Photochemistry of Acid Hydrazides

Samples of 3a in 2-propanol solvent (3.0 ml) were placed in the round-tube portion of a two-compartment cell and freeze-thaw degassed to a residual pressure of 10^{-4} mm. The cell was constructed from Pyrex glass tubing with a tubular compartment 13 mm o.d. by 55 mm and a cuvette compartment from 10 mm i.d. by 55 mm Trubore square tubing. Irradiations were carried out with the solution in the 13-mm tube and uv analyses were performed after transfer of the solution to the cuvette portion. cis-Piperylene, present at the concentrations shown in Table II, was employed as a triplet quencher for the photoreduction. At the end of the experiment formation of trans- piperylene was detected by glpc using the β,β' -oxydipropionitrile column (vide supra). Samples of 3c in benzene solvent (3.00 ml) of the various concentrations shown in Table III were placed in Pyrex tubes (13×70 mm) and freezethaw degassed to a residual pressure of 10^{-5} mm. After irradiation in the quantum yield apparatus formation of 5.6-dihydro-3,5.5-trimethyl-1,4-oxazin-2-one (3a) was measured by glpc using a 6 ft \times 0.25 in. column of 5% FS-1265 on 30-60 mesh Haloport F at 115° (He 60 cm³/min) using benzisoxazole as an internal standard. The quantum yields of formation of 3a as a function of the initial concentration of 3c are reported in Table III.

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Registry No-3a, 53153-46-1; 3b, 53153-47-2; 3c, 53153-48-3; 4a, 53153-49-4; 4b, 53153-50-7; 5a, 53153-51-8; 6, 53153-52-9; 7, 53153-53-0; N - (2 - (1 - hydroxy-2-methylpropyl))benzoylformamide, 53153-54-1; ethyl pyruvate, 617-35-6; N - (2-(1-hydroxy-2methylpropyl)acetylformamide, 53153-55-2; 2-amino-2-methylpropanol, 124-68-5; ethyl hexan-2-onate, 5753-96-8.

References and Notes

- (1) T. H. Koch and R. M. Rodehorst, Tetrahedron Lett., 4039 (1972).
- (2) J. A. Hyatt and J. S. Swenton, J. Chem. Soc., Chem. Commun., 1144 (1972); J. S. Swenton and J. A. Hyatt, J. Amer. Chem. Soc., 96, 4879 (1974)
- (3) E. Biekert and J. Sonnenbichler, *Chem. Ber.*, **94**, 2785 (1961).
 (4) O. L. Chapman and J. D. Lassila, *J. Amer. Chem. Soc.*, **90**, 2499
- (1968).
- (5) H. L. Goering, J. N. Eikenberry, and G. S. Koermer, J. Amer. Chem. Soc., 93, 5913 (1971).
- (6) A. Padwa, W. Bergmark, and D. Pashayan, J. Amer. Chem. Soc., 91,
- A. Padwa, W. Bergmark, and D. Pashayah, J. Amer. Chem. Soc., 91, 2653 (1969).
 M. Fischer, Chem. Ber., 100, 3599 (1967); W. F. Smith, Jr., and B. W. Rossiter, J. Amer. Chem. Soc., 89, 717 (1967); E. V. Doncht and G. Porter, J. Chem. Phys., 46, 1173 (1967); T. Okada, K. Saeki, M. Kawanisi, and H. Nozaki, Tetrahedron, 26, 3661 (1970).
 J. C. Dalton and H. -F. Chan, J. Amer. Chem. Soc., 95, 4805 (1973).
- (9) T. H. Koch, J. A. Olesen, and J. DeNiro, J. Amer. Chem. Soc., submitted for publication.
- V. I. Danilov, Y. A. Kruglyak, V. A. Kuprievich, and V. V. Ogloblin, *Theor. Chim. Acta*, 14, 242 (1969).
- (11) T. H. Koch, R. J. Sluski, and R. H. Moseley, J. Amer. Chem. Soc., 95, 3957 (1973); T. H. Koch and K. A. Howard, Tetrahedron Lett., 4035 (1972).
- (12) T. H. Koch and R. M. Rodehorst, unpublished results.
 (13) I. I. Lapkin and N. A. Karavanov, *Uch. Zap. Perm. Gos. Univ.*, 13, 101 (1959); *Chem. Abstr.*, 57, 11010i (1962).
- (14) ASTM Committee E-14 on Mass Spectrometry, "Index of Mass Spectral Data," ASTM Special Technical Publication No. 356. American Society for Testing Materials, Philadelphia, Pa., 1963, p 1.
- (15) F. G. Moses, R. S. H. Liu, and B. M. Monroe, Mol. Photochem., 1, 245 (1969).
- (16) C. G. Hatchard and C. A. Parker, Proc. Roy. Soc., Ser. A, 235, 518 (1956).

