5-Substituted-3-(substituted)phenyl-1,3,4-oxadiazolin-2(3*H*)-ones. Synthesis and Reactions With Nucleophilic Reagents

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A new synthesis of 4,4-dialkyl-2-(substituted)phenylsemicarbazides has been developed. The procedure begins with a 5-substituted-3-(substituted)phenyl-1,3,4-oxadiazolin-2(3*H*)-one, **3**, which is treated with dialkylamine to give a 1-acyl-4,4-dialkyl-2-(substituted)phenylsemicarbazide, **7**. Subsequent base-catalyzed hydrolysis of **7** gives 4,4-dialkyl-2-(substituted)phenylsemicarbazides, **14**, in high yield. With a variety of nucleophilic reagents, the compounds **3** also undergo ring opening.

J. Heterocyclic Chem., **19**, 823 (1982).

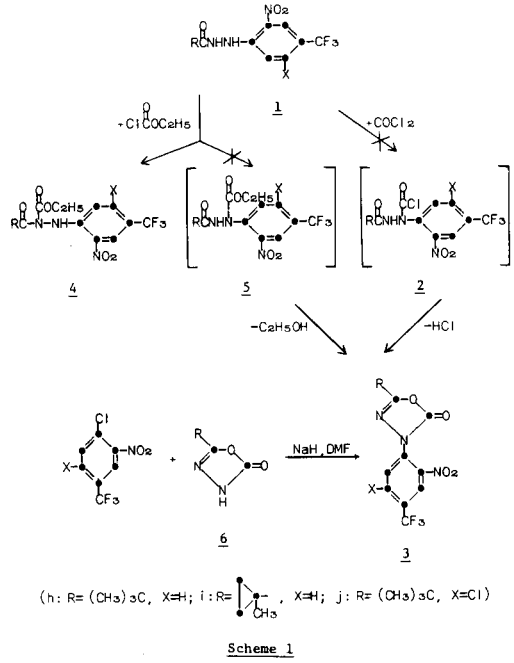
Introduction.

1,3,4-Oxadiazolin-2(3*H*)-ones have been of considerable chemical (1,2) and biological (3) interest for many years. In an attempt to displace the chlorine atom in the substituted 3-phenyl-1,3,4-oxadiazol-2(3*H*)-one, **3j**, by dimethylamine, more extensive reaction occurred and only 4,4-dimethyl-2-pivalolyl-2-(2-nitro-4-trifluoromethyl-5-dimethylamino-phenyl)semicarbazide, **7j**, was isolated (Scheme 2). This observation appeared to offer a new practical method for the formation of 4,4-dialkyl-2-substituted-phenylsemicarbazides having selective herbicidal properties (4,5). The present study demonstrates the feasibility and explores the scope of this new synthetic method.

Results and Discussion.

Synthesis of 1,3,4-Oxadiazolin-2-(3*H*)-ones.

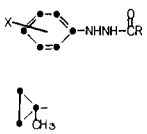
A representative selection of 3-(substituted)phenyl-5-substituted-1,3,4-oxadiazol-2(3*H*)-ones, **3a-g**, was prepared by the classical procedure of Freund and Goldsmith (6),



Scheme 1

Table 1

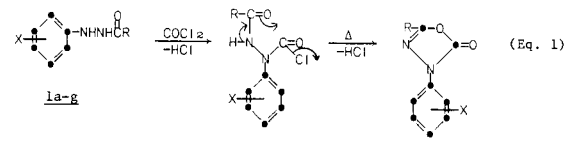
2-Acyl-1-(substituted)phenylsemicarbazides, **1**



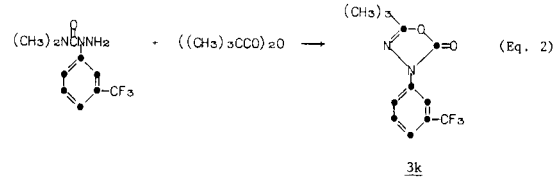
Compound	R	X	% Yield	Mp °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
1a	CF_3	2,4-Cl_2	70	127-128	$C_8H_5Cl_2F_3N_2O$	38.8	38.5	1.8	1.8	10.3	10.1
1b	C_2H_5O	H	56 (a)	76- 76	$C_9H_{12}N_2O_2$	60.0	60.3	6.7	7.0	15.5	15.2
1c	C_2H_5O	3-Cl	78 (b)	68- 69	$C_9H_{11}ClN_2O_2$	50.3	50.4	5.1	5.0	13.1	13.2
1d	C_2H_5O	3,4-Cl_2	55, (a) 96 (b)	108-111	$C_9H_{10}Cl_2N_2O_2$	43.4	43.6	4.0	4.1	11.2	11.2
1e	C_2H_5O	3-Cl,4-F	42 (a)	99-100	$C_9H_{10}ClFN_2O_2$	46.5	46.2	4.3	4.1	12.0	12.0
1f	C_6H_5O	3,4-Cl_2	76 (a)	153-155	$C_{13}H_{10}Cl_2N_2O_2$	52.5	52.6	3.4	3.4	9.4	9.4
1g	C_6H_5O	3-Cl,4-F	42 (a)	145-150	$C_{13}H_{10}ClFN_2O_2$	55.6	55.7	3.6	3.5	10.0	9.9
1h	$(CH_3)_3C$	2-NO_2,4-CF_3	95	187-188	$C_{12}H_{14}F_3N_3O_3$	47.2	47.2	4.6	4.7	13.8	13.8
1i		2-NO_2,4-CF_3	91	144-145	$C_{12}H_{12}F_3N_3O_3$	47.5	47.5	3.9	4.0	13.9	13.8

