1,3,4-Oxadiazolin-2-ones from Carbo-*t*-butoxyhydrazones

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5-Substituted-1,3,4-oxadiazolin-2-ones **2** were synthesized by the oxidation of carbo-*t*-butoxyhydrazones **1** of aromatic aldehydes with lead tetraacetate or, preferably, iodosobenzene diacetate. In some instances 5-acetoxy-1,3,4-oxadiazoles **3** were obtained along with **2**. The oxidation of carboethoxyhydrazones **4** gave 2-ethoxy-1,3,4-oxadiazoles **5**.

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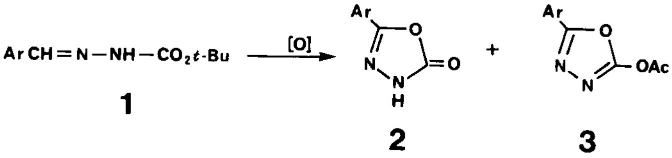
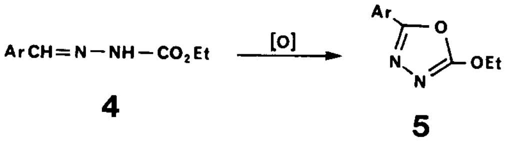
A recent paper by Milcent and Barbier [1] that describes the synthesis of 2,5-disubstituted-1,3,4-oxadiazoles by the oxidation of *N*-acylhydrazones of aromatic aldehydes with lead dioxide has prompted us to report a somewhat similar oxidation carried out in our laboratory. As a part of a general exploratory study of the use of carbo-*t*-butoxyhydrazones and carboethoxyhydrazones in synthesis we had examined earlier the oxidation of these substances with lead tetraacetate (LTA), a reaction that led to the formation of 1,3,4-oxadiazole derivatives in generally modest yields [2]. In recent years we have observed that several oxidative reactions typically carried out with LTA may give better yields of product when carried out with iodosobenzene diacetate (IBDA). Therefore, recently we reexamined two examples of our earlier work and found that IBDA does afford better yields of oxadiazoles. Our results and some other observations from this study are reported here.

LTA oxidative cyclizations of hydrazine derivatives of various types are effective routes to several heterocyclic ring systems. A number of these have been reviewed by Warkentin [3] and by Butler [4,5], and descriptions of new syntheses continue to appear [6]. Two studies of LTA oxidations of carboalkoxyhydrazones have been reported. The oxidation of benzophenone carbethoxyhydrazone has been found to give the acetoxylation product, ethyl acetoxydiphenylmethylazocarboxylate [7] (a commonly observed product type in hydrazone oxidations [4,5]). Thus, the only reported oxidative cyclization of carboalkoxyhydrazones of aromatic aldehydes appears to be that of Matsumura, Otseiji, and Imato [6f], which appeared after our LTA study had been completed. The details of their work are not available to us, but apparently they examined the oxidation of aldehyde carboalkoxyhydrazones and obtained 5-substituted-2-alkoxy-1,3,4-oxadiazoles and acetoxylation products, results similar to those we obtained with aldehyde carboethoxyhydrazones **4**.

In the present work the oxidations of aldehyde carbo-*t*-butoxyhydrazones **1** with LTA and IBDA were studied in different solvents as these sometimes markedly affect the outcome of oxidations carried out with both reagents. These oxidations afforded good to moderate yields of 5-substituted-1,3,4-oxadiazolin-2-ones **2**. Thus, when LTA was allowed to react with the benzaldehyde carbo-*t*-butoxyhydrazone (**1a**) in *t*-butyl alcohol the best yield of the 5-phenyl-1,3,4-oxadiazolin-2-one (**2**) was 45%. Use of methylene chloride, methylene chloride/*t*-butyl alcohol, or 2,2,2-trifluoroethanol did not improve the yield. In all of these cases a yellow oil was obtained as the major side product. In several experiments with various aldehydes, the oily byproducts were analyzed by nmr, ir, uv, and mass spectroscopy. Generally, the oil was found to consist of unrecovered product, the parent aldehyde, and acetoxylation products; however, small amount of other unidentified materials were present. When cinnamaldehyde carbo-*t*-butoxyhydrazone (**1c**) was oxidized with LTA in methylene chloride only 5% of **2c** was obtained, the principal product being 2-acetoxy-5-(2-phenylethenyl)-1,3,4-oxadiazole (**3c**) in 14% yield. In general the acetoxy compounds **3** were easily hydrolyzed to **2** in nearly quantitative yields in acidic ethanol-water.

