2} + \underset{\mathbf{10}}{C_6H_5CONHC_6H_5} \qquad (3)$$

Nitrosation of hydrazone **2b** gave the acetoxy azide **6b** as a short-lived intermediate. An nmr spectrum of the reaction mixture showed methyl singlets at δ 1.91 and 2.11 that are assigned to **6b**; the ir spectrum showed a strong azide absorption at 2120 cm^{-1} and a carbonyl band at 1760 cm^{-1}. In addition, the nmr spectrum indicated that a small amount (5–10%) of another product, α-azidostyrene, was also present by the appearance of olefinic protons at δ 4.91 (d, J = 2 Hz) and 5.37 (d, J = 2 Hz). Furthermore, on standing for 24 hr, the signals assigned to **6b** were observed to decrease in size accompanied by a proportional increase in the area of the peaks belonging to the α-azidostyrene. Thus, acetoxy azide **2b** slowly eliminates acetic acid to give α-azidostyrene (eq 4), presumably *via* an E1-type pathway.

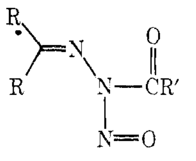


The azides **6c** and **6d** showed no tendency to decompose to vinyl azides. An attempt was made to promote elimination of acetic acid from azide **6c** by using the "proton sponge" bis-1,8-(dimethylamino)naphthalene;[5] no reaction occurred during 24 hr.

By analogy with the nitrosation of amides and carbamates,[1] we propose that in the first step of the reaction (Chart I) nitrosation occurs to give the unstable N-nitroso-N-acetylhydrazone **3** followed by rapid rearrangement to a diazo ester **4** and dissociation to the ion pair **5**. Efforts to detect **3** in the reaction mixture were unsuccessful. An ir spectrum run immediately after the addition of nitrosyl chloride showed only acetoxy azide **6** and unreacted hydrazone. The stability of N-nitrosoamides and related compounds is a sensitive function of the size of the alkyl group (R in **11**); large groups favor conformer **b** in which the nitroso group is favorably positioned for attack on the carbonyl group (Chart I).[6] In the nitrosoacylhydrazones, the reactive system is undoubtedly planar and nonbonded interactions of the nitroso function with the R groups should favor the reactive conformer shown in **12**, leading to instability of the compounds.



11a **11b**



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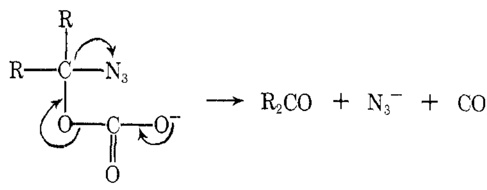
External anions are known to participate in the nitrosoamide reaction.[1] Similarly, when sodium propionate was substituted for the sodium acetate in the nitrosation of **2a**, 1-propionoxy-1-azidodiphenylmethane (14%) was detected as one of the products together with the corresponding acetate **6a** (82%). A control experiment showed that the acetate group of **6a** does not exchange with sodium propionate under the reaction conditions. Thus, the exchange occurs with **4** or more probably with **5**.

A second example of the involvement of anions from the medium was found in the nitrosation of **2b** in the presence of sodium carbonate.[7] Only acetophenone was formed, presumably *via* **13**. Similar reactions of nucleophiles with the acetoxy azides **6** can account for the excess of carbonyl compounds formed over acetyl azide (Table I).



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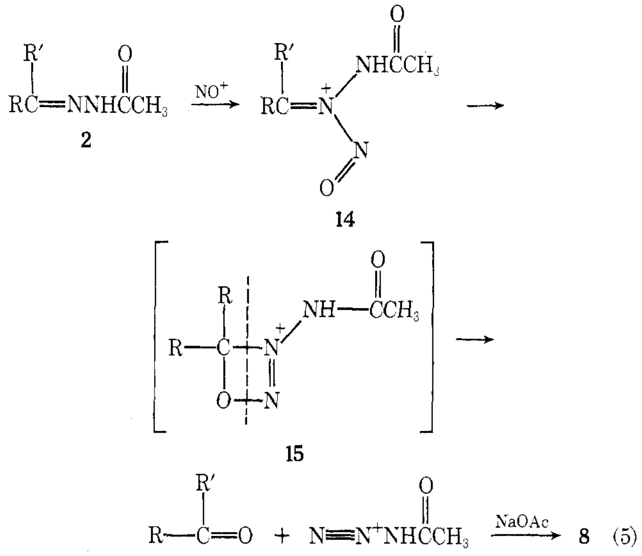
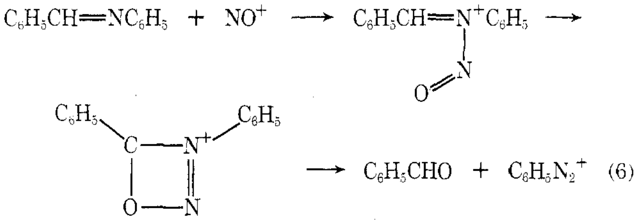
The formation of acetyl azide cannot be readily explained by the mechanism outlined in Chart I. This compound probably stems from the processes outlined in eq 5.