Photochemistry of Acid Hydrazides. Determination of Modes of Reaction and Identification of Photoproducts^{1a,b}

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The photochemical reaction pathways of a number of benzoic and acetic acid hydrazides of the type $R_1CONZNR_2R_3$ ($R_1 = CH_3$, C_6H_5 ; Z = H, CH_3 , C_6H_5CO , $p - CH_3C_6H_4SO_2$; $R_2R_3 = C_6H_5$, CH_3 , C_6H_5CO , CH_3CO) have been determined with 254-nm light. All reaction products are the result of dissociative processes with the two primary processes being nitrogen-nitrogen and carbonyl carbon-nitrogen cleavage. The first of these processes yields amides and amines, while the second yields aldehydes and acids. The amount and direction of cleavage appear to depend on the relative dissociation energies of the bonds in the vicinity of the carbonyl group of hydrazides. Secondary products of the type R1CONZR2 and R1COR2 are observed and shown to arise via known photochemical processes of the initial photoproducts of the acid hydrazides.

Although the photochemistry of amides² has been well studied, the corresponding aza analogs, acid hydrazides, have received scant attention in the literature.³ Generally, amides undergo photochemical reactions similar to those of ketones, namely α cleavage and Norrish type II cleavage⁴ (Scheme I). The analogous α -amino ketones undergo, almost exclusively, elimination reactions.^{5,6} However, cyclization in very high yields has been reported for α -N-alkylaminoacetophenones to produce 3-azetidinols7 similar to the cyclobutanol formation of ketones.^{8–11}

Scheme I **Photolytic Reactions of Amides**

 $CH_3CH_2CH_2CONH_3 \xrightarrow{h_{\nu}} CH_3CH_2CH_3NH_3 + CO$ α cleavage

type II $CH_3CH_2CH_2CONH_2 \xrightarrow{h_{\nu}} CH_2 \longrightarrow CH_2 \longrightarrow CH_2 CH_2$

Considering the large volume of previous work on the ketones and amides, as well as their variety of photochemical reactions, it appeared reasonable to investigate the photochemistry of acylhydrazides as aza analogs of amides and diaza analogs of ketones to determine their comparative modes of reaction. Of particular interest was the potential for synthetic routes to diazetidinols via an internal cyclization of the hydrazides.

Results and Discussion

The results of the photolysis of the compounds reported in this study are summarized in Table I. Percentage yields are not corrected for unreacted starting material as they could not be assayed via gas chromatography. However, in the preparative runs, analyzed by column chromatography, the unreacted starting material was recovered, accounting for approximately 90-95% of the material balance. There-

Tal	ble I
Summary of Pho	otolysis Products
O R'CN- Z	$-NR_2$ $\begin{vmatrix} \\ R_3 \end{vmatrix}$

Comp	od R ₁	Z	R ₂	R ₃	Primary N-N bond cleavage products	Primary CO-N cleavage products	Secondary products
3a	C ₆ H ₅	C ₆ H ₅ CO	CH3	CH3	$C_{6}H_{5}CONH_{2}$ (7a) (14%)	C_6H_5CHO (4a) (8.1%)	7c (11%)
					$(C_6H_5CO)_2NH (70) (4.5\%)^{\circ}$ (CH ₂) ₂ NH (8a) (23%) ^b	3D (19.6%)"	$C_6H_5COCH_3$ (6) (trace)
3 b	C_6H_5	н	CH_3	CH_3	7a (19%)	4a (5.4%)	7c (11%)
							6a (trace)
3c	C_6H_5	$p-CH_3C_6H_4SO_2$	CH3	CH_3	7a (10%)	4a (4.3%)	7c (5.2%)
							$C_{6}H_{5}CH_{3}$ (14%)
							6a (trace)
3d	$\mathbf{C}_{6}\mathbf{H}_{5}$	H	$(CH_3)_2CH$	$(CH_3)_2CH$	7a (25%)	4a (4.3 %)	7f (20%)
					$[(CH_3)_2CH]_2NH (8b) (21\%)$		
3e	$\mathbf{C}_{6}\mathbf{H}_{5}$	CH_3	C_6H_5CO	CH_3	$C_{6}H_{5}CONHCH_{3}$ (7c) (30%)	4a (9.2 %)	6 (2.9%)
						C ₆ H ₅ CO ₂ H (2.1%)	
3f	CH_3	CH_3	CH_3CO	CH_3	$CH_{3}CONHCH_{3}$ (7d) (2.6%)	$CH_{3}CHO$ (4b) (1.2%)	$CH_{3}CON(CH_{3})_{2}$ (9a) (3.0%)
3g	CH_3	(CH ₃) ₂ CH	н	(CH ₃) ₂ CH	$CH_{3}CONHCH(CH_{3})_{2}$ (7e) (27%)	4b (10%)	
					$(CH_3)CHNH_2$ (8c) (11%)		
3h	C_8H_5	Н	C ₆ H ₅ CO	$(CH_3)_2CH$	7a (11%)	4a (8.3%)	
						$C_{6}H_{5}CO_{2}H$ (9.9%)	
10a	C_6H_5	H	C_6H_5	C_6H_5	7a (24%)	4a (4.7%)	
					$(C_6H_5)_2$ NH (11) (37%)		
10b	CH_3	H	C_6H_5	C_6H_5	11 (23%)°		
10c	$C1CH_2$	C_6H_5	н	C_6H_5		12 (52%)	

^a Determined by column chromatography. ^b Determined by bubbling hydrogen chloride through the solution and isolating the amine hydrochloride. ^c Photolyzed 5.5 hr.

fore, the total yields listed may be considered as a good approximation to the percentage conversion.