When IBDA was used to oxidize **1a** in the same solvent systems, or preferably in methanol, under mild conditions, the yield of **2a** was at best 47%, but the workup of the





a	Ar = Ph	f	Ar = 2-NO$_2$Ph
b	Ar = 4-Pryidyl	g	Ar = 4-iPrPh
c	Ar = PhCH=CH	h	Ar = 3,5-DiMeOPh
d	Ar = 2-Naphthyl	i	Ar = 2-Furyl
e	Ar = 2-ClPh		

Table I

Oxidation of Aldehyde Carbo-*t*-butoxyhydrazones

Ar-	Oxidant (equivalents)	Solvent	Reaction Conditions [a]	Yield of Oxadiazolone
Phenyl	LTA (1.0)	methylene chloride	RT	19
	LTA (2.0)	methylene chloride	RT [b]	56
		methylene chloride	RT	40
		t-butyl alcohol	RT	45
		t-butyl alcohol-methylene chloride	RT	40
		2,2,2-trichloroethanol	RT	40
		acrylonitrile	RT	8 [c]
	IBDA (2.0)	*t*-butyl alcohol-methylene chloride	RT	35
		2,2,2-trichloroethanol	RT	9
		methanol	RT	47
		methanol	0°	25
		methanol	65° [d]	67
		methanol	65° [e]	0
	IBDA (4.0)	methanol	65° [d]	10
2-Phenylethenyl	LTA (2.0)	methylene chloride	RT	5 [f]
1-Naphthyl	LTA (1.5)	methylene chloride	RT	47
4-Isopropylphenyl	LTA (1.5)	methylene chloride	RT	45
2-Chlorophenyl	LTA (1.5)	methylene chloride	RT	10
2-Nitrophenyl	LTA (1.0)	methylene chloride	RT	29
3,5-Dimethoxyphenyl	LTA (1.5)	methylene chloride	RT	30
4-Pyridyl	LTA (2.0)	*t*-butyl alcohol	RT	10
		methylene chloride	RT	10
	IBDA (2.0)	methanol	RT	36
		methanol	65° [d]	47
	IBDA (4.0)	methanol	65° [d]	27

[a] RT = room temperature. Time = overnight unless specified. [b] One equivalent of dimethyl acetylenedicarboxylate was added to the reaction mixture. [c] The major product was 5-phenyl-2-acetoxy-1,3,4-oxadiazole (**3a**) (34%). [d] Four hours under reflux. [e] Six-eighteen hours under reflux. [f] The major product was 5-phenyl-2-acetoxy-1,3,4-oxadiazole (**3a**) (14%).

reaction mixture for the product was much simpler.

Since semicarbazones of aromatic aldehydes can be oxidatively cyclized to oxadiazoles both by LTA oxidation [6c] or by electrochemical oxidation [8], we attempted to oxidatively cyclize **1a** in a variety of solvents under the reaction conditions reported for semicarbazones at a platinum anode. No cyclization was observed.

In view of the possible pharmaceutical importance of these compounds an attempt was made to optimize the yields of the 5-phenyl- (**2a**) and 5-(4-pyridyl)- (**2b**) derivatives using IBDA as oxidant by varying the time and temperature of the reaction. Although the yellow-colored byproducts were observed when the oxidation of **1a** was carried out with IBDA at 0° or at room temperature, when the oxidation was conducted at 65° in methanol solution for 3-4 hours, the solution became colorless and an improvement of the yield of **2a** to 67% resulted. Reaction times longer than 4 hours resulted in the formation of undesirable side products and very low yields. The yield of the **2a** was also very poor when the ratio of oxidant to the substrate exceeded 2:1. Similarly, compound **2b** was obtained in a very low yield when the oxidant was LTA; but the yield improved considerably when IBDA was used as oxidant in methanol at 65°. In this case heating the reaction mixture longer than 4 hours and/or using excess IBDA also resulted in low yields of 1,3,4-oxadiazoline-2-one, suggesting that **2** is susceptible to further oxidation by these reagents. The results of our experiments are presented in Table I.

Three carboethoxyhydrazones, **4a**, **4d**, **4i**, of aromatic aldehydes were oxidized with LTA in methylene chloride solution to give poor to good yields of 5-aryl-2-ethoxy-1,3,4-oxadiazoles **5**, as shown in Table 2. In view of the work of Matsumura, Otseiji, and Imato [6f] no attempt was made to optimize these yields.