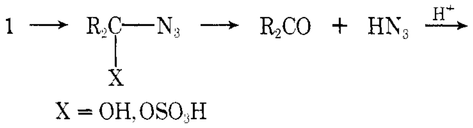
Since the basicities of the two nitrogens in the hydrazones **2** are comparable,[8] nitrosation should be capable of occurring at either site. It appears reasonable that the N-nitrosoimine **14** could decompose to a ketone and acetyl azide through the oxadiazetine intermediate **15**. Doyle, *et al.*,[9] and others[10] have proposed analogous four-membered intermediates to account, for example, for the formation of benzaldehyde and benzenediazonium ion from nitrosation of N-benzylideneaniline (eq 6).[11a,b]



In an effort to avoid the processes outlined in eq 5 and favor nitrosation of the amide nitrogen, the sodium salt of hydrazone **2c** was prepared and treated with nitrosyl chloride in the usual manner. The yield of acetoxy azide **6c** was greater than in the normal procedure (62% *vs.* 45%) and acetyl azide was not detected. Acetyl azide was never detected in the nitrosation of **2a** or **2b** implying that the phenyl groups make the imine nitrogen less susceptible to nitrosation compared with the amide nitrogen, probably due to an electron withdrawal effect.

Relationship to the Beckmann and Schmidt Reactions. The reactions described above show that if the counterion in species **1** is a strong base such as acetate ion, elimination of nitrogen does not compete with ion recombination to form species **6**. That is, in the nitrosation of compound **2a**, **6a** was formed, not benzanilide, of which only a trace was detected.

In the deamination analogy to the Beckmann reaction (eq 2),[2] 90% sulfuric acid was used as the medium, and it is possible that the availability of only bisulfate ion or water (low concentration) as nucleophiles conferred a sufficient lifetime to species 1 to allow nitrogen elimination to occur (eq 2). However, it is also possible that the reaction really proceeds *via* eq 7. In any case, the first two steps of eq 7 al-



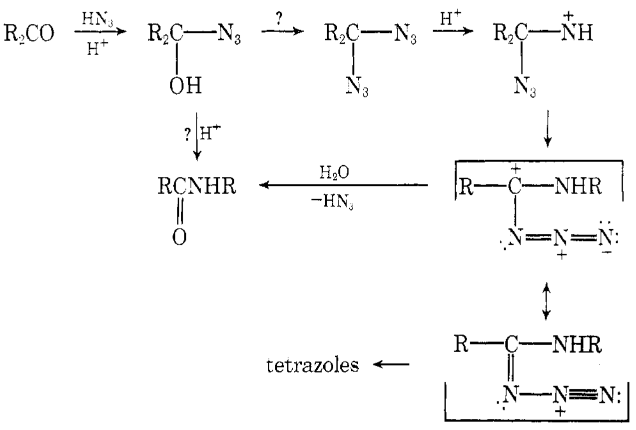
$$1 \longrightarrow \underset{\displaystyle X}{R_2C}-N_3 \longrightarrow R_2CO + HN_3 \xrightarrow{H^+}$$

$$X = OH, OSO_3H$$

"Schmidt-type reactions" (7)

most certainly occur in dilute acid solutions in view of the high yields of carbonyl compounds formed under those conditions.[8b]

The conversion of **6a** to **9** under acidic conditions suggests the possibility, furthermore, that diazidoalkanes may be involved as intermediates in the Schmidt reaction.



(8)

Experimental Section

All melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 457A spectrometer and ultraviolet spectra on a Cary Model 14 spectrophotometer. The nmr spectra were recorded with Varian Model A-60 and HA-100 instruments.

Acetylhydrazones (2a–d). Following the procedure of Grammaticakis,[12] equimolar amounts of the ketone or aldehyde and acetylhydrazine[13] were mixed. The reaction mixture became warm and homogeneous followed by formation of a solid mass. After 18–24 hr, the solid product was recrystallized to afford white crystals (40–80%). For benzophenone, the ketone and acetylhydrazine (2 molar excess) were dissolved separately in absolute methanol and then mixed. A drop of sulfuric acid was added and the reaction solution was refluxed for 6 hr. Water and ether were then added, and the ether layer was separated, dried over $MgSO_4$, and concentrated to give a white solid. A small amount of unreacted benzophenone was removed by recrystallization from methanol.

