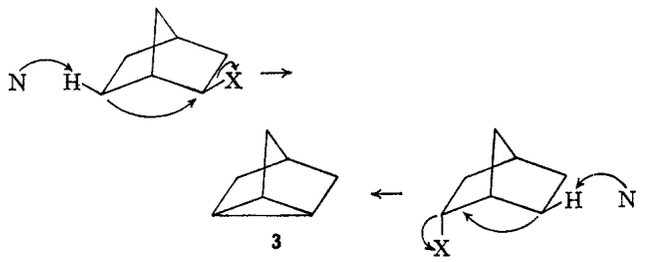
was 19:81; dehydrobrosylation in *s*-collidine and quinoline resulted in a 22:78 and a 12:88 ratio, respectively. Low yields (5–15%) of olefinic product were obtained using the *endo*-brosylate and *t*-hexoxide, a method reported[9] to give 53–59% yields with the *exo*-brosylate. However, the poor yield was not unexpected in light of the fact that the *exo*-dimethylaminonorbornane provided yields of 65–77% while the *endo* epimer **5** afforded yields of 2–4%.[3]

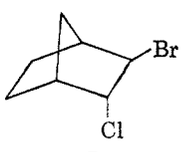
The elimination of a substituent in the *exo* position results in the formation of nortricyclene with smaller amounts of norbornene. Formation of **5** can be easily rationalized by the nucleophilic attack on the *exo* proton



3

attached to C-6. However, the formation of **3** from the isomer is not readily understood since consideration of electronic and stereochemical factors should make such attack unfavorable.

Reagents which add to the norbornene double bond under a variety of conditions without undergoing skeletal rearrangement do so to afford the *exo–cis* product (see for example, oxymercuration,[10] hydroboration,[11] deuteration,[12,13] hydrocarboxylation,[14] nitrosylation,[15] and diimidization[16]). The preference for *exo–cis* elimination in *exo*-2-substituted norbornanes has been demonstrated[17] from the fact that 2-chloro- and 2-bromonorbornene are obtained from the reaction of *exo*-2-bromo-3-*endo*-chloronorbornane (**7**) and *exo*-2-chloro-3-*endo*-bromonorbornane (**8**), respectively, with alkoxide. The formation of norbornene (**2**) from either



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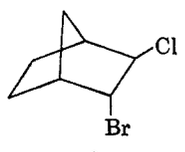

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an *exo* or *endo* leaving group is readily apparent; however, the *endo–cis* elimination is a much slower and a less favorable process.

(9) H. Kwart, T. Takeshita, and J. L. Nyce, *J. Am. Chem. Soc.*, **86**, 2606 (1964).

(10) T. G. Traylor and A. W. Baker, *Tetrahedron Letters*, **No. 19**, 14 (1959).

(11) R. B. Wetherill, H. C. Brown, and K. J. Murray, *J. Org. Chem.*, **26**, 631 (1961).

(12) D. R. Arnold, D. J. Trecker, and E. B. Whipple, *J. Am. Chem. Soc.*, **87**, 2596 (1965).

(13) J. K. Stille and F. M. Sonnenberg, manuscript in preparation.

(14) C. W. Bird, R. C. Cookson, I. Hudec, and R. O. Williams, *J. Chem. Soc.*, 410 (1963).

(15) J. Meinwald, Y. C. Meinwald, and T. N. Baker, *J. Am. Chem. Soc.*, **85**, 2513 (1963).

(16) E. E. van Tamelen and R. J. Timmons, *ibid.*, **84**, 1067 (1962).

(17) N. A. LeBel, P. D. Beirne, and P. M. Subramanian, *ibid.*, **86**, 4144 (1964).

Experimental Section

General Procedure.—To 50 ml of the alcohol employed was added 1.0 g of potassium metal. After solution occurred 3.31 g (0.01 mole) of *endo*-2-norbornyl brosylate, mp 59–60° (lit.[18] mp 60.0–61.7°), was added and the system was heated at 100–120° for 3 hr while being swept with nitrogen. The trap cooled in Dry Ice–isopropyl alcohol was analyzed by vpc for the products (see Table I). Reactions in solvents such as nitrobenzene, quinoline, and *s*-collidine were carried out in an analogous manner except that no potassium was added.