Table 2

Oxidation of Aldehyde Carboethoxyhydrazones (**4**)

Ar-	Oxidant (equivalents)	Yield of **5**
Phenyl	LTA (2.0)	36
2-Naphthyl	LTA (1.5)	79
2-Furyl	LTA (1.5)	16

[a] The reactions were carried out at room temperature in methylene chloride solution for 3 hours.

In general there often are several plausible mechanisms for the oxidation of the more complex organic nitrogen compounds with LTA or IBDA, and, in the absence of supporting evidence, it is difficult to choose among the possibilities [4,5,9]. For the oxidative cyclization of variously substituted hydrazones of aromatic aldehydes [4,5], nitrilimines have been proposed most frequently as intermediates, and these proposals have been supported by the successful trapping of nitrilimines from arylhydrazones of aromatic aldehydes with styrene, acrylonitrile, and other dipolarophiles [6a,10]. Nitrilimines have not been trapped successfully in LTA oxidations of aldehyde acylhydrazones. However, in the present work two attempts were made to trap nitrilimine intermediates from the LTA oxidation of **1a** with dimethyl acetylenedicarboxylate and with acrylonitrile. In neither case was any pyrazoline, or its further oxidation product, a pyrazole, detected. In the former instance, the product was **1b** in 56% yield (the highest obtained with LTA). In the latter example, the product was a mixture of **2a** (8%) and **3a** (34%). Although these results do not prove that nitrilimines are not intermediates in these oxidative cyclizations, reasonable mechanisms can be written that do not involve a nitrilimine *per se*. Thus, Gladstone, Aylward, and Norman [6a] originally proposed a nitrilimine intermediate for the oxidation cyclization of benzaldehyde benzoylhydrazone; however, based on failure to trap nitrilimines and other evidence, Norman, Purchase, Thomas, and Aylward [6d] later suggested an alternative mechanism similar to that shown here (a mechanism that we have favored for some years [2]). In this mechanism (or one of its minor variations) it is assumed that the oxidant (shown as LTA) will form a complex **6** at the more basic nitrogen atom. Elimination of acetic acid with cyclization gives the organolead intermediate **7**. Oxidative dehydrogenation then gives the 2-*t*-butoxy

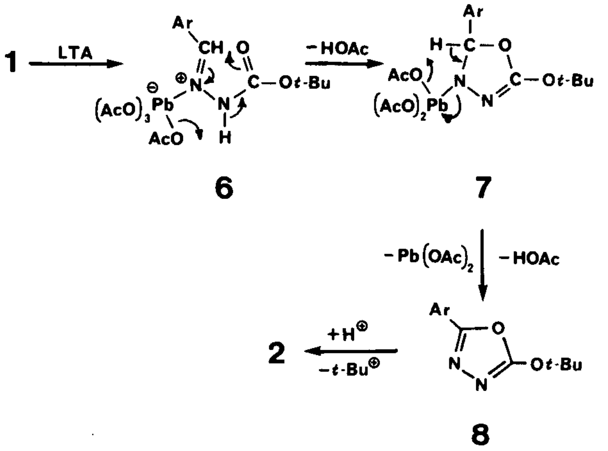


Table 3

Properties of Oxadiazoles

Compound	Mp °C	IR [a] cm^{-1}	NMR [b] δ	Analysis Calcd./Found		
				C	H	N
2a	134-136 [c]	3445	7.3-7.95	59.25	3.70	17.28
		1790		59.46	3.70	17.31
2b	270-273 [d]					
2c	194-195.5	3450	6.48-6.95 (s, 2H, CH=CH) [e]	62.61	4.35	12.17
			7.18-7.50 (m, 5H, Ar)	62.47	4.43	12.17
2d	182-184	3200 [f]	7.5-8.1	67.83	3.77	13.2
		1815,1730		67.85	3.76	13.32
2e	166-168	3100 [f]	7.35-7.0 [e]	48.88	2.56	18.03
		1790		49.13	2.66	18.33
2f	161-162	3250 [f]	7.6-7.95	46.24	2.38	20.54
		1780		46.39	2.41	20.29
2g	126-128	3430	1.25 (d, 7H, Me)	64.62	6.00	13.50
		1790	2.5-3.1 (m, 1H, CH)	64.69	5.92	13.71
2h	158-161	3120 [f]	3.85 (s, 6H, MeO)	54.05	4.53	12.60
		1780	6.6-7.25 (m, 3H, Ar)	53.72	4.52	12.25
4a	36-39	2975	1.52 (t, 3H, Me)	63.15	5.26	14.74
		1630	4.60 (q, 2H, CH_2)	63.36	5.46	14.66
			7.35-8.0 (m, 5H, Ar)			
4d	50-52	1675 [g]	1.48 (t, 3H, Me)	64.69	5.92	13.50
		1610	4.58 (q, 2H, CH_2)	64.62	6.00	13.50
			7.2-8.25 (m, 7H, Ar)			
4i	90-91	2995	1.52 (t, 3H, Me)	53.33	4.44	15.56
		1600	4.03 (q, 2H, CH_2)	53.30	4.52	15.72