(a) In this method, triethylamine was used as hydrogen chloride acceptor. (b) Ethyldiisopropylamine was used as hydrogen chloride acceptor.

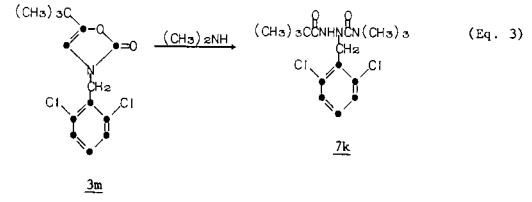
which consists of the reaction of phosgene with an acylated hydrazine derivative, **1** (Table 1). The experimental conditions employed involve heating a xylene or toluene solution of **1** containing an excess of phosgene (Method A in Table 2). In the present work, no hydrogen chloride acceptor was used. The course of the reaction (Eq. 1) is conveniently followed by thin-layer chromatographic (tlc) analysis. Reaction times vary; they are shorter where R^1 is alkyl (1-3 hours) and considerably longer where R^1 is alkoxy and phenoxy (7-48 hours). The intermediate chlorocarbonyl compounds **2**, were not isolated in these experiments.



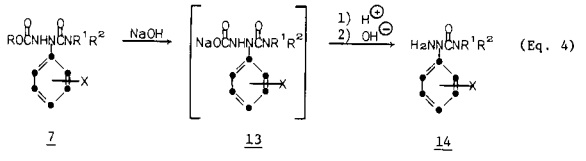
(Eq. 1)



(Eq. 2)



(Eq. 3)



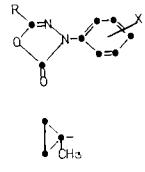
(Eq. 4)

Attempted reaction of the hydrazides **1h** and **1i** with phosgene in refluxing toluene (72 hours) failed to bring about ring-closure to **3h** and **3i** (Scheme 1). Likewise, no ring-closure occurred on treatment with refluxing ethyl chloroformate (72 hours), which can be substituted for phosgene (6). Instead, the reaction stopped at the carbethoxylation stage, the 1,1-diacylated 2-(substituted) phenylhydrazines, **4h** and **4i**, being formed exclusively and in high yield. The absence of the amide-II band (7) in their infrared spectra confirms the assigned structures for **4h** and **4i**, and eliminates from consideration structure **5**. However, when 4-chloro-3-nitrobenzotrifluoride and 2,4-dichloro-5-nitrobenzotrifluoride were allowed to react with 5-*t*-butyl-1,3,4-oxadiazol-2(3*H*)-one (8), **6h**, and 5-(1-methylcyclopropyl)-1,3,4-oxadiazol-2-(3*H*)-one, **6i**, in dimethylformamide in the presence of one molar equivalent of sodium hydride, the respective 5-substituted-3-(substituted)phenyl-1,3,4-oxadiazol-2(3*H*)-ones, **3h**, **3i**, and **3j** were isolated in good yield (9) (Scheme 1, Method B in Table 2).