Benzophenone-*N*-acetylhydrazone (2a): mp 105–106° (lit.[14] 107°); ir (CCl_4) 3335 (w, NH), 1710 (s), 1680 (m), 1450 (m), 1370 cm^{-1} (m); nmr ($CDCl_3$) δ 2.42 (s, 3 H), 7.1–7.7 (m, 10 H), 8.4 (s, NH).

Acetophenone-*N*-acetylhydrazone (2b) (recrystallized from methanol): mp 128–131° (lit.[15] 131–132°); ir (CCl_4) 3200 (w), 3100 (w), 1670 (s), 1395 (m), 1345 cm^{-1} (m); nmr (CCl_4) δ 2.33 (s, 6 H), 7.2–7.4 (m, 3 H), 7.6–7.9 (m, 2 H), 10.7 (s, NH).

Cyclohexanone-*N*-acetylhydrazone (2c) (recrystallized from methanol–ether): mp 123–124°; ir (CCl_4) 3195 (w), 3095 (w), 1670 (s), 1395 cm^{-1} (m); nmr (CCl_4) δ 1.5–1.9 (br m, 6 H), 2.18 (s, 3 H), 2.1–2.65 (m, 4 H), 10.3 (s, NH).

Heptaldehyde-*N*-acetylhydrazone (2d) (recrystallized from ether): mp 40–45°; ir (CCl_4) 3190 (w), 3090 (w), 1670 (s), 1400 (m), 1340 cm^{-1} (m); nmr (CCl_4) δ 0.90 (t, 3 H), 1.1–1.8 (m, 8 H), 2.15 (s, 3 H), 2.0–2.4 (m, 2 H), 7.25 (t, 1 H), 10.8 (s, NH).

Nitrosation of Benzophenone-*N*-acetylhydrazone. (A) With Dinitrogen Tetroxide. In a 50-ml flask was placed 0.61 g (2.56 mmol) of hydrazone **2a**, 3 g (37 mmol) of anhydrous sodium acetate, and 10 ml of dichloromethane. The reaction vessel was equipped with a drying tube and cooled in a Dry Ice–acetone bath. Dinitrogen tetroxide (0.5 ml, 0.7 g, 8.1 mmol) was added as a liquid in one portion, and the Dry Ice–acetone bath was replaced with an ice bath. After 2.5 hr of stirring, the mixture was filtered and evacuated under vacuum (25°, 20 μ) to remove acetic acid. The product was an oily residue, largely the acetoxy azide **6a:** ir (CH_2Cl_2) 2120 (s), 1760 (s), 1495 (m), 1450 (m), 1370 (m), 1220 (s), 1190 (m), 1185 (m), 1000 cm^{-1} (m); nmr ($CDCl_3$) δ 2.2 (s, 3 H), 7.0–7.9 (m, 10 H); mass spectrum *m/e* (rel intensity) 239 (4, P − 28), 197 (54), 194 (19), 182 (100), 105 (100). The yield was 70% as determined by nmr using ethylene dibromide as an internal standard. The presence of benzophenone was indicated by a weak carbonyl band at 1660 cm^{-1} in the ir spectrum; the absolute yield was estimated to be about 10% from the nmr integration.

Anal. Calcd for $C_{15}H_{13}N_3O_2$: C, 67.42; H, 4.87; N, 15.73. Found: C, 68.04; H, 5.08; N, 15.08.

This analysis is correct if 3–4% benzophenone is present. Ir and nmr spectra indicate this is probably so. Attempts to further purify the sample led to decomposition of **6a.**

Refluxing the crude product in carbon tetrachloride for 24 hr or hexane for 72 hr caused no apparent change in **6a.** Treatment of **6a** dissolved in carbon tetrachloride with aqueous sodium carbonate (saturated) caused a 15% increase in benzophenone within 4 hr at room temperature.

The oily azido compound **6a** (3.5 g) was chromatographed on silica gel (50 g) and fractions of 125 ml were taken. Five fractions of 100% petroleum ether, then two each of 2.5, 5.0, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and 90% ether in petroleum ether, and finally five fractions of 100% ether were collected. Fractions 2 and 3 contained 1.27 g (5.1 mmol, 39%) of a white, crystalline solid that was recrystallized from pentane and identified as diazidodiphenylmethane: mp 40.5–41.0° (lit.[4a] 42°); ir (CCl_4) 3320 (w), 3060 (w), 2440 (w), 2120 (s), 2005 (s), 1220 cm^{-1} (s); mass spectrum *m/e* (rel intensity) 194 (51), 119 (39), 103 (100), 93 (39), 91 (26), 77 (21), 76 (34); uv (hexane) 259 nm (ϵ 620).