An examination of the products obtained as well as their percentage yields in Table I reveals that three types of bond cleavage occur in the photochemical reaction of acid hydrazides: nitrogen-nitrogen (NN) bond cleavage, carbonyl carbon-nitrogen (CON) cleavage, and alkyl carbon-nitrogen (CN) cleavage. A detailed consideration of these reactions including comparison with ketones and amides is included in the following discussion.

Nitrogen-Nitrogen Bond Cleavage. Rupture of the nitrogen-nitrogen bond is evidenced by the presence of amines and amides as major products of the reaction. This mode of cleavage is a logical consequence of the low-energy requirements of the nitrogen-nitrogen bond (i.e., a dissociation energy of 38 kcal/mol¹²). The carbonyl excitation energy of benzamide, analogous to the hydrazides studied, is 79 kcal/mol,¹³ more than enough to induce NN cleavage. Dissipation of photoexcitation energy of the hydrazides may then occur by rupture of the bonds near the chromophore in order of their stability. Since the nitrogen-nitrogen bond is the least stable bond, the primary photoreaction then is the NN cleavage. A comparison of the NN cleavage products in Table I indicates the yields parallel the ability of the substituents to stabilize the radical produced. Compounds 3b,d and 10a,b particularly illustrate this trend. In particular, 10b cleaving to give the relatively stable diphenylamino radical produced 23% NN cleavage in just 5.5 hr, while the alkyl hydrazides took much longer to produce a similar reaction yield. The results of Davidson and Lewis³ also agree with this conclusion. A summary of the mode of formation of the photolysis is contained in Schemes II and III.

It is also apparent that substituents on the nitrogen α to the carbonyl also facilitate the NN cleavage, although a distinction between steric and electronic factors is not clear-cut. Compounds **3f** and **3g** indicate that bulky α substituents not only facilitate NN cleavage but also induce a greater reactivity in the photoreaction.

Compounds 3c and 10c are two notable exceptions to the predominance of NN cleavage in Table I. Their behavior, however, can be easily explained. Compound 3c has a relatively weak nitrogen-sulfur bond (i.e., approximately 45 kcal/mol¹⁴) which makes it nearly as susceptible to rupture as the nitrogen-nitrogen bond. In fact, a comparison of 3b and 3c shows that the combination of nitrogen-sulfur and NN cleavage in 3c is essentially the same as the NN cleavage for 3b. It is assumed that the formation of toluene from 3c results from nitrogen-sulfur cleavage to give the tosyl radical which, in turn, loses sulfur dioxide to give the tolyl radical. The tolyl radical then abstracts a hydrogen atom from the solvent to give the toluene product. The lack of toluene product in the other benzoic acid hydrazides supports the contention that the tosyl group is the source of toluene.

The second exception is 10c which gives azobenzene and hydrogen chloride as the only identifiable products. In this particular case, the ease of oxidation of N-substituted hydrazobenzenes¹⁵ can account for the cleavage of the carbonyl-nitrogen bond, the driving force being the formation of the very stable azobenzene molecule. This reaction path is indicated in path b, Scheme III.

The above results indicate that acyl hydrazides differ considerably in their mode of reaction when compared to the ketones^{10,11} and amides.² It is readily apparent that the NN cleavage is not the typical Norrish type II cleavage as

Scheme II Photolysis of N-Alkyl Acid Hydrazides



indicated in Scheme II, path a. Although the amides would be expected from such a cleavage, there is no evidence that the imine is formed in the reaction, either in this work or in that of Davidson and Lewis.³ Therefore, paths b and c in Scheme II indicate a much better representation of the NN cleavage reaction.

Carbonyl Carbon-Nitrogen Cleavage. The second type of cleavage observed, namely the carbonyl carbon-nitrogen cleavage (CON), is evidenced by the presence of **4a** and **b**. Additionally, the benzoic acid found may be considered as a CON cleavage product, either formed by oxidation of **4a** during work-up procedure or from trace amounts of oxygen present in the nitrogen gas used for purging the reaction solutions.^{16,17} The percentage yields of the aldehydes or benzoic acid must be considered as minimum yields since the acyl radicals formed can readily decarbonylate to give either benzene or methyl radicals leading to products that would not be detected using our method of assaying the reaction products.