[a] Ir spectra in methylene chloride unless specified otherwise. [b] Nmr spectra in deuteriochloroform unless specified otherwise. Oxadiazolone spectra were due to the Ar-group and had the characteristic shape thereof. [c] Lit [10] mp 138°. [d] With sublimation, lit [11] mp 273-275°. [e] In dimethyl sulfoxide-d_6-deuteriochloroform. [f] Potassium bromide disk. [g] In carbon tetrachloride.

derivative **8**, acid-catalyzed hydrolysis of which yields the product **2**. Possibly **5** is an intermediate in the cleavage of **8**. Since the ethoxy substituent would be expected to be more stable than the *t*-butoxy substituent, the product from the oxidation of **4** is **5** rather than **2**.

EXPERIMENTAL

Dichloromethane was distilled from phosphorus pentoxide under nitrogen. *t*-Butyl alcohol was refluxed over calcium hydride for 24 hours and distilled under nitrogen. *t*-Butyl carbazate, ethyl carbazate, and lead tetraacetate were purchased from Aldrich Chemical Co. The preparation of iodosobenzene diacetate used in this Laboratory will be described elsewhere; however, the commercial material is satisfactory for these oxidations. Melting points were obtained with a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra were determined with Perkin Elmer Models 621 and 1430. The ^{1}H nmr spectra were determined with Varian A-60A or EM-390 spectrometers. Chemical shifts are given in ppm downfield from TMS. Mass spectra were provided by the Midwest Center for Mass Spectrometry, Lincoln, Nebraska. Microanalyses were obtained from Micro- Tech Laboratories, Skokie, Illinois or Galbraith Laboratories, Knoxville, Tennessee. All yields quoted are for isolated and purified products.

Aldehyde Carbo*t*-butoxyhydrazones **1** and Carboethoxy hydrazones **4**.

Equimolar amounts of *t*-butyl carbazate or ethyl carbazate and the corresponding aldehyde were dissolved in an appropriate amount of absolute ethanol, and the reaction mixture was stirred at room temperature until a precipitate was formed. A few drops of glacial acetic acid were added if the reaction mixture had stirred for more than 24 hours without formation of a precipitate. The precipitate was collected, and further crops were obtained by adding small amounts of water to the filtrate. The combined precipitates were recrystallized from 95% ethanol (with added water as necessary). The compounds prepared and their properties are listed below. Unless otherwise specified the ir spectra were run in methylene chloride and the nmr spectra in deuteriochloroform.

Benzaldehyde Carbo-*t*-butoxyhydrazone (**1a**).

This compound was obtained in a yield of 99%, mp 185-185° (lit [11] mp 190-191°); ir (potassium bromide): 3240, 2960, 2965 cm^{-1}; nmr: δ 1.52 (s, 9H, *t*-Bu), 7.25-7.8 (m, 5H, Ar), 8.01 (s, 1H, NH), 9.03 (s, 1H, −CH=).

4-Pyridinecarboxaldehyde *t*-Butoxycarbohydrazone (**1b**).

This compound was obained in a yield of 77%, mp 122-124°; ir: 3330, 2960, 1745 cm^{-1}; nmr (deuteriochloroform-acetone-d$_6$): δ 1.51 (s, 9H, *t*-Bu), 7.51-7.61, 8.03; 8.55 (m, Ar and/or NH).

Anal. Calcd. for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.92; N, 18.99. Found: C, 59.37; H, 6.92; N, 19.35.

Cinnamaldehyde *t*-Butoxycarbohydrazone (**1c**).