2,6-Dichlorobenzyl chloride reacted analogously with

Table 2

5-Substituted-3-(substituted)phenyl-1,3,4-oxadiazolin-2(3*H*)-ones, **3**



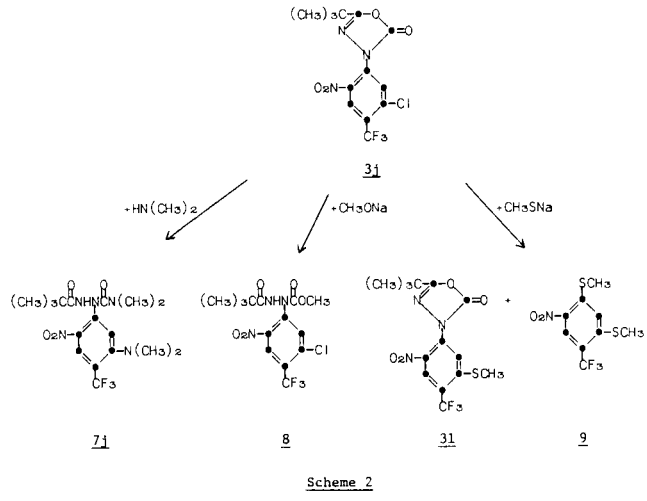
Compound	R	X	Method	% Yield	Mp °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
3a	CF_3	2,4-Cl_2	A	55	44- 45	$C_9H_3Cl_2F_3N_2O_2$	35.1	35.2	1.0	1.0	9.5	9.4
3b	C_2H_5O	H	A	95	58- 60	$C_{10}H_{10}N_2O_3$	58.3	58.4	4.8	4.8	13.6	13.5
3c	C_2H_5O	3-Cl	A	80	88- 90	$C_{10}H_9ClN_2O_3$	49.9	49.9	3.7	3.9	11.6	11.7
3d	C_2H_5O	3,4-Cl_2	A	71	95- 97	$C_{10}H_8Cl_2N_2O_3$	43.6	43.5	2.9	3.0	10.2	10.1
3e	C_2H_5O	3-Cl,4-F	A	94	48- 50	$C_{10}H_8ClFN_2O_3$	46.4	46.5	3.1	3.0	10.8	10.8
3f	C_6H_5O	3,4-Cl_2	A	23	92- 93	$C_{14}H_8Cl_2N_2O_3$	52.0	52.1	2.5	2.4	8.6	8.8
3g	C_6H_5O	3-Cl,4-F	A	79	97-100	$C_{14}H_8ClFN_2O_3$	54.8	54.8	2.6	2.7	9.1	9.2
3h	$(CH_3)_3C$	2-NO_2,4-CF_3	B	65	90- 92	$C_{13}H_{12}F_3N_3O_4$	47.1	46.8	3.6	3.6	12.7	13.0
3i		2-NO_2,4-CF_3	B	81	67- 68	$C_{13}H_{10}F_3N_3O_4$	47.4	47.3	3.0	3.1	12.8	12.9
3j	$(CH_3)_3C$	2-NO_2,4-CF_3 5-Cl	B	51	89- 91	$C_{13}H_{11}ClF_3N_3O_4$	42.7	42.7	3.0	2.9	11.5	11.6
3k	$(CH_3)_3C$	3-CF_3	C	84	110-111	$C_{13}H_{13}F_3N_2O_2$	54.6	54.5	4.5	4.5	9.8	9.9
3l	$(CH_3)_3C$	2-NO_2,4-CF_3, 5-SCH_3	-	24	133-135	$C_{14}H_{14}F_3N_3SO_4$	44.5	44.4	3.7	3.7	11.1	11.3

the anion of **6h** in dimethyl formamide to give 5-*t*-butyl-3-(2,6-dichlorobenzyl)-1,3,4-oxadiazolin-2(3*H*)-one, **3m** (mp 96-98°, 93% yield).

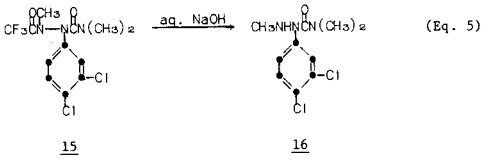
5-*t*-Butyl-3-(3-trifluoromethylphenyl)-1,3,4-oxadiazolin-2(3*H*)-one, **3k**, was prepared by treatment of 4,4-dimethyl-2-(3-trifluoromethyl)phenylsemicarbazide with pivalic anhydride following a literature procedure (10) (Eq. 2, Method C in Table 2).

Reaction of 3,5-Disubstituted-1,3,4-oxadiazol-2(3*H*)-ones with Nucleophiles.

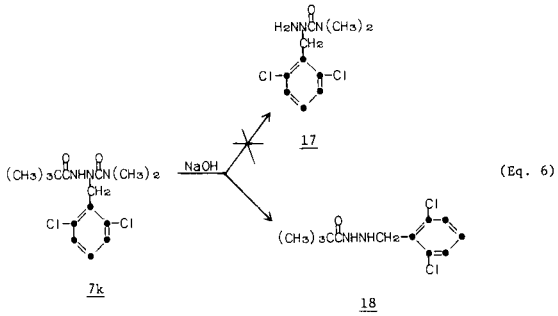
3,5-Disubstituted-1,3,4-oxadiazolin-2(3*H*)-ones are easily cleaved by alkali hydroxide or carbonate into hydrazine derivatives (2). Milder conditions allow isolation of hydrazides and more vigorous conditions give hydrazines.