The carbonyl carbon-nitrogen bond energy is greater than that of the nitrogen-nitrogen bond (i.e., approximately 80 kcal/mol for benzoic hydrazides and 96 kcal/mol for acetic hydrazides¹⁸), and therefore less likely to rupture. As a first approximation, it appears that the amount of CON cleavage is related to the number of carbonyl groups in the molecule. Compounds 3b-d and 10a all have one benzoyl group and give approximately the same amount of CON cleavage products, about 5%. However, photolysis of the amide photoproducts alone, under the same conditions, gives an identical yield of CON cleavage product, about 5%, no matter what the nature of the N substituent. It would appear then that small yields of the CON cleavage products of about 5% are due to cleavage of the photoproduct amide rather than the direct cleavage of the acid hydrazide. Compound 3e may be included in this group, since, with two carbonyl groups on different nitrogens, it yields 11% CON

Scheme III Photolysis of N-Aryl Acid Hydrazides



scission products, approximately double that of a single carbonyl. It is known that photolysis of amides does indeed proceed with CON cleavage.^{19–21} To effectively discuss the CON cleavage reaction then, one must consider that approximately 5% of such products arise from further photolysis of the amide photoproducts.

There are, however, several compounds, **3a,g,h** and **10c**, that exhibit a substantially greater degree of CON scission. This increase in CON cleavage arises from a general weakening of the CON bond through decreased resonance interaction of the nitrogen lone-pair electrons and the carbonyl group. Since **3a** exhibits the greatest amount of CON scission, 45%, consideration of its mode of reaction may be used to illustrate the concept of decreased resonance interactions as the primary cause of such cleavage. The 45% figure for CON cleavage is arrived at by the summation of the yield of photoproducts **3b**, **7a**, and **7c**. Direct CON scission of **3a** gives **3b**, while **7a** and **7c** are produced by further reaction of **3b**. Appearance of **7a** and **7c** in the reaction

Table II		
Photolysis Products of 3d as a Function		
of Added $8c^{a,b}$		

Hydrazide/amine	7£/7a	
No amine	0.48	
7.35	0.54	
2.45	0.55	
1.33	0.56	
1.05	0.58	
0.61	0.61	

^a Molarity of hydrazide = 3.88×10^{-2} . ^b Photolyzed in 15-ml quartz tubes in a merry-go-round, without purging with nitrogen. It was found that purging reactions gave increased yields of photoproducts while unpurged solutions gave, in addition to lower yields, an increase in the amount of tars formed on the sides of the reaction vessel. This would be expected with a reaction involving radical intermediates.

does not arise from 7b, the NN cleavage product, since 7b was unreactive under the conditions of photolysis.

Examination of a molecular model of **3a** reveals that the coplanarity of the carbonyls, nitrogen atom, and benzene rings, required for maximum resonance stabilization, cannot be achieved. In addition, coplanarity of the carbonyl system alone introduces unfavorable steric and electrostatic interactions with the benzene rings. It is fairly obvious that decreased resonance interaction will be the result of these steric and electrostatic effects. This would tend to weaken the CON bond and render it more susceptible to rupture in the photoexcited hydrazide.

A similar argument may be advanced for the other compounds, **3g**,**h** and **10c**, to rationalize the increased degree of scission observed for these substances. All have a substituent on the nitrogen α to the carbonyl which is either bulky or capable of resonance interaction with the lone-pair electrons on the nitrogen. Both types of groups would tend to weaken the CON bond via decreased resonance interaction and lead to increased susceptibility to cleavage in the photoreaction. An additional possibility for **10c** has already been presented above.

It appears that there are some similarities between ketones and hydrazides in this type of reaction since the trend in CON cleavage parallels the α cleavage of ketones. The greater the bulk of the α substituent, the greater the degree of α cleavage.²² In addition, a number of amides containing supplementary chromophoric groups have exhibited CON cleavage.²

The high reactivity of 3a appears to be in direct contrast with the results of Davidson and Lewis³ who observed a lack of reactivity of compound 13. This could either be due



to a solvent effect, or, since the five-numbered phthalimido group is planar, there is ample opportunity for resonance interaction of the nitrogen lone-pair electrons with both carbonyls and the benzene ring. The CON bond would thus be much more stable and less likely to cleave in the photoexcited hydrazide. In support of this, we observed only 4.5% NN cleavage in **3a** in 24 hr, while Davidson and Lewis observed no reaction in **13** in 6 hr. It would appear then that increased resonance interaction reduces the suscepti-

Table IIIPhotolysis Function of 3d as a Function of Time a,b

Time, hr	% 7a	% 7f	
1.4	9.8	0.0	
2.8	11.5	2.9	
5.2	19.1	3.8	
6,9	14.8	4.5	
12.0	14.6	7.2	
24.0	12.0	10.8	

 a Molarity of acid hydrazide = 3.74 \times 10^{-2}. b See footnote b in Table II.

bility toward photoreaction of hydrazides, while a decreased resonance interaction increases the photoreactivity.