This compound was obtained in a yield of 90%, mp 179-181°; ir (potassium bromide): 3210, 3010, 2965, 1695 cm^{-1}; nmr: δ 1.53 (s, 9H, *t*-Bu), 7.17-7.40 (m, 5H, Ar), 6.8, 6.92, 7.6, 7.2, 8.24 (−CH=CH− and/or −CH=, NH).

Anal. Calcd. for $C_{14}H_{18}N_2O_2$: C, 68.23; H, 7.36; N, 11.42. Found: C, 68.12; H, 7.46; N, 11.42.

Naphthaldehyde *t*-Butoxycarbohydrazone (**1d**).

This compound was obtained in a yield of 85%, mp 167-168°; ir: 3330, 2965, 1740 cm^{-1}; nmr (deuteriochloroform-dimethyl sulfoxide-d$_6$): δ 1.53 (s, 9H, *t*-Bu), 7.35-7.9 (m, 7H, Ar).

Anal. Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.05; H, 6.71; N, 10.40. Found: C, 71.03; H, 6.79; N, 10.38.

2-Chlorobenzaldehyde *t*-Butoxycarbohydrazone (**1e**).

This compound was obtained in a yield of 95%, mp 174-176°; ir: 3330, 3225, 2960, 1745 cm^{-1}; nmr: δ 1.53 (s, 9H, *t*-Bu), 7.2-7.4, 8.0-8.2 (m, 4H, Ar), 8.29 (s, 1H, NH), 8.5 (s, 1H, −CH=).

Anal. Calcd. for $C_{12}H_{15}ClN_2O_2$: C, 56.58; H, 5.94; N, 10.99; Cl, 13.92. Found: C, 56.78; H, 6.04; N, 11.02; Cl, 14.04.

2-Nitrobenzaldehyde *t*-Butoxycarbohydrazone)**1f**).

This compound was obtained in a yield of 77%, mp 151-152°; ir: 3335, 2970, 1745 cm^{-1}; nmr: δ 1.53 (s, 9H, *t*-Bu), 7.28-8.25 (m, 4H, Ar).

Anal. Calcd. for $C_{12}H_{15}N_3O_4$: C, 54.29; H, 5.69; N, 15.89. Found: C, 54.21; H, 5.82; N, 15.95.

4-Isopropylbenzaldehyde *t*-Butoxycarbohydrazone (**1g**).

This compound was obtained in a yield of 78%, mp 162-164°; ir: 3340, 2955, 1740 cm^{-1}; nmr: δ 1.25 (d, 6H, CH$_3$), 2.5-3.1 (m, 1H, CH), 7.1-8.0 (m, 4H, Ar), 1.52 (s, 9H, *t*-Bu).

Anal. Calcd. for $C_{15}H_{22}N_2O_2$: C, 68.64; H, 8.45; N, 10.72. Found: C, 68.65; H, 8.58; N, 10.63.

3,5-Dimethoxybenzaldehyde *t*-Butoxycarbohydrazone (**1h**).

This compound was obtained in a yield of 91%, mp 161-163°; ir: 3325, 2950; 1735 cm^{-1}; nmr: δ 1.52 (s, 9H, *t*-Bu), 3.75 (s, 6H, CH$_3$O), 6.31-6.41, 6.72 (m, 3H, Ar), 7.8 (s, 1H, NH), 8.3 (s, 1H, CH=).

Anal. Calcd. for $C_{14}H_{20}N_2O_4$: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.73; H, 7.35; N, 10.07.

Benzaldehyde Ethoxycarbohydrazone (**4a**).

This compound was obtained in a yield of 99%, mp 138-139° (lit [12] mp 138°); ir: 3335, 3030, 2960, 1740 cm^{-1}; nmr: δ 1.32 (t, 3H, CH$_3$), 4.28 (q, 2H, CH$_2$), 7.2-7.75 (m, 5H, Ar), 7.9 (s, 1H, NH), 8.7 (s, 1H, −CH=).

1-Naphthaldehyde Ethoxycarbohydrazone (**4d**).

This compound was obtained in a yield of 85%, mp 137-138°; ir: 3330, 2970, 1745, 1720 cm^{-1}; nmr: δ 1.32 (t, 3H, CH$_3$), 4.3 (q, 2H, CH$_2$), 7.3-7.9 (m, 7H, Ar).