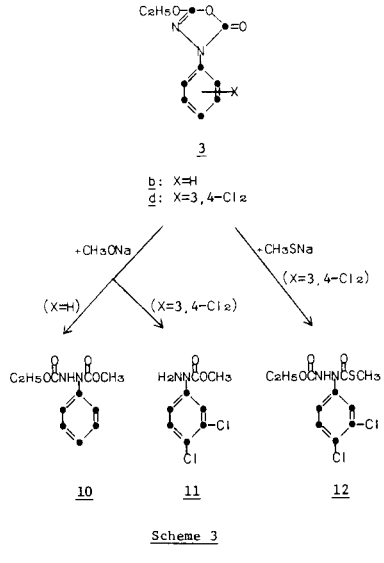
Scheme 2



(Eq. 5)



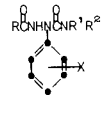
(Eq. 6)



Scheme 3

Table 3

1-Acylated-4,4-dialkyl-2-(substituted)phenylsemicarbazides, **7**



Compound	R	R¹	R²	X	% Yield	Mp °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
7a	CF_3	CH_3	CH_3	2,4-Cl_2	93	137-138	$C_{11}H_{10}Cl_2F_3N_3O_2$	38.4	38.4	2.9	2.9	12.2	12.2
7b	C_2H_5O	C_2H_5	C_2H_5	H	76	74- 76	$C_{14}H_{21}N_3O_3$	60.2	60.3	7.5	7.6	15.1	14.9
7c	C_2H_5O	CH_3	CH_3	3-Cl	90	110-112	$C_{12}H_{16}ClN_3O_3$	50.4	50.4	5.6	5.8	14.7	14.7
7d	C_2H_5O	C_2H_5	C_2H_5	3-Cl	79	90- 93	$C_{14}H_{20}ClN_3O_3$	53.6	53.7	6.4	6.4	13.4	13.3
7e	C_2H_5O	C_2H_5	C_2H_5	3,4-Cl_2	82	107-110	$C_{14}H_{19}Cl_2N_3O_3$	48.3	48.4	5.5	5.4	12.1	11.9
7f	C_2H_5O	$-CH_2(CH_2)_3CH_2-$		3,4-Cl_2	56	125-127	$C_{15}H_{19}Cl_2N_3O_3$	50.0	50.1	5.3	5.3	11.7	11.6
7g	C_2H_5O	CH_3	CH_3	3-Cl,4-F	69	69- 73	$C_{12}H_{15}ClFN_3O_3$	47.4	47.5	4.9	5.0	13.8	14.0
7h	C_6H_5O	CH_3	CH_3	3,4-Cl_2	99	101-104	$C_{16}H_{15}Cl_2N_3O_3$	52.2	52.3	4.1	4.0	11.4	11.7
7i	C_6H_5O	CH_3	CH_3	3-Cl,4-F	75	114-118	$C_{16}H_{15}ClFN_3O_3$	54.6	54.6	4.8	4.8	11.9	12.2
7j	$(CH_3)_3CO$	CH_3	CH_3	2-NO_2,4-CF_3 5-$N(CH_3)_2$	67	220	$C_{17}H_{24}F_3N_5O_4$	48.7	49.1	5.7	5.9	16.7	16.8

Dimethylamine, diethylamine and piperidine reacted readily at room temperature, or slightly elevated temperature, with the 3,5-disubstituted-1,3,4-oxadiazolin-2-(3*H*)-ones, **3a-g**, to give the ring-opened derivatives, **7a-i** (Table 3). The reaction proceeds rapidly in ethyl acetate, tetrahydrofuran or xylene to give the **7** compounds in high yields and high purity.

The oxadiazolinone **3m** reacted analogously with dimethylamine to give 2-(2,6-dichlorobenzyl)-4,4-dimethyl-1-pivalolylsemicarbazide, **7k** (mp 145-147°, 66% yield) (Eq. 3).

When 5-*t*-butyl-3-(5-chloro-2-nitro-4-trifluoromethylphenyl)-1,3,4-oxadiazolin-2(3*H*)-one, **3j**, was allowed to react with dimethylamine in dimethyl sulfoxide at 25° (1 hour), the only product formed and isolated in 67% was the acylated semicarbazide **7j** (Scheme 2) in which the reactive chlorine atom in position-3 on phenyl is replaced by dimethylamino. A departure from the anticipated reaction of **3j** with a nucleophilic reagent was realized when sodium methoxide was employed. The only product, isolated in 45% yield, was the hydrazinecarboxylic acid derivative **8**; the chlorine atom para to nitro on phenyl was not replaced. A further departure from the reactions of **3j** with nucleophilic reagents was observed when a solution containing four equivalents of sodium methylmercaptide in dimethyl sulfoxide was allowed to react with **3j** (25°, 0.5 hour). Under these reaction conditions, the heterocylcic ring moiety remained intact, but the chlorine atom on phenyl was replaced by methylthio to give **31** in 24% yield. A second compound, isolated in 23% yield, was characterized as 2,4-bis(methylthio)-5-nitrobenzotrifluoride, **9**. The identity of **9** is evident from its correct elemental analysis and nmr spectrum which shows the presence in the molecule of two methyl groups at δ 2.6 (s) and 2.65 (s), and two aromatic protons at 7.1 (s) and 8.4 (s) ppm. The formation of **9** illustrates that the 1,3,4-oxadiazol-2(3*H*)-one-3-yl moiety is itself an excellent leaving group competing with the good nucleofugic nitro group (11).

