

formed. The product was *N,N'*-bis(propionamido)formamidine: mp 200°; $\lambda_{\text{max}}^{\text{MeOH}}$ 245 μ (ϵ 14,720); λ_{max} 3.12, 6.10, 6.44, 8.33, 9.24, 9.98, and 10.77 μ (mull).

Anal. Calcd for $\text{C}_7\text{H}_{14}\text{N}_4\text{O}_2$: C, 45.15; H, 7.58; N, 30.09. Found: C, 44.88; H, 7.63; N, 29.93.

C.—A solution of 8.8 g (0.1 mole) of propionic acid hydrazide and 50 ml of triethyl orthoacetate was heated under mild reflux overnight. Distillation gave 7 g (62% yield) of 2-ethyl-5-methyl-1,3,4-oxadiazole (Table I).

n-Butyric Acid Hydrazide and Ortho Esters. A.—A solution of 10.2 g (0.1 mole) of *n*-butyric acid hydrazide and 50 ml of triethyl orthoformate was heated on a steam bath overnight. On cooling a solid separated, and it was collected. The filtrate was distilled under reduced pressure and gave 2 g (13% yield) of 1-*n*-butyryl-2-ethoxymethylenehydrazine, bp 125° (1 mm). A sample was recrystallized from ethyl acetate-petroleum ether (60–70°) (see Table II).

The solid that formed initially was recrystallized from ethyl acetate and gave 5 g (23% yield) of *N,N'*-bis(*n*-butyramido)formamidine, mp 180–183°.

Anal. Calcd for $\text{C}_9\text{H}_{18}\text{N}_4\text{O}_2$: C, 50.45; H, 8.47; N, 26.15. Found: C, 50.75; H, 8.72; N, 25.84.

B.—A solution of 10.2 g of *n*-butyric acid hydrazide and 50 ml of triethyl orthoformate was heated under reflux overnight. Distillation under reduced pressure gave 5 g (45%) of 2-*n*-propyl-1,3,4-oxadiazole [λ_{max} 3.18, 6.32, 6.55, 9.06, 10.28, 10.42, and 11.85 μ (CHCl_3) (see Table I)] and a small amount of 1-*n*-butyryl-2-ethoxymethylenehydrazine.

C.—A solution of 10.2 g (0.1 mole) of *n*-butyric acid hydrazide and 100 ml of triethyl orthoacetate was heated under mild reflux overnight. Distillation under reduced pressure gave 5 g (40%) of 2-methyl-5-*n*-propyl-1,3,4-oxadiazole (see Table I).

Phenylacetic Acid Hydrazide and Triethyl Orthoformate.—A solution of 10 g (0.066 mole) of phenylacetic acid hydrazide and 100 ml of triethyl orthoformate was heated under reflux overnight. Distillation under reduced pressure gave 5.5 g (51%) of 2-benzyl-1,3,4-oxadiazole: λ_{max} 3.19, 3.34, 6.34, 6.58, 6.67, 9.09, 10.19, 11.82, and 14.42 μ (CHCl_3).

Oxalic Acid Dihydrazide and Triethyl Orthoformate.—A mixture of 4.5 g (0.05 mole) of oxalic acid dihydrazide and 200 ml of triethyl orthoformate was heated under reflux overnight. The solution was concentrated to dryness on a steam bath under reduced pressure. The residue was recrystallized from ethanol and gave 2 g (22%) of 1-ethoxymethylene-2-(1,3,4-oxadiazolyl-2-carbonyl)hydrazine:¹⁰ mp 192–194°; λ_{max} 3.09, 3.23, 6.00, 6.21, 7.32, 7.88, 9.01, 9.65, 11.10, and 11.92 μ (mull); nmr, τ 1.45 s, 2.25 s, 5.65 q, and 8.65 t in the ratio 1:1:2:3 (DMSO-*d*₆; see Table I).

N,N'-Bis(benzamido)formamidine and Triethyl Orthoformate.—A 3-g sample of *N,N'*-bis(benzamido)formamidine^{3b,5} and 25 ml of triethyl orthoformate was heated under reflux overnight. Distillation under reduced pressure gave 2 g of 2-phenyl-1,3,4-oxadiazole.²

Acknowledgment.—The microanalyses were performed by W. L. Brown and associates, and the physical data were determined by L. G. Tensmeyer and D. O. Woolf, Jr.

(10) C. Runti, *et al.*,^{3b} obtained *N,N'*-bis(ethoxymethylene)oxalylidihydrazine by heating the reactants for 2 hr.