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.37; H, 5.82; N, 11.61. Found: C, 69.14; H, 5.89; N, 11.43.

2-Furaldehyde Ethoxycarbohydrazone (**4i**).

This compound was obtained in a yield of 97%, mp 135-138°; ir: 3330, 2955, 1735 cm^{-1}; nmr: δ 1.82 (m, 3H, CH$_3$), 4.28 (m, 2H, CH$_2$), 6.4-6.72;, 7.15-7.65, 7.92 (m, 4H, furan ring protons and/or NH).

Anal. Calcd. for $C_8H_{10}N_2O_3$: C, 52.74; H, 5.83; N, 15.37. Found: C, 52.76; H, 6.02; N, 15.42.

Oxidation of Benzaldehyde Carbo-*t*-butoxyhydrazone.

(1) With Lead Tetraacetate in Various Solvents.

In a typical experiment a solution of 9.0 g (0.02 mole) of lead tetraacetate in 100 ml of *t*-butyl alcohol was added to a vigorously stirred solution of 3.0 g (0.02 mole) of benzaldehyde carbo-*t*-butoxyhydrazone in 100 ml of the same solvent during an interval of 30 minutes in the ice bath. The reaction mixture was stirred overnight at room temperature; then the insoluble lead salts were filtered off through a celite packed filter with suction. The celite was washed with the solvent, and the combined washings were collected and evaporated under reduced pressure. To the residue 100 ml of water was added, and the aqueous layer was extracted with chloroform. The organic layer was washed with dilute sodium bicarbonate solution and then with water and dried over magnesium sulfate. Evaporation of the chloroform yielded a pale yellow residue which was recrystallised from petroleum ether and benzene to give 1.45 g (45%) of 5-phenyl-1,3,4-oxadiazolin-2-one, mp 137-139° (lit [13] mp 138°); ir (methylene chloride): 3445 (NH), 1790 (ester C=O) cm^{-1}; nmr: δ 7.3-7.8 (m, 5H, aromatic); ms: m/e (% intensity, formula, Calcd. mass), 162.0437 (100, $C_8H_6N_2O_2$, 162.0510), 118.0535 (40, $C_7H_6N_2$, 118.0530), 105.0343 (26, C_7H_5O, 105.0381), 103.0419 (46, C_7H_5N), 91.0422 (14, C_6H_5N, 91.0421), 77.0398 (48, C_6H_5, 77.0391), 76.0321 (14, C_6H_4, 76.0313), 51.0245 (22, C_4H_3, 51.0234).

Anal. Calcd. for $C_8H_6N_2O_2$: C, 59.25; H, 3.70; N, 17.28. Found: C, 59.46; H, 3.72; N, 17.34.

Analysis of the yellow oil remaining by tlc and spectroscopy indicated the presence of benzaldehyde. The ir, uv, and nmr spectra of the remaining oily liquid indicated a mixture, consisting largely of **2** but probably containing acetoxylation products.

In other experiments the ratio of LTA to substrate varied from 1.0:1.0 to 2.0:1.0 and a variety of solvents were used. In some experiments LTA was added in one lot to a solution of the substrate without noticeably affecting yields.

(2) With Lead Tetraacetate in Acrylonitrile.

Lead tetraacetate (17.80 g, 0.0364 mole [14]) was added in one lot to a stirred solution of 4 g (0.0182 mole) of benzaldehyde carbo-*t*-butoxyhydrazone in 100 ml of acrylonitrile. A strong exothermic reaction was observed. The mixture was stirred for 20 minutes, during which time the solution turned pasty; therefore, an additional 60 ml of acrylonitrile was added, and the mixture was stirred overnight at room temperature. Extraction with ether gave a mixture of a yellow oil and white solid, which appeared to be a polymer of acrylonitrile (ir band at 2250-2230 cm^{-1}). The solid was removed by filtration and washed with ether and chloroform. Evaporation of the solvents left a residue from which a white solid slowly deposited. Recrystallization of the solid from chloroform-petroleum ether gave 1.25 g (34%) of **3a**, mp 108-110°; ir (methylene chloride): 1830-1800, 1730 cm^{-1}; nmr (deuteriochloroform): δ 2.6 (s, 3H, CH_3), 7.5-8.0 (m, 5H, Ar).

Anal. Calcd. for $C_{10}H_8N_2O_3$: C, 56.82; H, 3.90; N, 13.72. Found: C, 59.01; H, 3.94; N, 13.98.