5-Ethoxy-3-phenyl-1,3,4-oxadiazolin-2(3*H*)-one, **3b**, reacted smoothly with sodium methoxide in methanol (25°, 0.5 hours) to give the 1,2-hydrazinedicarboxylic acid diester **10** in 83% yield. However, when the similarly constituted **3d** was allowed to react with sodium methoxide under similar reaction conditions, the only compound isolated (37% yield) was the hydrazinecarboxylic acid ester **11**. Sodium methylmercaptide reacted as expected with **3d** to give the thioester, **12**, albeit in low (9%) yield (Scheme 3).

Hydrolysis of 1-Acyl-4,4-dialkyl-2-(substituted)phenylsemicarbazides.

Under acidic conditions, the compounds **7b-7i** are hydrolytically very stable. However, under alkaline conditions, they hydrolyse readily affording 4,4-dialkyl-2-(substituted)phenylsemicarbazides, **14**, in high yield (Table 4). In a typical experiment, a solution containing 0.01 mole of **7** and 0.05 mole of sodium hydroxide in 80 ml of 35% aqueous ethanol is heated to reflux. After 3 to 6 hours, the reaction mixture is first made slightly acidic, perfecting the *N*-decarboxylation of intermediate **13**, then made alkaline to p*H* 8 with sodium hydroxide and extracted with ether. Evaporation of the solvent gives **14** in 35 to 95% yield (Eq. 4).

For the deacylation of the trifluoroacetylated semicarbazide, **15**, aqueous sodium or potassium hydroxide proved satisfactory and gave the desired semicarbazide, **16**, in good yield (4) (Eq. 5). However, when the pivalolyl derivative, **7k**, was so treated (50% aqueous ethanol 85°, 2 hours), the desired semicarbazide, **17**, was not obtained. Instead, the hydrazide, **18**, was isolated in essentially quantitative yield (Eq. 6).

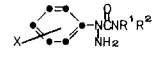
EXPERIMENTAL

Materials and Methods.

Melting points are uncorrected and were taken on a Thomas Hoover

Table 4

4,4-Dialkyl-2-(substituted)phenylsemicarbazides, **14**



Compound	R¹	R²	X	% Yield	Mp °C	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
14a	C_2H_5	C_2H_5	H	78	(a)	$C_{11}H_{17}N_3O$	63.8	63.8	8.2	8.5	20.3	19.5
14b	C_2H_5	C_2H_5	3,4-Cl_2	97	59- 62	$C_{11}H_{15}Cl_2N_3O$	47.8	48.0	5.4	5.3	15.2	15.3
14c	$-CH_2(CH_2)_3CH_2-$		3,4-Cl_2	54	105-108	$C_{12}H_{15}Cl_2N_3O$	50.0	50.1	5.2	5.6	14.6	14.2
14d	CH_3	CH_3	3-Cl,4-F	88 (b)	88- 90	$C_9H_{11}ClFN_3O$	46.7	46.7	4.8	4.8	18.1	17.9
14e	CH_3	CH_3	3-Cl,4-F	44 (c)	84- 86	$C_9H_{11}ClFN_3O$	46.7	46.9	4.8	4.9	18.1	18.1

(a) Liquid at room temperature. (b) Hydrolysis of **7g**. (c) Hydrolysis of **7i**.

capillary apparatus. Infrared absorption was measured with a Digilab FTS-15B spectrometer. Nmr Spectra were recorded on a Varian EM-360 spectrometer. Chemical shifts are expressed in parts per million (δ) downfield from internal TMS.

All intermediates prepared by reported procedures had analytical and physical constants in agreement with reported values.

Hydrazinecarboxylic Acid, 2-(3-Chloro-4-fluorophenyl)-, Ethyl Ester, **1e**.