Anal. Calcd for $C_{13}H_{10}N_6$: C, 62.40; H, 4.00; N, 33.60. Found: C, 62.22; H, 4.03; N, 34.14.

Pyrolysis of the diazide and recrystallization of the product from chloroform yielded a crystalline solid which was identified as 1,5-diphenyltetrazole: mp 143–145° (lit.[4b] 146°).

Fractions 7–10 gave 1.34 g (7.4 mmol, 56%) of a viscous liquid that was identified as benzophenone by ir comparison. Fractions 14–17 contained a solid that was identified as benzanilide (0.24 g, 1.2 mmol, 9%) by comparison of the ir spectrum with authentic material. Recrystallization from carbon tetrachloride yielded white crystals melting at 161–162° (lit.[16] 163°).

Similar yields of benzophenone (65%) and benzanilide (15%) were obtained when the azide **6a** was treated with gaseous hydrogen chloride in ether at 25° for 3 days.

(B) With Nitrosyl Chloride. In a flask fitted with a drying tube and serum cap was placed 0.28 g (1.18 mmol) of hydrazone **2a,** 1.6 g (20 mmol) of anhydrous sodium acetate, and 6 ml of dichloromethane. The reaction vessel was cooled in an ice–acetone bath (∼−5°) and 26 ml (78 mg, 1.2 mmol) of gaseous nitrosyl chloride was injected from a syringe into the rapidly stirred mixture. After 30 min at 0°, an ir spectrum of the reaction mixture showed the presence of unreacted **2a** plus new bands at 2120 (s), 1760 (s), 1715 (s), 1295 (s), and 1220 cm^{-1} (s). An additional 48 ml of nitrosyl chloride was added in three portions until the hydrazone could not be detected by ir. The reaction mixture was filtered; the filtrate was concentrated on a rotary evaporator and evacuated further (30 μ) to remove most of the acetic acid. An ir spectrum of the oily residue was identical with **6a** as prepared using dinitrogen tetroxide. The yield of **6a** was calculated to be 78% by nmr. Benzophenone (5%) was also present. Similar results were obtained in other runs when the nitrosyl chloride was added in one batch.

(C) In the Presence of Sodium Propionate. To a mixture of 0.193 g (0.81 mmol) of **2a** and 1.5 g (14 mmol) of sodium propionate in 6 ml of dichloromethane was added 50 ml (2.3 mmol) of gaseous nitrosyl chloride. After 25 min, the reaction mixture was filtered. The filtrate was washed sequentially with water and a saturated solution of sodium carbonate; it was then dried over sodium sulfate and concentrated on a rotary evaporator. The residue was dissolved in carbon tetrachloride and a weighed amount of ethylene bromide was added as an internal standard. The nmr spectrum showed that **6a** (82%) was present and also 1-azido-1-propionoxydiphenylmethane (14%): nmr (CCl_4) δ 1.1 (t, 3 H), 2.3 (q, 2 H), 7.2–7.5 (m, 10 H). Benzophenone (3%) was also present.

For a control, a mixture of 188 mg (0.70 mmol) of **6a,** 1.5 g (14 mmol) of sodium propionate, 85 mg (1.14 mmol) of propionic acid, and 25 ml of nitrosyl chloride was stirred for 25 min at 0°, filtered, and worked up exactly as described above. The nmr spectrum of the product showed **6a** was recovered unchanged. No signals in the nmr spectrum were detected that could be attributed to a propionate group (<1%).

(D) With Pyridine. To a mixture of 0.55 g (2.3 mmol) of **2a,** 0.2 ml (2.5 mmol) of pyridine, and 10 ml of dichloromethane was added 55 ml (2.3 mmol) of gaseous nitrosyl chloride. An ir spectrum showed that **6a** had formed, but some unreacted **2a** still remained. Addition of more nitrosyl chloride (25 ml) caused decomposition of **6a** to benzophenone and diazidodiphenylmethane as determined by the ir spectrum.