(18) S. Winstein and D. Trifan, *ibid.*, **74**, 1132 (1952).

Alkyl-1,3,4-oxadiazoles

C. AINSWORTH[1] AND R. E. HACKLER

The Lilly Research Laboratories, Indianapolis, Indiana

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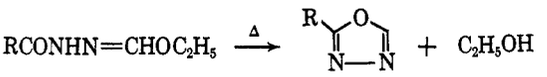
Although 2,5-diaryl- and alkylaryl-1,3,4-oxadiazoles have been known for a long time, the first monosubstituted 1,3,4-oxadiazoles were reported in 1955 by two independent laboratories.[2] Since 1955 other workers[3] have extended this reaction.

This paper describes unreported monoalkyl-1,3,4-oxadiazoles, 2,5-dialkyl-1,3,4-oxadiazoles, and details related to the preparation of unsubstituted 1,3,4-oxadiazole.[4] The monosubstituted 1,3,4-oxadiazoles listed in Table I were prepared by heating 1-acyl-2-ethoxymethylenehydrazines (Table II) that were made from alkylcarboxylic acid hydrazides and triethyl orthoformate. Reaction of alkylcarboxylic acid hydrazides,



and triethyl orthoacetate furnished the 2-alkyl-5-methyl-1,3,4-oxadiazoles (see Table I). The nmr data for these compounds are included in Table I.

It was found during the study of the reaction of triethyl orthoformate and carboxylic acid hydrazides that the ethoxymethylene intermediate, RCONHN=$CHOC_2H_5$, and the carboxylic acid hydrazide reacted further to form the bis compound, RCONHN=CHNHNHCOR.[3b,5] The reaction of the bis compound and triethyl orthoformate also gave the 1,3,4-oxadiazole system. These reactions are operative for both the alkyl- and arylcarboxylic acid series.

The above reactions are envisioned in terms of reversible equations similar to those proposed by Roberts and DeWolfe[6] for aryl amines and triethyl orthoformate and confirmed by us.[7]

The condensation products formed by reaction of formic acid hydrazide and triethyl orthoformate were

(1) To whom correspondence should be addressed: Department of Chemistry, Colorado State University, Fort Collins, Colo.

(2) (a) E. Muller and D. Ludsteck, *Chem. Ber.*, **88**, 921 (1955); (b) C. Ainsworth, *J. Am. Chem. Soc.*, **77**, 1148 (1955).

(3) (a) A. P. Grekov, O. P. Shvaika, and L. M. Egupova, *J. Gen. Chem. USSR*, **29**, 1996 (1959); (b) C. Runti, L. Sindellari, and C. Nisi, *Ann. Chim.* (Rome), **49**, 1649 (1959); *Chem. Abstr.*, **54**, 22601 (1960).

(4) C. Ainsworth, *J. Am. Chem. Soc.*, **87**, 5800 (1965).

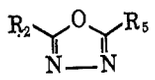
(5) K. T. Potts, *J. Org. Chem.*, **28**, 543 (1963).

(6) R. M. Roberts and R. H. DeWolfe, *J. Am. Chem. Soc.*, **76**, 2411 (1954).

(7) C. Ainsworth, *ibid.*, **78**, 1973 (1956).