Ethyl chloroformate, 37.2 g (0.343 mole), was added dropwise within 45 minutes at 5°, to a stirred solution containing 50.0 g (0.312 mole) of 3-chloro-4-fluorophenylhydrazine and 14.8 g (0.343 mole) of triethylamine in 500 ml of tetrahydrofuran. After 0.5 hour, the reaction mixture was filtered and washed with tetrahydrofuran. The filtrate was concentrated to dryness, and the residue was dissolved in ether and washed well with water. Concentration of the dried solution followed by crystallization from ether-hexane gave 30.7 g (42%) of **1e** as tan crystalline solid; mp 99-100°; ir (potassium bromide): 3290 (NH), 1695 (C=0) and 1505 cm^{-1} (amide II); nmr (DMSO-d_6): δ 1.2 (3, t, CH_3)., 4.1 (2, q, CH_2), 6.5-7.5 (3, m, CH=), 7.9 (1, s, NH) and 9.1 (1, s, NH).

Pivalic Acid, (2-(2-Nitro-4-trifluoromethyl)phenyl)hydrazide, **1h**.

To a solution containing 22.1 g (0.1 mole) of 2-nitro-4-(trifluoromethyl)phenylhydrazine in 125 ml of pyridine was added dropwise, at 10°, 13.2 g (0.11 mole) of pivalyl chloride. The mixture was stirred at ambient temperature for 2 hours, poured into ice water, and filtered. Recrystallization of the filter cake from methanol gave 29.0 (95%) of **1h** as yellow crystalline solid, mp 187-188°; ir (potassium bromide): 3430 and 3380 (NH), 1700 (C=O), 1540 and 1330 (NO_2), 1135 cm^{-1} (CF_3); nmr (DMSO-d_6): δ 1.25 (9, s, $(CH_3)_3C$), 7-8.5 (3, m, CH=), 9.6 (1, s, NH), and 10.1 ppm (1, s, NH).

5-Ethoxy-3-(3-chloro-4-fluorophenyl)-1,3,4-oxadiazol-2(3*H*)-one, **3e**.

A solution containing 14.9 g (0.064 mole) of **1e** and 14.9 g (0.15 mole) of phosgene in 200 ml of xylene was stirred and gradually heated to reflux. After 8 hours, the reaction mixture was concentrated under reduced pressure. The residue crystallized from ether-hexane to give 15.5 g (94%) of **3e** as tan crystalline solid, mp 48-50°, ir (potassium bromide): 1795 (C=O) and 1660 cm^{-1} (C=); nmr (deuteriochloroform): δ 1.45 (3, t, CH_3), 4.45 (2, q, CH_2), and 7-8 ppm (3, m, CH=).

Hydrazinecarboxylic Acid, 1-Pivaloly-2-(2-nitro-4-(trifluoromethyl)-phenyl)-, Ethyl Ester, **4h**.

A solution containing 15.25 g (0.05 mole) of **1h** in 250 ml of ethyl chloroformate was refluxed for 72 hours. The reaction mixture was concentrated under reduced pressure, and the residue was crystallized from ether-hexane to give 16.9 g (89.9%) of **4h** as colorless crystalline solid; mp 134-135°; ir (potassium bromide): 3280 (NH), 1750, 1730, 1680 (C=O), 1630 (CH=), no apparent amide II, 1550 and 1340 cm^{-1} (NO_2); nmr (DMSO-d_6): δ 1.26 (3, s, CH_3), 1.3 (9, s, $(CH_3)_3$), 4.1 (2, q, CH_2O), 7-8.3 (3, m, CH=), and 10.8 ppm (1, s, NH); m/e 377 (M^+).

Anal. Calcd. for $C_{15}H_{18}F_3N_3O_5$ (377.2): C, 47.7; H, 4.8; N, 11.1. Found: C, 47.6; H, 4.7; N, 11.1.

Hydrazinecarboxylic Acid, 1-(1-Methylcyclopropylcarbonyl)-2-(2-nitro-4-(trifluoromethyl)phenyl)-, Ethyl Ester, **4i**.

This compound was prepared analogously to **4h** in 81.5% yield, mp 149-150°; ir (potassium bromide): 3400 (NH), 1745 and 1700 cm^{-1} (C=O); nmr (DMSO-d_6): δ 0.5-1.5 (10, m, $(CH_2)_2$ and $(CH_3)_2$), 4.1 (2, q, CH_2O), 7.0-8.5 (3, m, CH=) and 10.6 ppm (1, s, NH).

Anal. Calcd. for $C_{15}H_{16}F_3N_3O_5$ (375.1): C, 48.0; H, 4.3; N, 11.2. Found: C, 47.8; H, 4.1; N, 11.3.

Hydrazinecarboxylic Acid, 2-(Dimethylcarbamoyl)-2-(3-chloro-4-fluorophenyl)-, Ethyl Ester **7g**.