Alkyl Carbon-Nitrogen Cleavage. A secondary product arising in the photochemical reaction is that of the Nalkylamides shown in Table I. The presence of such products may arise by paths f + i or g + i in Scheme II. That the latter path is involved, while the first does not appear to be operative, is supported by the following discussion.

Path g + i is evidenced by the data in Table II, which show the ratio of the *N*-alkylamide photoproducts of **3d** as a function of added **8b**. As the amount of added amine is increased (*i.e.*, lowering the hydrazine/amine ratio) the ratio of **7f**/**7a** increases. This result is indicative of the involvement of the amine in the formation of **7f**. It is well known that amines may cleave in the manner indicated by path g,²³ suggesting that at least a portion of **7f** arises *via* path g + i.

A consideration of the data in Table III shows the rate of appearance of the two amide products as a function of time. It may be seen that the primary NN cleavage product, 7a, appears early in the reaction, before the appearance of N-isopropylbenzamide. This means that considerable NN cleavage is necessary for the production of the Nalkylamide product. Since the amine is a product of NN cleavage, this is indirect evidence of the pathway g + i. In addition, it appears that, late in the reaction, 7f is formed at the expense of 7a. This is indicative of path k + i and/or k. A reaction path such as f + i would be expected to have a constant 7f/7a ratio since the radical generated by f would be in the vicinity of the benzamido radical. Thus a constant rate of NN cleavage coupled with a constant rate of path f should give a ratio that is relatively constant throughout the reaction. The constantly changing ratio as indicated by the data in Table III makes f + i an unlikely reaction pathway. Additionally, attempts to trap the nitrene intermediate that would be generated by path f were unsuccessful.

The yield of this secondary amide product appears to be related to the stability of the alkyl radical produced, the isopropylhydrazides giving higher yields than the methylhydrazides.

The appearance of **9a** from **3f** does not arise from alkylnitrogen cleavage but rather from the photolysis of **7d**, initially formed to give methyl radicals *via* carbonyl carboncarbon cleavage which combine with the *N*-methylacetamido radicals formed by NN cleavage. Such photolytic reactions have been observed previously²⁴ and the photostability of *N*-alkyl bonds of amides is also documented.^{25,26} This would also support path g + i.

Small amounts of 16 appeared in the photolysis of **3a,b,c**, and **e**. It would seem likely that its formation is due to diffusive encounters of benzoyl and methyl radicals since both are produced during the course of the photoreaction. Also, the greatest yield of 6 was observed with 3e, which also exhibited a high percentage of CON cleavage.

Conclusions

From a consideration of the results in Table I and the above discussion it is clear that the photochemical processes of hydrazides in 254-nm light are exclusively dissociative processes. No rearrangement or cyclization products were detected in the compounds studied. It also appears that the amount of bond dissociation parallels the strengths of the bonds in the vicinity of the carbonyl group of hydrazides.

The weakest bond, the nitrogen-nitrogen bond, undergoes cleavage in most of the compounds, with greater amounts of cleavage occurring with substituents that either weaken the nitrogen-nitrogen bond and/or stabilize the incipient radicals. In one case, compound IV, with the presence of the relatively weak N-S bond, the nitrogen-nitrogen dissociation is reduced by the amount of N-S cleavage which occurs.

With the carbonyl carbon-nitrogen bond, the dissociation energy is presumably in the vicinity of energy of the radiation used for photolysis, approximately 78 kcal. Therefore, substituents which interfere with resonance interactions of the nitrogen lone pair and the carbonyl group lower the bond dissociation energy and thus increase the amount of carbonyl carbon-nitrogen bond cleavage.

The results of Davidson and Lewis³ are consistent with the bond dissociation energy hypothesis. With compound 14 predominantly nitrogen-nitrogen bond cleavage occurs and with type 15 cleavage occurs at the weaker carbonyl carbon-carbon bond.

$C_6H_5CONHNR_1R_2$	$C_6H_5CH_2CONHNR_1R_2$
14	15

In addition to the primary dissociative process, secondary dissociative processes occur in the initial products to give N-alkylamides and acetophenone. These products may be rationalized on the basis of known photochemical processes of the initial photoproducts.

Experimental Section

General Methods. Melting points were determined on a Thomas-Hoover (Unimelt) apparatus and are uncorrected. Microanalyses were carried out on a Perkin-Elmer Model 240 carbonhydrogen-nitrogen analyzer.

Nuclear magnetic resonance spectra were obtained with Hitachi-Perkin-Elmer Models R-10 and R-24 spectrometers. Infrared spectra were obtained with a Beckman Model IR-10 recording spectrophotometer. Ultraviolet spectra were determined on a Cary 14 recording spectrophotometer.