TABLE I

1,3,4-OXADIAZOLES



R_2	R_5	Bp, °C (mm)	$n^{25}D$	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Proton position, τ[a] R_2	Proton position, τ[a] R_5
H	H	150	1.4300	$C_2H_2N_2O$	34.29	2.88	40.00	34.56	3.19	39.71	1.27	1.27
CH_3	H	164	1.4340	$C_3H_4N_2O$	42.85	4.80	33.32	43.04	5.00	33.26	7.42	1.47
C_2H_5	H	171	1.4375	$C_4H_6N_2O$	48.97	6.17	28.56	48.77	6.77	28.33	7.06, 8.60	1.52
n-C_3H_7	H	80 (12)	1.4410	$C_5H_8N_2O$	53.55	7.19	24.99	53.69	7.40	24.71	*b*	1.57
$CH_2C_6H_5$	H	120 (0.3)	1.5430	$C_9H_8N_2O$	67.48	5.03	17.49	67.67	5.02	17.12	2.75, 5.80	1.74
c	H	*d*	...	$C_6H_8N_4O_3$	39.13	4.38	30.43	39.27	4.46	30.37	*c*	
CH_3	CH_3	65 (12)[e]	1.4400	$C_4H_6N_2O$	48.97	6.17	28.56	48.96	6.41	28.21	7.50	7.50
CH_3	C_2H_5	75 (12)	1.4423	$C_5H_8N_2O$	53.55	7.19	24.99	53.26	7.44	24.81	7.49	7.15, 8.63
CH_3	n-C_3H_7	87 (12)	1.4434	$C_6H_{10}N_2O$	57.11	7.99	22.21	57.35	8.32	21.97	7.50	*f*

[a] Nmr shift values measured in $CDCl_3$. [b] 7.12, 8.14, and 8.98. [c] R_2 = $CONHN{=}CHOC_2H_5$; see Experimental Section. [d] Mp 192°. [e] H. Weidinger and J. Kranz [*Chem. Ber.*, **96**, 1049 (1963)] reported bp 172–176° (745 mm). [f] 7.20, 8.20, and 8.99.

TABLE II

1-ACYL-2-ETHOXYMETHYLENEHYDRAZINES[a]

$RCONHN{=}CHOC_2H_5$

R	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
H	88–92[b]	$C_4H_8N_2O_2$	41.37	6.94	24.13	41.11	7.25	24.63
CH_3	95–100[b]	$C_5H_{10}N_2O_2$	46.14	7.75	21.53	46.50	7.72	21.22
C_2H_5	83–85	$C_6H_{12}N_2O_2$	49.98	8.39	19.43	49.35	8.37	19.85
n-C_3H_7	108–110	$C_7H_{14}N_2O_2$	53.14	8.92	17.71	53.31	8.95	17.37

[a] Transformed on standing to the bis compounds (see ref 7). [b] Mixture of two isomers; see text.

readily converted to other products,[4] and these are described in the Experimental Section.

The nmr spectra of compounds of Table II showed both *syn* and *anti* isomers in the crude product, each form displaying restricted rotation. Unusual solvent effects were seen with these compounds, and this study is currently in progress.

Experimental Section[8]

1,3,4-Oxadiazoles by Heating 1-Acyl-2-ethoxymethylenehydrazines.—A 10-g sample of 1-acyl-2-ethoxymethylenehydrazine was heated at atmospheric pressure and gave a forerun of ethanol followed by the oxadiazole. The crude product was redistilled using a spinning-band column. The first three 1,3,4-oxadizoles listed in Table I were prepared in this manner in about 50% yield.

Formic Acid Hydrazide and Triethyl Orthoformate. A.—A solution of 24 g (0.4 mole) of freshly prepared formic acid hydrazide, 100 ml (0.6 mole) of triethyl orthoformate, and 300 ml of absolute ethanol in a 500-ml, round-bottom flask was heated on a steam bath for 4 hr. The solution was concentrated to about 80 ml and after storing this overnight in a refrigerator a solid formed. It was collected and air dried, mp 85–88°, yield 24 g. The filtrate was distilled under reduced pressure to give an additional 5 g (84% total yield) of product, bp 110° (1 mm). Recrystallization from ethyl acetate gave 1-ethoxymethylene-2-formylhydrazine, mp 88–92° (see Table II).

The residue from the distillation contained a small amount of 4-formylamino-1,2,4-triazole,[9] mp 123°.

When 95% ethanol was used in place of absolute ethanol, the product isolated was mainly 4-formylamino-1,2,4-triazole.

B.—The reaction was sensitive to variation of reaction conditions. As an example, equimolar quantities of formic acid hydrazide and triethyl orthoformate, heated at 100° or heated in absolute ethanol overnight, gave product containing large amounts of 4-formylamino-1,2,4-triazole and 1,2-diformylhydrazine. The same solids were formed when formic acid hydrazide and excess triethyl orthoformate were heated under reflux overnight.