Dimethylamine, 2.6 g (58 mmoles), was introduced into a solution containing 13.8 g (53 mmoles) of **3e** in 150 ml of tetrahydrofuran. After 1 hour, the reaction mixture was concentrated to dryness, and the residue was recrystallized from ether-hexane to give 8.5 g (69%) of 7 g as white crystalline solid; mp. 69-73°; ir (potassium bromide): 3300 (NH), 1755 (C=O) and 1560 cm^{-1} (amide II); nmr (deuteriochloroform): δ 1.35 (3, t, CH_3), 4.25 (2, q, CH_2), 2.9 (6, s, $(CH_3)_2$), 7.1 (3, m, CH=) and 7.8 ppm (1, s, NH).

4,4-Dimethyl-1-pivaloyl-2-(2-nitro-4-(trifluoromethyl)-5-(dimethylamino)-phenyl)semicarbazide, **7j**.

Dimethylamine, 2 g (excess), was added to a solution containing 3.65 g (0.0l mole) of **3j** in 50 ml of DMSO. After 1 hour, the mixture was poured into water, acidified (hydrochloric acid) and filtered. The filter cake crystallized from methanol to give 2.8 g (67%) of **7j** as a yellow solid, mp 220° dec; ir (potassium bromide): 3320 and 3280 (NH), 1695 and 1675 (C=O), 1615 cm^{-1} (C=); nmr (DMSO-d_6): δ 1.2 (9, s, $(CH_3)_3$) 2.8 (12, d, $(CH_3)_2N)_2$), 6.7 (1, s, CH=), 8.2 (1, s, CH=), and 10.6 ppm (1, s, NH).

Hydrazinecarboxylic Acid, 1-(2-Nitro-4-trifluoromethyl)-5-chlorophenyl)-2-pivaloyl-, Methyl Ester, **8**.

Sodium methoxide, 0.54 g (0.101 mole) was added with stirring to a solution of 3.65 g (0.01 mole) of **3j** in 75 ml of DMSO. After 1 hour, the reaction mixture was poured into ice water, acidified (hydrochloric acid), and filtered. Recrystallization of the filter cake from ether-hexane gave 1.8 g (45%) of **8**, an off-white solid, mp 136-138°; ir (potassium bromide): 3300 (NH), 1750 (C=O), 1615 (C=), and 1145 cm^{-1} (CF_3); nmr (DMSO-d_6): δ 1.2 (9, s, $(CH_3)_3C$), 3.7 (3, s, CH_3O), 7.5-8.35 (2, m, CH=) and 10.8 ppm (1, s, NH).

Anal. Calcd. for $C_{14}H_{15}ClF_3N_3O_5$ (397.6): C, 42.3; H, 3.8; N, 10.6. Found: C, 42.6; H, 3.9; N. 10.9.

5-*t*-Butyl-3-(2-nitro-4-(trifluoromethyl)-5-methylthio)phenyl)-1,3,4-oxadiazolin-2(3*H*)-one, **31**, and 2,4-Bis(methylthio)-5-nitrobenzotrifluoride, **9**.

To a stirred solution of 3.65 g (0.01 mole) of **3j** and 2.0 g concentrated aqueous solution of 0.44 g (0.011 mole) of sodium hydroxide. After 0.5 hour, the reaction mixture was poured into water and acidified. The solid product was filtered, washed with water, and purified by silica chromatography (eluent, by volume: hexane (96), THF (4)) to give 0.9 g (24%) of **31** as a white crystalline solid, mp 133-135°. The second fraction consisted of **9**, 0.7 g (23%), mp 145-147°; ir (potassium bromide) 1595 (C=O), 1550 (NO_2) and 1135 cm^{-1} (CF_3); nmr (deuteriochloroform): δ 2.6 (3, s, CH_3), 2.65 (3, s, CH_3), and 7.1 (1, s, CH=) and 8.4 ppm (1, s, CH=).

Anal. Calcd. for $C_9H_8F_3NS_2O_2$ (283.2): C, 38.2; H, 2.8; N, 4.9. Found: C, 37.8; H, 2.8; N, 4.7.

Hydrazinecarboxylic Acid, 2-(Methoxycarbonyl)-2-phenyl-, Ethyl Ester, **10**.

A solution containing 4.5 g of (0.022 mole) of **3b** and 1.3 g (0.024 mole) of sodium methoxide in 75 ml of methanol was stirred for 0.5 hours, concentrated under reduced pressure and then treated with water. Extraction with ether gave 4.3 g (83%) of dark oil that solidified on standing, mp 62-65°; ir (potassium bromide): 3290 (NH), 1745 and 1710 cm^{-1} (C=O); nmr (deuteriochloroform): δ 1.3 (3, t, CH_3C), 4.2 (2, q, CH_2O), 3.8 (3, s, CH_3O) and 7.4 ppm (6, m, CH=, and NH).