An Improved Synthesis of 1,2,4-Triazoline-3,5-diones

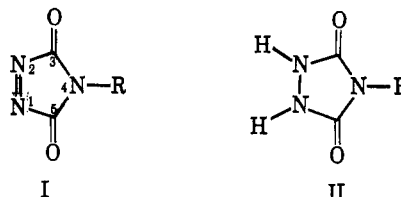
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The unusual reactivity which makes 1,2,4-triazoline-3,5-diones (I) of interest also makes them hard to prepare and purify. These compounds are sensitive to

acids, bases, moisture, and alcohols,^{1a} many nucleophiles, light, and many olefins,^{1b} as well as to heat and conjugated dienes.^{1c} Only three of these compounds (I, R = C_6H_5 , NH_2 , and NCHC_6H_5) have been isolated and characterized,^{1a} although it is claimed that the unsubstituted parent (I, R = H) has been prepared, but could not be isolated.^{1a}



All known syntheses of these diones require oxidation of the corresponding 1,2,4-triazolidine-3,5-diones (II), more commonly known as urazoles, as the final step. A variety of reagents is capable of effecting these oxidations. Thiele used lead peroxide in cold dilute sulfuric acid;² Stollé oxidized heavy metal salts of the urazoles with iodine;^{1a} Cookson used *t*-butyl hypochlorite in acetone;^{1a} Gillis and Hagarty have recently used lead tetraacetate in acetonitrile.³ The latter two oxidizing systems had previously been used by Clement⁴ and Kealy⁵ to oxidize phthalhydrazides to the corresponding phthalazine-1,4-diones. Manganese dioxide, calcium hypochlorite, and *N*-bromosuccinimide will also effect the oxidation of urazoles.⁶ The latter reagent has since been used by Bock to prepare a number of azobisphosphonic acid derivatives.⁷ However, all the aforementioned reagents produce by-products which either destroy or are difficult to remove from the sensitive dione.

We wish to report that nitrogen tetroxide is superior to all the previously cited oxidizing agents in convenience, yield, and purity of the isolated 1,2,4-triazoline-3,5-diones.⁸ Passage of gaseous nitrogen tetroxide into a suspension of a urazole in cold methylene chloride results in rapid formation of the corresponding red dione with concomitant dissolution of the urazole. Evaporation of the methylene chloride yields quantitatively the crystalline dione. Analytically pure samples are obtained in good yield after two sublimations.⁹ Table I gives data relevant to the preparation and characterization of several 4-substituted 1,2,4-triazoline-3,5-diones, some of which are previously unreported.

(1) (a) R. Stollé, *Ber.*, **45**, 273 (1912); (b) J. C. Stickler and W. H. Pirkle, unpublished observations; (c) R. C. Cookson, S. S. H. Gilani, and I. D. R. Stevens, *Tetrahedron Letters*, No. 14, 615 (1962).

(2) J. Thiele and O. Stange, *Ann.*, **233**, 1 (1894).

(3) B. T. Gillis and J. D. Hagarty, the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, Abstract K74.

(4) R. A. Clement, *J. Org. Chem.*, **25**, 1724 (1960).

(5) T. J. Kealy, *J. Am. Chem. Soc.*, **84**, 966 (1962).

(6) E. J. Corey and W. H. Pirkle, unpublished observations.

(7) H. Bock, G. Rudolph, and E. Baltin, *Ber.*, **98**, 2054 (1965).

(8) Owing to the equilibrium between nitrogen dioxide and nitrogen tetroxide, one cannot be certain which of the two is the active reagent. There are, however, numerous claims in the literature [see J. L. Riebsomer, *Chem. Rev.*, **36**, 157 (1945)] of oxidations by agency of nitrogen tetroxide. The report [E. H. White, *J. Am. Chem. Soc.*, **77**, 6008 (1955)] of nitrosation of amides by nitrogen tetroxide further implicates this reagent.

(9) The sole exception to this is the *p*-nitrophenyl-substituted dione which shows some propensity toward spontaneous decomposition until it has been further purified by sublimation. Once pure, this dione is stable for at least 2 weeks if stored in the dark at 0°.

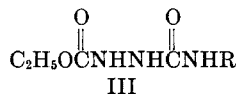
TABLE I
4-R-1,2,4-TRIAZOLINE-3,5-DIONES

Structure of R	Yield, % ^b	Mp, °C ^c	Anal, % ^a				Visible absorption ^e	
			Carbon		Hydrogen		λ_{\max} , m μ	ϵ
			Calcd	Found	Calcd	Found		
C ₆ H ₅	86	Dec	545 ^d	135
CH ₃	81	98.0-98.5	31.87	31.95	2.67	2.61	538 ^d	152
<i>n</i> -C ₄ H ₉	71	44.0-44.5	46.45	46.60	5.85	5.79	544 ^e	211
C ₆ H ₁₁	86	95-96 ^f	53.03	53.03	6.12	6.13	545 ^e	205
<i>p</i> -NO ₂ C ₆ H ₄	20	128-129 ^f	43.65	43.48	1.83	1.76	540 ^d	150
<i>p</i> -CH ₃ OC ₆ H ₄	60	130-131 ^f	52.69	52.71	3.44	3.37	546 ^d	151

^a Analyses were performed by Mr. J. Nemeth and associates of the University of Illinois. ^b Purified material. ^c Uncorrected. ^d In methylene chloride. ^e In cyclohexane. ^f There is some prior decomposition (Kofler block).