Thin-layer chromatography (tlc) was carried out using Eastman or Brinkmann precoated silica gel or alimina plastic plates. Prepartive thin-layer chromatography (plc) was run on Brinkmann precoated silica gel plates of 2 mm thickness. Tlc was used to examine the purity of products and plc was used for purifying samples whenever necessary. Vapor phase chromatography was conducted on a Gow-Mac Model 550 gas chromatograph equipped with a thermal conductivity detector and a Kontron Model 1100 recorder fitted with an electronic integrator. Quantitative data were obtained using the relative weight response technique²⁷ with an internal standard added after photolysis. For the benzoylhydrazides, benzophenone was the internal standard, and toluene was likewise used for the acetylhydrazides. Blanks were also run to ascertain that the observed products were the result of photolysis and not due to a thermal reaction during the gas chromatographic analysis. The quantitative values listed are the average of at least three determinations and are accurate to $\pm 4\%$ of the indicated value.

Photolysis Procedure. Photolyses were carried out in a Rayonet Photochemical Reactor at 253.7 nm using a 100-ml quartz tube for exploratory and quantitative runs and a 1500-ml quartz tube for preparative runs. Benzene solutions, 0.1-0.01~M, were purged by bubbling dry nitrogen into the solutions for at least 0.5hr, and then photolyzed for 24 hr. Initially, the photolysis solutions were analyzed by column chromatography to characterize the products. All products isolated by column chromatography were identified by comparison of their melting point and infrared and nmr spectra with an authentic sample as well as a mixture melting point determination. Quantitation of products was conducted by gas chromatography. At the end of the photolysis, 10 ml of the solution was removed and analyzed for the presence of volatile materials using a 4 ft \times 0.25 in. Carbowax column. The reminder of the photolysis solution was evaporated under reduced pressure into an oil or slurry, dissolved in 2–5 ml of benzene and transferred to a 10-ml flask. A known weight of the internal standard was introduced and enough benzene was added to make a total volume of 10.0 ml. These solutions were analyzed on a 4 ft \times 0.25 in. DC200 on Chromosorb P column. Relative weight response values were determined with standard solutions and used in the analysis of the photolysis solutions.

N, N-**Dibenzoyl**-N', N'-**dimethylhydrazine (3a)** was prepared by the method of Hinamann²⁸ mp 152–153° (lit. 152–153°); λ_{max} (MeOH) 323 (ϵ 1800), 236 nm (15,000).

N'-**Benzoyl**-*N*,*N*-**dimethylhydrazine (3b)** was prepared by the method of Hinmann:²⁸ mp 104–105° (lit. 106–107°); λ_{max} (MeOH) 214 nm (ϵ 9300).

N,N-Dimethyl-N'-(p-toluenesulfonyl)hydrazine (16) was prepared by the method of Wawazonek and Meyer:²⁹ mp 80-81° (lit. 79-81°).

N-Benzoyl-N', N'-dimethyl-N-(p-toluenesulfonyl)hydra-

zine (3c). A well-stirred suspension of 32.4 g (0.15 mol) of 16 in 300 ml of ether and 15.3 g (0.15 mol) of triethylene, cooled to 0°, was treated, dropwise, with 20.1 ml (0.19 mol) of benzoyl chloride. After the addition the mixture was stirred for 1 hr and then allowed to stand overnight. The white needles of triethylamine hydrochloride were filtered off and washed with ether. The filtrate was evaporated and the brown viscous residue recrystallized from methanol. Two crops gave 6.0 g (10.5%) of 3c: mp 95–95.5°; ir (film) 1680, 1600, 1350, 1290, 1170, 1030, and 820 cm⁻¹; nmr (CDCl₃) δ 2.45 (s, 3 H), 3.00 (s, 6 H), 7.3–8.1 (m, 9 H); λ_{max} (MeOH) 233 nm (ϵ 21,900)

Anal. Calcd for $\rm C_{16}H_{18}N_{2}O_{3}S:$ C, 60.36; H, 5.70; N, 8.80; S, 10.07. Found: C, 60.71; H, 5.98; N, 8.60; S, 10.04.^{30}

N,N-Diisopropylhydrazine (17) was prepared by the method of Lemal, et al.³¹ bp 135-136° (lit. 130-132°).

N'-Benzoyl-*N*,*N'*-diisopropylhydrazine (3d). A solution of 31 g (0.22 mol) of benzoyl chloride in 60 ml of ether was cooled to 5° and 13 g (0.11 mol) of diisopropylhydrazine in 50 ml of ether was added dropwise, with stirring, over a period of 1 hr, keeping the temperature between 5 and 10°. After stirring an additional hour, the white crystals that separated were collected and recrystallized from ethanol-water and then carbon tetrachloride to yield 7.0 g (29%) of 3d: mp 140–141°; ir (Nujol) 3260, 1625, 1130, 915, and 695 cm⁻¹; nmr (CDCl₃) δ 1.10 (d, 12 H, J = 6 Hz), 3.20 (m, 2 H), 6.60 (s, 1 H), and 7.3–7.9 (m, 5 H); λ_{max} (MeOH) 222 nm (ϵ 11.200).

