Thomas J. Giacobbe

Ag-Products Department, Dow Chemical U.S.A., Walnut Creek, California 94598

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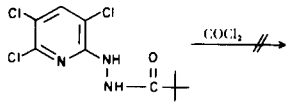
The synthetic objective of preparing halo- and halo- plus alkoxy-substituted pyridyloxadiazolones was achieved by allowing an alkali metal salt of an oxadiazolone to displace a leaving group on a halo- or halo- plus alkoxy-substituted pyridine, respectively. Other routes failed to give the desired compounds, and they are briefly discussed.

J. Heterocyclic Chem., 15, 1221 (1978)

A sequence of reactions which allows one to prepare halo-substituted, and halo- plus alkoxy-substituted pyridyloxadiazolones is described. Adherence to the sequence was necessary in order to obtain the desired products. These compounds are structurally similar to the halo- and halo- plus alkoxy-substituted phenyloxadiazolones, a known class of herbicides (1).

The frequently employed method of preparing oxadiazolones by ring closure of an acid hydrazide with phosgene (2) failed to cyclize **1** to the desired trichloropyridyloxadiazolone. The failure of this cyclization probably results from a low electron density on the nitrogen atom adjacent to the pyridine ring.



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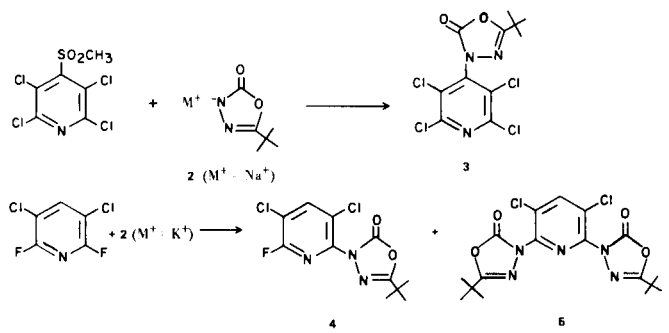
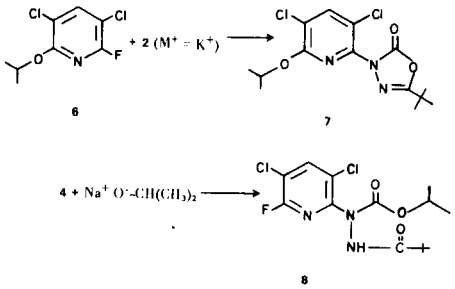
The desired halo-substituted pyridyloxadiazolones were obtained by synthesizing an oxadiazolone and then allowing an alkali metal salt of the oxadiazolone to displace a leaving group on the pyridine. Polar, aprotic solvent were used for this displacement reaction, as protic solvents (*e.g.* ethanol) completely inhibited it. Bis-substituted products (*e.g.* **5**) were easily formed which suggested that the oxadiazolone moiety has a strong electron-withdrawing effect. The oxadiazolone **2** (M = H) was prepared by the ring closure of pivaloyl hydrazide with phosgene. Pivaloyl hydrazide was prepared by allowing pivalic acid (3) or methylpivalate (4) to react with hydrazine, or by treatment of trimethylacetyl urea with potassium hypobromite (5,6). Preparation of the halo-substituted pyridyloxadiazolones **3** and **4** are two examples of this rather general displacement reaction



The final synthetic objective was to prepare pyridines containing halo, alkoxy, and oxadiazolone groups. This was achieved by displacing a leaving group from a halo- and alkoxy-substituted pyridine using the salt of an oxadiazolone. The preparation of **7** is an example of such a molecule, and the last step in the synthetic sequence is shown below. It was observed that the isopropoxy group could also be displaced in this reaction, as some of the bis-oxadiazolone (**5**) was obtained. Isolation of **5** points to the electron-withdrawing effect of an oxadiazolone moiety and the subsequent activation of a relatively poor leaving group (isopropoxide) towards nucleophilic displacement. Reversing the addition order of the isopropoxy and oxidazolone groups to the pyridine ring in the synthetic sequence failed to give the desired product. Rupture of the oxadiazolone ring was observed, and compound **8** was obtained when **4** and sodium isopropoxide were allowed to react.