Equimolar quantities of 1-ethoxymethylene-2-formylhydrazine and formic acid hydrazide in dry dioxane were allowed to stand at room temperature overnight. The dioxane was removed by being heated under reduced pressure, and the residue, recrystallized from methanol, gave N,N′-bis(formamido)formamidine: mp 126–127° (50% yield); λ_{max}^{EtOH} 245 mμ (ε 12,200); λ_{max} 3.13, 5.89, 5.99, 6.14, 6.45, 7.31, and 7.42 μ (mull).

Anal. Calcd for $C_3H_6N_4O_2$: C, 27.69; H, 4.65; N, 43.07. Found: C, 28.00; H, 4.93; N, 42.81.

Acetic Acid Hydrazide and Ortho Esters. A.—A solution of 12.5 g (0.2 mole) of acetic acid hydrazide and 100 ml of triethyl orthoformate was heated under mild reflux overnight. Distillation under reduced pressure gave 12 g (46% yield) of 1-acetyl-2-ethoxymethylenehydrazine: bp 135–140° (10 mm); λ_{max} 2.98, 5.88, 6.00, 6.64, 9.04, and 9.58 μ ($CHCl_3$) (see Table II).

B.—A solution of 12.4 g (0.2 mole) of acetic acid hydrazide, 14.8 g (0.1 mole) of triethyl orthoformate, and 100 ml of ethanol was heated on a steam bath for 2 hr. The solution was concentrated to about 25 ml and on cooling deposited 8 g (51% yield) of N,N′-bis(acetamido)formamidine: mp 173°; λ_{max}^{EtOH} 242 mμ (ε 14,050); λ_{max} 3.12, 3.26, 5.95, 6.00, 6.17, 6.54, 7.91, and 10.04 μ (mull).

Anal. Calcd for $C_5H_{10}N_4O_2$: C, 37.97; H, 6.37; N, 35.43. Found: C, 38.24; H, 6.77; N, 35.57.

A 10-g sample of N,N′-bis(acetamido)formamidine and 50 ml of triethyl orthoformate was heated under reflux for 4 hr. Distillation under reduced pressure gave 2-methyl-1,3,4-oxadiazole and 1-acetyl-2-ethoxymethylenehydrazine.

C.—A solution of 12.4 g (0.2 mole) of acetic acid hydrazide and 100 ml of triethyl orthoacetate was heated under mild reflux overnight. Distillation under reduced pressure gave 10 g (51% yield) of 2,5-dimethyl-1,3,4-oxadiazole (see Table I).

Propionic Acid Hydrazide and Ortho Esters. A.—A solution of 8.8 g (0.1 mole) of propionic acid hydrazide and 100 ml of triethyl orthoformate was heated under reflux for 6 hr. Distillation under reduced pressure gave a small forerun of 2-ethyl-1,3,4-oxadiazole and 5 g (51% yield) of 1-ethoxymethylene-2-propionylhydrazine, bp 118° (1 mm). A sample was recrystallized from ethyl acetate (see Table II).

B.—Equimolar quantities of propionic acid hydrazide and triethyl orthoformate were heated to about 140°, and a solid

(8) Melting points were taken on a Fisher-Johns apparatus.

(9) Identical with material prepared according to C. Bulow, *Ber.*, **42**, 2715 (1909).

formed. The product was N,N′-bis(propionamido)formamidine: mp 200°; λ_{max}^{MeOH} 245 mμ (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 $C_7H_{14}N_4O_2$: 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 $C_9H_{18}N_4O_2$: 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)oxalyldihydrazine by heating the reactants for 2 hr.

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

J. C. STICKLER AND W. H. PIRKLE

Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois 61801

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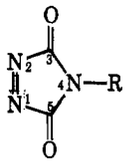
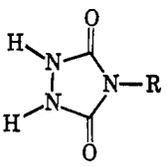
The unusual reactivity which makes 1,2,4-triazoline-3,5-diones (I) of interest also makes them hard to prepare and purify. These compounds are sensitive to acids, bases, moisture, and alcohols,[1a] many nucleophiles, light, and many olefins,[1b] as well as to heat and conjugated dienes.[1c] Only three 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]



I



II

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 Clement[4] and Kealy[5] 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 concommitant 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.*, **283**, 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°.