Nitrosation of Acetophenone-*N*-acetylhydrazone. (A) A mixture of 300 mg (1.8 mmol) of hydrazone **2b** and 1.9 g (23 mmol) of sodium acetate in 8 ml of dichloromethane was allowed to react with 30 ml (1.3 mmol) of gaseous nitrosyl chloride in the same manner as previously described for **2a.** After 30 min an ir spectrum of the reaction mixture showed the presence of unreacted **2b** in addition to new bands at 2120 (s), 1760 (s), 1715 (s), and 1220 cm^{-1} (m). An additional 30 ml of nitrosyl chloride was added and after stirring the reaction mixture for 30 min more, it was filtered. The nmr spectrum of the filtrate showed methyl singlets at δ 1.90 and 2.1 that are assigned to the acetoxy azide **6b,** at δ 2.04 (acetic acid), δ 2.24 and 2.34 (unreacted **3b**), and δ 2.54 (acetophenone). After standing for 24 hr at room temperature in dichloromethane, the singlets at δ 1.90 and 2.1 decreased in size by 67% with a corresponding increase in the acetic acid peak. After 2 days, ir and nmr spectra showed that compound **6b** had completely disappeared. The filtrate was washed with a saturated solution of sodium carbonate, dried, and concentrated on a rotary evaporator. The nmr and ir spectra of the residue indicated that α-azidostyrene (0.60 mmol, 33%), acetophenone (0.04 mmol, 2%), and unreacted **2b** (0.2 mmol, 11%) were present. The α-azidostyrene was identified by the following data which agreed with the nmr and ir values reported in the literature:[17] nmr (CCl$_4$) δ 4.91 (d, J = 2.0 Hz, 1 H), 5.37 (d, J = 2.0 Hz, 1 H), 7.2–7.8 (m, 5 H); ir (CCl$_4$) 2220 (w), 2140 (s), 2105 (s), 1615 (m), 1300 (s), and 840 cm^{-1} (m).

In a duplicate run, 0.76 g (4.3 mmol) of **2b,** 5.0 g of sodium acetate, 19 ml of dichloromethane, and 200 ml of nitrosyl chloride were treated in the same manner. After 2 days at room temperature, the reaction mixture was worked up as before. The volatiles were collected and analyzed by ir for acetyl azide; none was detected (<1%). The residue was dissolved in CCl$_4$ and ethylene bromide was added as an internal standard. The nmr spectrum showed that α-azidostyrene (2.7 mmol, 63%), acetophenone (0.2 mmol, 5%), unreacted hydrazone **2b** (0.8 mmol, 19%), and some **6b** (0.26 mmol, 6%) were present.

(B) With Sodium Carbonate. Nitrosation was carried out in 50 ml of dichloromethane with 1.76 g (10.0 mmol) of **2b,** 5.3 g (50 mmol) of sodium carbonate, and 480 ml (20 mmol) of nitrosyl chloride as described above. The nitrosyl chloride was added over 20 min, and after an additional 20 min, the reaction mixture was filtered and evaporated at 0.01 Torr. The nmr spectrum of the resulting oil showed acetophenone (δ 2.5), acetic acid (δ 2.0), and unidentified peaks (δ 1.9–2.3) in a relative ratio of 16:1:3. The total product was distilled under reduced pressure (20 mm) to give 0.86 g (7.2 mmol, 72%) of acetophenone.

Nitrosation of Cyclohexanone-*N*-acetylhydrazone. A mixture of 0.58 g (3.75 mmol) of hydrazone **2c** and 4.0 g of anhydrous sodium acetate in 16 ml of dichloromethane was allowed to react with 30 ml (1.38 mmol) of gaseous nitrosyl chloride in the usual manner. The ir spectrum of the mixture showed an azide absorption at 2125 cm^{-1} (m), a strong carbonyl band at 1715 cm^{-1} (unreacted **2c**), and weak bands at 1745, 1220, and 1200 cm^{-1}. An additional 120 ml of nitrosyl chloride was added in two portions to bring the total to 150 ml (5.9 mmol). The reaction mixture was stirred another 20 min, then filtered and washed with a saturated solution of sodium carbonate. An ir spectrum of the resulting solution showed the following strong absorptions: 2125, 1745, 1715, 1375, 1220, and 1200 cm^{-1}. The solvent was removed under vacuum (20 mm) and the volatiles were trapped. The ir spectrum of the volatiles showed the presence of acetyl azide: 2135 (s), 1715 (s), 1370 (m), 1200 (s), 1150 (w), 990 cm^{-1} (m). This spectrum was identical with a spectrum of acetyl azide prepared from acetyl chloride and sodium azide in dichloromethane.[18] The nmr spectrum of the volatiles showed a singlet for acetyl azide at δ 2.0, and the yield was calculated to be 9% by using ethylene bromide as an internal standard. The yield was 11% on a duplicate run.