EXPERIMENTAL

Nuclear magnetic resonance spectra (nmr) were recorded on a Varian T-60 spectrometer and tetramethylsilane was used as an internal standard. Infrared spectra were recorded using a Beckman Acculab-3 spectrometer. Melting points were taken using a Thomas-Hoover capillary melting point apparatus and are corrected. Elemental analyses were performed by Mary J. Gade of these laboratories.

2-(3,5,6-Trichloro-2-pyridinyl)-2,2-dimethylpropanoic Acid Hydrazide (**1**).

Pivaloyl chloride (5.62 g., 0.0466 mole) and 2-hydrazino-3,5,6-trichloropyridine (9.0 g., 0.042 mole) were allowed to react in dry pyridine (75 ml.) for 5 hours at room temperature. The reaction mixture was poured onto a mixture of concentrated hydrochloric acid and crushed ice. The crude product was recrystallized from ethanol to give tan needles, m.p. 147.5-149°; ir (mull): 3400, 3170, 3100 (N-H stretch), 1675 cm^{-1} (C=O); nmr (deuterio-

chloroform): δ 8.22 (d, 1, J = 5 Hz, -NHNHCO), 7.6 (s, 1, aromatic H), 7.37 (d, 1, J = 5 Hz, -NHNHCO), 1.39 (s, 9, -C(CH_3)$_3$).

Anal. Calcd. for $C_{10}H_{12}Cl_3N_3O$: C, 40.4; H, 4.3; N, 14.1. Found: C, 40.6; H, 4.1; N, 13.9.

3-(2,3,5,6-Tetrachloro-4-pyridinyl)-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3*H*)one (**3**).

Into a mixture of 2,3,5,6-tetrachloro-4-methylsulfonylpyridine (13 g., 0.044 mole) and **2** (7.1 g., 0.05 mole) in a 1:1 (v/v) mixture of HMPA and glyme was added sodium hydride (2.11 g. of 57% oil dispersion). The reaction mixture was heated under reflux for 0.75 hour, poured onto crushed ice, and the crude solid was purified on a silica column using benzene as eluent. A white solid (2 g.) was identified as the title compound, m.p. 148-150°; ir (mull): 1805 cm^{-1} (C=O of oxadiazolone); nmr (deuteriochloroform): δ 1.37 (s, 9, -C(CH_3)$_3$).

Anal. Calcd. for $C_{11}H_9Cl_4N_3O_2$: C, 37.0; H, 2.5; N, 11.8. Found: C, 37.1; H, 2.7; N, 11.5.

3-(3,5-Dichloro-6-fluoro-2-pyridinyl)-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3*H*)one (**4**), and 3,3'-(3,5-Dichloro-2,6-pyridinedyl)-bis-5(1,1-dimethethyl)-1,3,4-oxadiazol-2(3*H*)one (**5**).

A mixture of 3,5-dichloro-2,6-difluoropyridine (18.4 g., 0.1 mole) and the potassium salt of **2** (prepared by allowing potassium hydroxide and **2** to react in toluene) was allowed to react in acetonitrile (100 ml.) for 0.5 hour at room temperature. The reaction mixture was poured onto crushed ice and the crude product was purified on a silica column using chloroform as eluent. Compound **4** was isolated as an oil (10 g.) which crystallized, and was recyrstallized from hexane, m.p. 107-108°; ir (mull): 1795 cm^{-1} (C=O of oxidiazolone); nmr (deuteriochloroform): δ 7.95 (d, 1, J = 8 Hz, aromatic proton coupled to F), 1.38 (s, 9, -C(CH_3)$_3$).

Anal. Calcd. for $C_{11}H_{10}Cl_2FN_3O$: C, 43.2; H, 3.3; N, 13.7. Found: C, 43.1; H, 3.4; N, 13.4.

Compound **5** was eluted after compound **4** from the column, m.p. 156-158°; ir (mull): 1785 cm^{-1} (C=O of oxadiazolone); nmr (deuteriochloroform): δ 8.07 (s, 1, aromatic H), 1.37 (s, 18, -C(CH_3)$_3$).