The requisite 4-substituted urazoles were prepared by base-promoted cyclization¹⁰ of the appropriate 4-substituted-1-ethoxycarbonyl semicarbazides (III). These semicarbazides result from the addition of aryl or alkyl isocyanates to ethoxycarbonylhydrazine.¹¹ Tables II and III give data relevant to previously unreported semicarbazides and urazoles which were prepared in the course of this work. The physical properties of our samples of 4-phenyl, 4-methyl, 4-*n*-butyl, and 4-cyclohexyl urazoles agree with reported values.^{2,11-13}

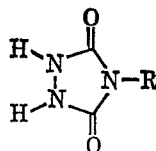
TABLE II
4-SUBSTITUTED-1-ETHOXYCARBONYL SEMICARBAZIDES



Structure of R	Yield, %	Mp, °C ^b	Anal, % ^a			
			Carbon		Hydrogen	
			Calcd	Found	Calcd	Found
CH ₃	100	141.0-141.5	37.26	37.55	6.88	6.89
<i>p</i> -NO ₂ C ₆ H ₄	92	218.0-218.5	44.78	44.50	4.51	4.46
<i>p</i> -CH ₃ OC ₆ H ₄	98	170.5-171.5	52.17	51.99	5.97	5.91

^a See footnote a in Table I. ^b Uncorrected.

TABLE III
4-SUBSTITUTED URAZOLES



Structure of R	Yield, %	Mp, °C ^b	Anal, % ^a			
			Carbon		Hydrogen	
			Calcd	Found	Calcd	Found
<i>p</i> -NO ₂ C ₆ H ₄	82	271.0-271.5	43.25	43.25	2.72	2.75
<i>p</i> -CH ₃ OC ₆ H ₄	55	219.5-220.5	52.17	52.04	4.38	4.30

^a See footnote a in Table I. ^b Uncorrected.

To our knowledge, this is the first instance of oxidation of diacylhydrazines to the corresponding azo compounds by nitrogen tetroxide.¹⁴ The mechanism of this oxidation is being investigated.

Experimental Section

Owing to the similarity of the nitrogen tetroxide oxidation procedures by which the various 1,2,4-triazoline-3,5-diones were

- (10) G. Zinner and W. Deucker, *Arch. Pharm.*, **294**, 370 (1961).
- (11) F. Arndt, L. Loewe, and A. Tarlan-Akón, *Rev. Fac. Sci. Forest Univ. Istanbul*, **13A**, 127 (1948); *Chem. Abstr.*, **42**, 8190 (1948).
- (12) T. Tsuji, *Pharm. Bull. (Tokyo)*, **2**, 403 (1954).
- (13) G. Zinner and B. Böhlke, *Arch. Pharm.*, **299**, 43 (1966).
- (14) Monoacylhydrazines have been shown [G. B. Bachman and W. Michalowicz, *J. Org. Chem.*, **23**, 1800 (1958)] to yield acylazides upon treatment with nitrogen tetroxide.

prepared, the experimental details of only one of these oxidations are presented, these being exemplary of the others.

Preparation of 4-Cyclohexyl-1,2,4-triazoline-3,5-dione.—Gaseous nitrogen tetroxide¹⁵ was passed through a narrow tube into a cold (0°) slurry of 1.00 g of 4-cyclohexylurazole (5.46 mmoles) and 10 g of anhydrous sodium sulfate in 50 ml of methylene chloride until all the urazole had dissolved. The solution was maintained at 0° during the reaction. The sodium sulfate was removed by filtration and the clear, red filtrate was evaporated to dryness at reduced pressure. The red, crystalline residue was twice sublimed (0.01 torr, 40°) in the dark to yield 0.784 g (86.5%) of analytically pure 4-cyclohexyl-1,2,4-triazoline-3,5-dione of indicated (Table I) melting point and composition.

(15) Commercial material obtained from the Matheson Co.

Perfluoroalkanesulfonate Esters. The Reaction of 2,2,2-Trifluoroethyl Trifluoromethanesulfonate with *p*-Dimethylaminophenylmagnesium Bromide

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Trifluoroethylation of diethylamine with 2,2,2-trifluoroethyl trifluoromethanesulfonate (I) has been described recently.¹ In the present work, ester I was further investigated as an alkylating agent of *p*-dimethylaminophenylmagnesium bromide (II), a typically reactive Grignard reagent under recent study in these laboratories.²

It is known that alkyl esters of arylsulfonic acids react with Grignard reagents in two ways. The "normal" reaction,³ first reported by Ferns and Lapworth,⁴ involves the alkylation of the Grignard reagent. It is most commonly employed for preparative purposes. In addition, sulfonic esters are capable of undergoing sulfone formation with Grignard reagents. This tendency appears to be intensified in the reaction of aryl Grignard reagents with alkyl esters of alkanesulfonic acids and aryl esters of aryl sulfonic acids.³ By analogy, one of the products expected from a reaction of Grignard reagent II with compound I was 1-(*p*-dimethylaminophenyl)-2,2,2-trifluoroethane (III). How-

- (1) R. L. Hansen, *J. Org. Chem.*, **30**, 4322 (1965).
- (2) A. Mendel, *J. Organometal. Chem.*, **6**, 97 (1966).
- (3) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954, pp 1278-1285.
- (4) J. Ferns and A. Lapworth, *J. Chem. Soc.*, **101**, 273 (1912).