After removal of the volatiles, the ir spectrum (CH$_2$Cl$_2$) of the residue showed bands at 2125 (s), 1750 (s), 1710 (s), 1370 (m), and 1220 cm^{-1} (m). These bands are consistent with the presence of **6c** and cyclohexanone. The yields were estimated by nmr to be 45 and 35%, respectively.

Nitrosation of the Sodium Salt of Hydrazone 2c with Nitrosyl Chloride. A three-necked 100-ml flask was fitted with a nitrogen inlet, condenser with a drying tube, stirring bar, and serum cap. Dry toluene (25 ml) and 0.51 g (3.3 mmol) of compound **2c** were added, and the mixture was heated in an oil bath. At 50–60°, the mixture became homogeneous, and 91 mg (3.95 mmol) of sodium was added. Hydrogen evolution was moderate. The reaction mixture was heated at 100–110° for 4 hr during which time the sodium slowly disappeared and a copious white precipitate formed. The reaction mixture was cooled, and the toluene was removed under vacuum (0.1 mm). To the white residue was added 20 ml of dichloromethane and 2.0 g (22 mmol) of sodium acetate. The mixture was cooled in an ice–acetone bath and 30 ml of gaseous nitrosyl chloride was injected *via* a syringe. This action was repeated over a 1-hr period until a total of 150 ml (6.9 mmol) of nitrosyl chloride had been added. The reaction mixture was filtered. An ir spectrum of the filtrate revealed the presence of the acetoxyazido compound **6c** and some cyclohexanone, but no acetyl azide (<5%). The ir spectrum of the filtrate showed no change after 24 hr or after shaking with an aqueous solution saturated with sodium carbonate. The solvent was removed on a rotary evaporator to give 0.41 g of a liquid. A portion (180 mg) was chromatographed over Florisil eluting with a 5% dichloromethane–hexane solution. The first three fractions contained a single component (60 mg) identified as the acetoxyazido compound **6c** on the following basis: ir (CCl$_4$) 2940 (s), 2860 (m), 2110 (s), 1750 (s), 1365 (m), 1265 (s), 1220 cm^{-1} (s); nmr (CCl$_4$, 100 MHz) δ 1.41–1.76 (m, 6 H), 1.86–2.06 (m, 2 H), 2.01 (s, 3 H), 2.12–2.41 (m, 2 H); mass spectrum *m/e* (rel intensity) 155 (26), 127 (27), 113 (40), 112 (27), 98 (22), 85 (92), 60 (100). The yield in the crude product mixture was estimated to be 62% by nmr using an internal standard (ethylene bromide). A small amount of cyclohexanone was also present (~10–20%) as indicated by a weak carbonyl absorption at 1715 cm^{-1}.

Nitrosation of Heptaldehyde-*N*-acetylhydrazone. A mixture of 0.61 g (3.6 mmol) of hydrazone **2d** and 4.0 g (44 mmol) of sodium acetate in 15 ml of dichloromethane was nitrosated with 200 ml (9.2 mmol) of nitrosyl chloride in the usual manner. An ir spectrum taken after adding 50 ml of nitrosyl chloride showed new absorptions at 2135, 1200 (acetyl azide), and 1715 cm^{-1}. After adding the remainder of the nitrosyl chloride, the reaction mixture was filtered. An ir spectrum of the filtrate showed large amounts of acetic acid in addition to acetyl azide. The filtrate was then washed with a saturated solution of sodium carbonate. An ir spectrum (CH$_2$Cl$_2$) showed that a second azide product (**6d**) was present together with heptaldehyde and acetyl azide. The solvent was removed under vacuum and the volatiles were collected. The ir spectrum of the volatiles showed that acetyl azide was present; the yield by nmr was 14%. The residue showed the presence of the acetoxy azide **6d** [ir (CH$_2$Cl$_2$) 2120 (s), 1760 (s), 1210 cm^{-1} (s); nmr (CCl$_4$) δ 2.05 (s, 3 H), 5.78 (t, 1 H)] and heptaldehyde [ir (CH$_2$Cl$_2$) 2720 (w), 1730 cm^{-1} (s); nmr (CCl$_4$) δ 9.65 (t, 1 H)]. The yields were 23% for aldehyde and 20% for **6d** as determined by nmr on the crude product using ethylene bromide as an internal standard.

The acetoxy azide **6d** remained unchanged at room temperature over a period of a week or when it was heated in refluxing carbon tetrachloride for several hours. The mixture of products was chromatographed over silica gel eluting with carbon tetrachloride. Decomposition of **6d** was not observed, but there was little separation of **6d** and heptaldehyde.