Anal. Calcd. for $C_{17}H_{19}Cl_2N_5O_4$: C, 47.6; H, 4.5; N, 16.3. Found: C, 47.5; H, 4.5; N, 16.1.

3,5-Dichloro-6-fluoro-2-(1-methylethoxy)pyridine (**6**).

Sodium hydride (3.3 g. of 53% oil dispersion, washed with hexane) was added cautiously (foaming) to a solution of 3,5-dichloro-2,6-difluoropyridine (12.9 g., 0.07 mole) in isopropanol (100 ml.). After the foaming ceased, the reaction was stirred at room temperature for 10 minutes, diluted with water (100 ml.) and extracted three times with hexane. The product (10 g.), a clear oil, was isolated by distillation, b.p. 165-170° (190 mm); ir (film): 1600 and 1565 cm^{-1}; nmr (deuteriochloroform): δ 7.58 (d, 1, J = 8 Hz, aromatic H coupled to F), 5.15 (7 line multiplet, 1, spacing = 6 Hz between lines, -OC*H*(CH_3)$_2$), 1.42 (d, 6, J = 6 Hz, -OCH(CH_3)$_2$).

Anal. Calcd. for $C_8H_8Cl_2FNO$: C, 42.8; H, 3.5; N, 6.2. Found: C, 42.4; H, 3.4; N, 6.4.

3-(3,5-Dichloro-6-(1-methylethoxy)-2-pyridinyl)-5-(1,1-dimethyl-ethyl)-1,3,4-oxadiazol-2(3*H*)one (**7**).

A mixture of **6** (5.6 g., 0.025 mole) and the potassium salt of **2** (5.41 g., 0.03 mole) in acetonitrile (60 ml.) was heated under reflux for 4.5 hours. The solvent was removed by distillation and the residual was triturated with water and extracted twice with dichloromethane. The crude product was purified on a silica column eluted with chloroform and then on preparative-layer silica plates eluted with benzene. Two grams of the bis compound (**5**), and 2.1 g. of a clear oil which slowly crystallized and was identified as **7** were isolated, m.p. 75-77°; ir (film): 1790 cm^{-1} (C=O of oxadiazolone); nmr (deuteriochloroform): δ 7.73 (s, 1, aromatic H), 5.3 (5 line multiplet, 1, spacing = 7 Hz between lines, -OC*H*(CH_3)$_2$), 1.4 (d, 6, J = 7 Hz, -OCH(CH_3)$_2$), 1.4 (s, 9, -C(CH_3)$_3$).

Anal. Calcd. for $C_{14}H_{17}Cl_2H_3O_2$: C, 48.6; H, 4.9; N, 12.1. Found: C, 48.4; H, 4.6; N, 12.0.

1-(3,5-Dichloro-6-fluoro-2-pyridinyl)-2-(2,2-dimethyl-1-oxopropyl)hydrazine Carboxylic Acid Methylethyl Ester Monohydrate (**8**).

Sodium hydride (0.8 g. of 57% oil dispersion) was added to a solution of **7** (4.6 g., 0.015 mole) in 2-propanol (50 ml.), and allowed to stir at room temperature for 16 hours. The solvent was removed under reduced pressure, and the residue was triturated with water to yield a sticky solid. This solid was digested with methanol, and the insoluble material was removed by filtration and discarded. A tan solid (0.53 g.) crystallized from the methanol and it was recrystallized twice from benzene, m.p. 171-172°; ir (mull): 3310 (N-H), 1735 (N-C(=O)-O), 1655 cm^{-1} (NHC(=O)-C), nmr (deuteriochloroform): δ 8.62 (s, 1, N-H), 7.92 (d, 1, J = 8 Hz, aromatic H coupled to F), 5.05 (7 line multiplet, 1, spacing = 6 Hz between lines, -OC*H*(CH_3)$_2$), 3.47 (s, 2, H_2O), 1.28 (d, 6, J = 6 Hz, -OCH(CH_3)$_2$), 1.26 (s, 9, -C(CH_3)$_3$).

Anal. Calcd. for $C_{14}H_{18}Cl_2FN_3 \cdot H_2O$: C, 43.7; H, 5.2. N, 10.9. Found: C, 43.3; H, 4.8; N, 10.6.

REFERENCES AND NOTES

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