(s, 1 H), and 7.3–7.9 (m, 5 H); λ_{max} (MeOH) 222 nm (ϵ 11,200). Anal. Calcd for C₁₃H₂₀N₂O: C, 70.87; H, 9.15; N, 12.71. Found: C, 70.67; H, 9.12; N, 12.52.

N,N'-**Dibenzoyl**-N,N'-**dimethylhydrazine** (3e) was prepared by the method of Craig, *et al.*³² mp 84–87° (lit. 84–87° ³³ and 88–89° ³²).

N,N'-Diacetyl-N,N'-dimethylhydrazine (3f) was prepared by the method of Hinmann:²⁸ mp 60-62° (lit. 61-62°).

N-Acetyl-N,N'-diisopropylhydrazine (3g) was prepared from N,N'-diisopropylhydrazine^{34,35} by the method of Straub and Zeller:³⁶ bp 52–54° (2 mm) [lit. 88–89° (12 mm)].

N,N'-**Dibenzoyl**-N-**isopropylhydrazine** (3h) was prepared from isopropylhydrazine by the method of Craig, *et al*:³² mp 163-164° (lit.^{32,37} 161.5°); λ_{max} (MeOH) 222 nm (ϵ 15,000).

N'-Benzoyl-N,N-diphenylhydrazine (10a) was prepared by the method of Fisher:³⁸ mp 192–193° (lit. 192°); λ_{max} (MeOH) 280 (ϵ 14,800), 226 nm (21,400).

N'-Acetyl-N,N-diphenylhydrazine (10b) was prepared by the method of Gattermann, et al.;³⁹ mp 185–186° (lit. 184°); λ_{max} (MeOH) 280 (ϵ 12,200), 226 nm (9240).

N-(Chloroacetyl)-N,N'-diphenylhydrazine (10c) was prepared by the method of Bauer:⁴⁰ mp 157–158° (lit. 163°); λ_{max} (MeOH) 225 nm (ϵ 19,000).

Anal. Calcd for $C_{14}H_{13}N_2OCl: C, 64.48; H, 5.03; N, 10.75.$ Found: C, 64.51; H, 5.08; N, 10.67.

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References and Notes

- (1) (a) Abstracted from the Ph.D. Thesis of S.A.S., Lowell Technological Institute, May 1974. (b) A preliminary account of this work was presented at the Fifth Northeast Regional Meeting of the American Chemical Society, Oct 1973, Abstract No. 267
- (2) For a review, see I. Rosenthal in "The Chemistry of Amides," J. Zab-icky, Ed., Interscience, New York, N. Y., 1970, pp 289–308.
- (3) While this work was in progress, a preliminary communication appeared: R. S. Davidson and A. Lewis, *Tetrahedron Lett.*, 4679 (1973).
 (4) E. H. Booth and R. G. W. Norrish, *J. Chem. Soc.*, 188 (1952).
- (4) L. H. Bodwa, W. A. Eisenhardt, R. Eruber, and D. Pashayan, J. Amer. Chem. Soc., 91, 1857 (1969).
 (6) R. A. Clasen and S. Searles, Chem. Commun., 289 (1966).

- E. H. Gold, J. Amer. Chem. Soc., 93, 2793 (1971).
 P. J. Wagner, Accounts Chem. Res., 4, 168 (1971).
 P. J. Wagner, P. A. Kelso, and R. G. Zepp, J. Amer. Chem. Soc., 94, 7480 (1972).
- (10) F. D. Lewis and T. A. Hilliard, J. Amer. Chem. Soc., 94, 3852 (1972).
 (11) J. C. Dalton and H. F. Chan, J. Amer. Chem. Soc., 95, 4085 (1973).
- K. S. Pitzer, J. Amer. Chem. Soc., 70, 2140 (1948).
 H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectrocopy," Wiley, New York, N. Y., 1962, p 180.
- (14) C. K. Barker, A. W. Cordes, and J. L. Margrave, J. Phys. Chem., 69, 334 (1965).
- (15) P. A. S. Smith, "Open Chain Nitrogen Componds," Vol. 2, W. A. Benjamin, New York, N. Y., 1966, Chapter 11.

- (16) R. O. Kan and R. L. Furey, *Tetrahedron Lett.*, 2573 (1966).
 (17) D. Elad, D. V. Rao, and V. I. Stenberg, *J. Org. Chem.*, **30**, 3252 (1965).
 (18) A. J. Gordon and R. A. Ford, "The Chemists Companion," wiley, New
- York, N. Y., 1972, p 113.
- (19) D. Elad, Tetrahedron Lett., 873 (1963)