From the remaining oily material 0.25 g (8.4%) of **2a** was obtained. Its properties were identical with those of an authentic sample.

(3) With Iodosobenzene Diacetate in Various Solvents.

A solution of 6.5 g (0.0091 mole) of IBDA in 100 ml of the chosen solvent was added dropwise to a vigorously stirred solution of 3.0 g (0.0132 mole) of benzaldehyde carbo-*t*-butoxyhydrazone in the same solvent over a period of 20-30 minutes. The reaction mixture was stirred overnight, and the solvent was evaporated under reduced pressure. To the residue 100 ml of water was added and the mixture was extracted with 100 ml of chloroform. The organic layer was washed with dilute sodium bicarbonate solution and then with water. The chloroform solution was dried (magnesium sulfate) and evaporated under reduced pressure. The residue was recrystallized from petroleum ether-benzene to yield **2a**. Results are given in Table I.

(4) With Iodosobenzene Diacetate in Methanol (the Optimum Procedure).

To a solution of 2.0 g of benzaldehyde carbo-*t*-butoxyhydrazone in 150 ml of methanol heated to reflux under nitrogen, a solution of 4.35 g of IBDA in 50 ml of warm methanol was added dropwise over a period of 30 minutes. The reaction mixture was heated under reflux for a period of 3-4 hours, by which time the color of the solution had changed from an initial yellow to nearly colorless. The solvent was removed under reduced pressure and the residue was recrystallized from carbon tetrachloride to yield 1.0 g (67%) of **2a**).

Oxidation of Pyridine-4-aldehyde Carbo-*t*-butoxyhydrazone.

(1) With Lead Tetraacetate.

The procedure described for benzaldehyde carbo-*t*-butoxyhydrazone was followed except that 14.78 g (0.033 mole) of LTA and 4.24 g (0.019 mole) of pyridine-4-aldehyde carbo-*t*-butoxyhydrazone (**1b**) were used. The reaction mixture was still positive to starch iodide paper after 24 hours but was worked up to give a yellow brown oil from which pale yellow crystals depositied on standing. Recrystallization of the precipitate from chloroform-benzene gave 0.6 g (10%) of 5-(4-pyridinyl)-1,3,4-oxadiazolin-2-one (**2b**), mp 269-271° (sublimes) (lit [15] mp 273-275°); ms: m/e (% intensity, formula, Calcd. mass), 163.0384 (100, $C_7H_5N_3O_2$, 163.0460), 119.0480 (41, $C_6H_5N_3$, 119.0483), 106.0293 (21, C_6H_4ON, 106.0333), 51.0174 (17, C_4H_3, 51.0234).

(2) With Iodosobenzene Diacetate in Methanol.

To a solution of 2.0 g (0.0090 mole) of **1b** in 100 ml of methanol heated to reflux under nitrogen, a solution of 4.35 g (0.0132 mole) of IBDA in 50 ml of warm methanol was added dropwise with stirring over a period of 25 minutes. Heating was continued for a further period of 4 hours. The methanol was evaporated to a small volume under reduced pressure. The white product was filtered, washed with methanol, and recrystallized from ethanol to yield 0.7 g (47%) of **2b**, mp 270-273° (lit [11] mp 273-275°).

Oxidation of Other Carboalkoxyhydrazones.

The procedures used for the oxidation cyclization of the other carboalkoxyhydrazones (**1,4**) were similar to that described above for **1a**. In general the amount of solvent used was slightly more than the amount required to bring all of the reactants into solution. The workup procedures were necessarily different as the product solubilities were also different, but the general approach was the same. Details of the isolation and purification procedures can be found in reference [4].

Hydrolysis of 2-Acetoxy-5-phenyl-1,3,4-oxadiazole.

To a solution of 0.70 g (0.0343 mole) of **5a** in 20 ml of 95% ethanol diluted with 5 ml of water a few drops of concentrated hydrochloric acid was added, and the reaction mixture was stirred and heated under reflux for 48 hours. The mixture was cooled to room temperature and neutralized with dilute sodium bicarbonate solution. The organic layer was extracted with three 20-ml portions of ether. Evaporation of the dried (magnesium sulfate) extract and recrystallization of the solid residue by adding a solution of it in a small amount of chloroform to a large amount of petroleum ether gave 0.54 g (96%) of white crystals, whose mp and ir and nmr spectra were identical with those of an authentic sample of **2a**.

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