Anal. Calcd. for $C_{11}H_{14}N_2O_4$ (238.1): C, 55.4; H, 5.9; N, 11.8. Found: C, 55.8; H, 6.0; N, 11.7.

Hydrazinecarboxylic Acid, 1-(3,4-Dichlorophenyl)-, Methyl Ester, **11**.

A solution containing 7.0 g (25 mmoles) of **3d** and 1.5 g (28 mmoles) of sodium methoxide in 100 ml of methanol was stirred at ambient temperature for 1 hour. The mixture was concentrated under reduced pressure, diluted with water, and extracted with ether. The ether extracts were dried and concentrated, and the residue was crystallized from ether-hexane to give 2.2 g (37%) of **11** as tan solid, mp 130-132°; ir (potassium bromide): 3290 (NH), 1710 cm^{-1} (C=O); nmr (DMSO-d_6) δ 3.6 (3, s, CH_3O), 6.5-7.5 (3, m, CH=), and 8.1 (1, s, NH) and 9.1 ppm (1, s, NH).

Anal. Calcd. for $C_8H_8Cl_2N_2O_2$ (235.0): C, 40.9; H, 3.4; N, 11.9. Found: C, 40.9; H, 3.7; N, 11.7.

Hydrazinecarboxylic Acid, 2-(3,4-Dichlorophenyl)-2-((methylthio)carbonyl)-, Ethyl Ester, **12**.

A solution of 7.0 g (25 mmoles) of **3d** in 75 ml of DMSO was treated at ambient temperature with 2.1 g (30 mmoles) of sodium methylmercaptide. After 0.5 hour, the reaction mixture was diluted with water and extracted with ether. The ether extract was concentrated. Crystallization of the residual dark oil, 4.5 g, from ether-hexane gave 0.7 g (9%) of **12** as off-white solid, mp 126-128°; ir (potassium bromide): 3260 (NH), 1715 and 1680 cm^{-1} (C=O); nmr (DMSO-d_6): δ 1.15 (3, t, CH_3), 4.15 (2, q, CH_2O), 2.2 (3, s, CH_3S), 7.5 (3, m, CH=) and 10.5 ppm (1, s, NH).

Anal. Calcd. for $C_{11}H_{12}Cl_2N_2SO_3$ (323.1): C, 40.9; H, 3.7; N, 8.7. Found: C, 40.9; H, 3.7; N, 8.7.

4,4-Dimethyl-2-(3-chloro-4-fluorophenyl)semicarbazide, **14d**.

A solution of 10.7 g (0.035 mole) of **7g** and 7.0 g (0.175 mole) of sodium hydroxide in 100 ml of ethanol and 150 ml of water was refluxed for 3.5 hours at 83° when tlc indicated complete hydrolysis. The reaction mixture was concentrated to a volume of about 150 ml, acidified (hydrochloric acid), then made alkaline to p*H* 8.5 (sodium hydroxide), and extracted with ether. The combined ether extracts were dried (magnesium sulfate) and concentrated, and the residue was recrystallized from ether-hexane to give 7.1 g (88%) of **14** as white crystalline solid, mp 88-89°; ir (potassium bromide) 3250 (NH) and 1645 cm^{-1} (C=O); nmr (deuteriochloroform) δ 2.9 (6, s, $(CH_3)_2N$), 4.6 (2, s, NH_2) and 7.2 ppm (3, m, CH=), and 1645 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.9 (6, s, $(CH_3)_2N$), 4.6 (2, s, NH_2) and 7.2 ppm (3, m, CH=).

Pivalic Acid, 2-(2,6-Dichlorobenzyl)hydrazide, **18**.

A solution containing 8.7 g (25 mmoles) of **7k** and 5.0 g (0.125 mole) of sodium hydroxide in 100 ml of ethanol and 50 ml of water was refluxed for 2 hours. The reaction mixture was acidified (hydrochloric acid) and then made alkaline (sodium hydroxide). The white solid that had formed was removed by filtration, washed with water, and dried to give 6.1 g (94%) of **18**, mp 118-121°; ir (potassium bromide): 3290 and 3260 (NH), 1655 cm^{-1} (C=O); nmr (deuteriochloroform): δ 1.15 (9, s, $(CH_3)_3C$), 4.3 (2, m, CH_2) and ca. 7.2 ppm (5, m, CH= and NH); m/z 274 (M^+), 259 (M^+-CH_3).

Anal. Calcd. for $C_{12}H_{16}Cl_2N_2O$ (275.1): C, 52.4; H, 5.8; N, 10.2. Found: C, 52.7; H, 6.1; N, 10.0.

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