Attempted Preparation of 1-Azidocyclohexene. To a solution of 28 mg of acetoxy azide **6c** in CCl$_4$ was added 65 mg of 1,8-bis(dimethylamino)naphthalene. The nmr spectrum was recorded several times over a 24-hr period. There was no change in **6c.**

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Registry No.—**2a,** 52919-86-5; **2b,** 28153-25-5; **2c,** 28766-50-9; **2c** Na salt, 52919-88-7; **2d,** 52919-87-6; **6a,** 52919-89-8; **6b,** 52919-90-1; **6c,** 52919-91-2; **6d,** 52919-92-3; **7a,** 119-61-9; **7b,** 98-86-2; **7c,** 108-94-1; **7d,** 111-71-7; acetylhydrazine, 1068-57-1; dinitrogen tetroxide, 10544-72-6; nitrosyl chloride, 2696-92-6; diazidodiphenylmethane, 17421-82-8; 1-azido-1-propionoxydiphenylmethane, 52964-38-2.

References and Notes

(1) E. H. White and D. J. Woodcock in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, New York, N.Y., 1968.

(2) D. E. Pearson, K. N. Carter, and L. M. Greer, *J. Amer. Chem. Soc.*, **75**, 5905 (1953); P. T. Lansbury and N. R. Mancuso, *J. Amer. Chem. Soc.*, **88**, 1205 (1966); K. N. Carter, *J. Org. Chem.*, **23**, 1409 (1958).
(3) To our knowledge the only prior report of an acetoxy azide was the synthesis of 2-azido-2-hexafluoroisopropyl acetate by R. J. Shozda and J. A. Vernon, *J. Org. Chem.*, **32**, 2876 (1967).
(4) S. Gotzky, *Chem. Ber.*, **64**, 1555 (1931); (b) F. R. Benson, *Chem. Rev.*, **31**, 1 (1947).
(5) R. W. Alder, P. S. Bowman, W. R. P. Steele, and D. R. Winterman, *Chem. Commun.*, 723 (1968).
(6) R. Huisgen and H. Reimlinger, *Justus Liebigs Ann. Chem.*, **599**, 11 (1956); E. H. White, M. C. Chen, and L. A. Dolak, *J. Org. Chem.*, **31**, 3038 (1966).
(7) For a related hydrolytic reaction, see E. H. White and W. J. Considine, *J. Amer. Chem. Soc.*, **80**, 626 (1958).
(8) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," W. A. Benjamin, New York, N.Y., 1965: (a) Vol. I, pp 139, 294; (b) Vol. II, p 164.
(9) M. P. Doyle, J. G. Kalmbacher, W. Wierenga, and J. E. DeBoer, *Tetrahedron Lett.*, 1455 (1974); M. P. Doyle, W. Wierenga, and M. A. Zaleta, *J. Org. Chem.*, **37**, 1597 (1972); M. P. Doyle, M. A. Zaleta, J. E. DeBoer, and W. Wierenga, *ibid.*, **38**, 1663 (1973).
(10) R. M. Scribner, *J. Org. Chem.*, **29**, 3429 (1964); C. J. Thoman and I. M. Hunsberger, *ibid.*, **33**, 2852 (1968).
(11) (a) It should be pointed out that these reactions can also be interpreted in terms of a chain reaction of the nitrosated material with water. (b) As a referee has pointed out, a chain reaction involving attack of azide on **6** would also lead to acetyl azide and the corresponding carbonyl compounds. On this basis, it is not clear, however, why **2a** and **2b** do not form as much acetyl azide as **2c** and **2d.**
(12) P. Grammaticakis, *Bull. Soc. Chim. Fr.*, 690 (1950).
(13) T. Curtius and T. S. Hoffman, *J. Prakt. Chem.* [2] **53**, 513 (1896).
(14) T. Curtius and F. Rauterberg, *J. Prakt. Chem.* [2] **44**, 192 (1891).
(15) R. A. Turner, *J. Amer. Chem. Soc.*, **69**, 875 (1947).
(16) "Dictionary of Organic Compounds," Vol. 1, Oxford University Press, New York, N.Y., 1965.
(17) A. Hassner and F. W. Fowler, *J. Org. Chem.*, **33**, 2686 (1968).
(18) P. A. S. Smith, *Org. React.*, **3**, 373 (1946).