- (19) D. Elad, *Tetrahedro Lett.*, 873 (1955).
 (20) D. V. Rao and V. I. Stenberg, *J. Org. Chem.*, **30**, 3252 (1965).
 (21) D. V. Rao and V. Lambreti, *J. Org. Chem.*, **32**, 3896 (1967).
 (22) For a review, see N. J. Turro, J. C. Dalton, K. Dawes, G. Farrington, R. Hautola, D. Morton, M. Niemczyk, and N. Schore, *Accounts Chem.* Res., 5, 92 (1972).
 (23) V. I. Stenberg, N. Kulevsky, and C. H. Niu, J. Org. Chem., 38, 1227
- (1973)
- (24) B. C. Spall and E. W. R. Steacie, Proc. Roy. Soc., Ser. A, 239, 1 (1957)
- (25) S. R. Bosco, A. Cirillo, and R. B. Timmons J. Amer. Chem. Soc., 91, P. W. Jones and H. D. Gesser, J. Chem. Soc. B, 1973 (1971).
- (26)
- (27) D. M. Bosie and E. F. Barry, J. Chromatogr., 11, 237 (1973).
 (28) R. L. Hinmann, J. Amer. Chem. Soc., 78, 1646 (1956).
 (29) S. Wawazonek and D. Meyer, J. Amer. Chem. Soc., 78, 2918 (1954). (29)
- Analysis by Werby Laboratories, Boston, Mass.
- (31) D. M. Lemal, F. Menger, and E. Coats, J. Amer. Chem. Soc., 86, 2395 (1964).
- (32) J. C. Craig, J. L. Garnett, and D. M. Temple, J. Chem. Soc., 4057
- d. Gradina (1964).
 H. H. Hatt, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., (33) 1943, p 208.
- H. L. Lochte, J. R. Bailey, and W. A. Noyes, J. Amer. Chem. Soc., 43, 2597 (1921); 44, 2556 (1922). (34)
- (35)
- J. C. Stowell, *J. Org. Chem.*, **32**, 2360 (1967). O. Straub and P. Zeller, U. S. Patent 3,031,479 (1900). A. L. Foster, S. M. Clark, J. E. Miller, and J. R. Bailey, *J. Amer. Chem.* (36)
- (37) Soc., 44, 1557 (1922).
- E. Fisher, Ann. Chem., **190**, 178 (1878).
 L. Gattermann, S. Johnson, and R. Holzle, Ber., **25**, 1076 (1892).
- (40) S. Bauer, Chem. Zvesti, 16, 19 (1956).

Synthesis and Properties of N-(2,3,5-Tri-O-acetyl-D-ribofuranosyl)maleimide

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Reaction of silver maleimide with 2,3,5-tri-O-acetyl-D-ribofuranosyl chloride afforded N- (2,3,5-tri-O-acetyl-D-ribofuranosyl)maleimide (5). The removal of the blocking acetyl groups to obtain the N-substituted analog of showdomycin was not possible owing to its instability. In water, 5 hydrolyzed to maleimide and 2,3,5-tri-O-acetyl-D-ribofuranose. In contrast, dissolution in methanol caused the maleimide ring to open, yielding the methyl ester of N- (2,3,5-tri-O- acetyl-D-ribofuranosyl)maleamic acid (6). Compound 5 was found to be a good storage form of a reactive ribofuranose derivative. It underwent transglycosylation reactions readily in boiling nitromethane. In this manner, adenosine and cytidine were prepared using N^6 - benzoyladenine and N^4 - acetylcytosine, respectively, N- (2,3,4,6-Tetra-O- acetyl-D-glucopyranosyl)maleimide was also prepared; only in this case mercuric maleimide was the reactant of choice. In addition, the preparation of N- trimethylsilylmaleimide and N^4 - adamantoylcytosine are described.

The preparation of $N - \beta$ -D-ribofuranosylmaleimide (1) was undertaken because such a compound would be an Nsubstituted analog of the naturally occurring antibiotic, showdomycin (2, 2- β -D-ribofuranosylmaleimide, Chart I).² Since there is a structural similarity between 1 and 2, it was thought that the N-substituted analog would be a biologically active substance, perhaps more so than showdomycin, but still maintain some of the biological selectivity of the





latter. Recognizing that compound 1 could be a more powerful sulfhydryl reagent than 2,3 it was of interest to determine if the ribofuranose ring would confer specificity of binding to enzymes of nucleic acid metabolism and allow the compound to act, in part, as an N-substituted maleimide. Such compounds would have a potential use as antitumor and antimicrobial agents⁴ and could conceivably function as "active-site-directed irreversible inhibitors."

The preparation of silver maleimide and its use in the formation of N-substituted aralkylmaleimides was recently reported.⁶ Reaction of silver maleimide (4) with 2,3,5-tri-O-acetyl-D-ribofuranosyl chloride (3) in hot benzene gave the blocked product, N- (2,3,5-tri-O-acetyl-D-ribofuranosyl)maleimide (5, Scheme I). Unless great care is utilized in the preparation of the chloride 3, and yields are maximized, the product 5 will be contaminated with unreacted tetra-O-acetyl-D-ribofuranose, an undesirable situation since purification by many of the standard procedures, as discussed below, is virtually impossible without degradation of