Peracid Oxidation of Imino Ethers[1]

Donald H. Aue* and Darryl Thomas[2]

Department of Chemistry, University of California, Santa Barbara, California 93106

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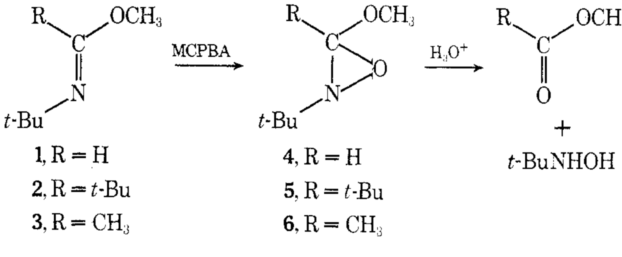
Peracid oxidation of imino ethers results in the formation of 3-alkoxyoxaziranes. The oxidation of the 2-alkoxyazetines **15**, **18**, and **22** leads to unstable 1-aza-5-oxabicyclo[2.1.0]pentanes and Baeyer–Villiger products, 2-alkoxy-2-oxazolines. The product distribution depends upon the substitution at the migrating center. These 2-alkoxy-2-oxazoline products represent the first examples of Baeyer–Villiger type oxidation of imines. The oxaziranes **9** and **10** derived from the cyclic imino ethers **7** and **8** can be isolated, but readily rearrange to imino esters **11** and **12** thermally. The hydrolysis of alkoxyoxaziranes yields esters and hydroxylamines, but hydrolysis of the bicyclic oxaziranes **9** and **10** leads to cyclic hydroxamic acids as well. Further oxidation of alkoxyoxaziranes gives esters and nitroso compounds. The nitroso compounds dimerize if tertiary or tautomerize to oximes if secondary. Oxidation of 2-alkoxyoxazoline **19** (an imino carbonate) results in the formation of a nitroso carbonate **29**, by a double oxidation sequence. Oxidation of imino ethers with 2 equiv of peracid provides a convenient synthetic method for cleavage of the C=N bond.

The oxazirane ring system was first synthesized in 1956 by peracid oxidation of imines.[3-8] Since then, many oxaziranes have been prepared by this method as well as new ones.[9-30] The ring strain and electronegative elements of the oxazirane ring make it unique in its physical and chemical properties. Oxaziranes, for example, have an unusually high barrier to nitrogen inversion (ref 4, 16, 17, 26, 27, 31, 32). Thermally, oxaziranes rearrange to nitrones (ref 3, 4, 6, 8, 11, 15, 26–28) (as low as −8°),[12] amides (generally above 150°) (ref 4, 9, 10b, 26–28, 30), or a carbonyl compound plus an imine (ref 4, 12, 13, 26, 27). Photochemically, oxaziranes open to give nitroxides,[28,33a] nitrenes,[28] or amides.[28,33b,c] Hydrolytically, oxaziranes can decompose to carbonyl compounds, hydroxylamines, and ammonia or imines, the products dependent upon the pH and the substituents of the oxazirane (ref 3, 4, 6, 9, 10b, 26, 27, 30, 34a,b, 35a,b). Some interesting cycloaddition reactions with heterocumulenes have recently been investigated by Agawa and coworkers.[36,37]

While many imines have been oxidized to oxaziranes, no imino ethers have been oxidized before.[1,22] Imino ethers are readily available by alkylation of amides and lactams[38-41] and other methods.[42] Of particular interest are the alkoxyazetines derived from alkylation[43,44a,b] of β-lactams available from addition of chlorosulfonyl isocyanate to olefins.[45,46] This constitutes nearly the only entry into the azetine ring system.[47] We describe here the oxidation of some cyclic and acyclic imino ethers and some properties of the derived alkoxyoxaziranes.

Results and Discussion

Oxidation of Acyclic Imino Ethers. Oxidation of imino ethers **1** and **2** using *m*-chloroperbenzoic acid (MCPBA) gives the oxaziranes **4** and **5** in good yields. Oxazirane **4** is stable to aqueous base, but treatment with aqueous acid results in the formation of methyl formate (95% by nmr) and *N-tert*-butylhydroxylamine (87% by nmr). This reaction sequence can be used to synthesize hydroxylamines from the corresponding amides in two steps.[4,27] The acid hydrolysis of 3-alkoxyoxaziranes yields products analogous to those obtained from 3-phenyloxaziranes.[3,4,10b,34a,b,35a] Two routes are possible, considering alkoxyoxaziranes as cyclic amide acetals.[48] Protonation on oxygen with C–O bond cleavage has been suggested for this process with most oxaziranes,[4,34a,b,35a] although protonation on nitrogen with C–N bond cleavage is the preferred mode for cleavage of acyclic amide acetals in acid.[48] The C–O cleavage is favored only in neutral hydrolysis of amide acetals.[48] Apparently no N–O cleavage occurs. If it had occurred, a simultaneous



1, R = H
2, R = *t*-Bu
3, R = CH$_3$

4, R = H
5, R = *t*-Bu
6, R = CH$_3$