JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

J. Agric. Food Chem. **2008,** *56,* 10779–10784 **10779**

Organophosphorus Derivatives Containing Isatin-3-hydrazones as Chemotherapeutants against Fungal Pathogens of Sugarcane

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A total of 20 novel organophosphorus derivatives have been synthesized by the reactions of *O,O*-diethylchlorophosphate/thiophosphate with isatin-3-(substituted benzoic acid/phenoxy acetic acid hydrazones). The derivatives have been characterized on the basis of analysis and spectral (IR and ^{1}H and ^{13}C NMR) data. Fungicidal activities of the derivatives against *Colletotrichum falcatum*, *Fusarium oxysporum*, and *Curvularia pallescence* have been evaluated. The screening results have been correlated with the structural features of the tested compounds. The greater potency has been observed with thiophosphates compared to phosphates, with substituted phenoxy acetic acid hydrazones compared to substituted benzoic acid hydrazones, and with substitutent Cl^{-} attached to the aromatic ring compared to other substitutents. *O,O*-Diethylchlorophosphate compounds containing isatin-3-(4-chlorophenoxy acetic acid hydrazone) (**IIe**) and the compound containing two molecules of *O,O*-diethylchlorophosphate attached to isatin-3-(4-hydroxy phenoxy acetic acid) hydrazone (**IIh**) were proven to be more active than some prevalent commercial synthetic fungicides.

KEYWORDS: Organophosphorus derivatives; hydrazones; synthesis; fungicidal; sugarcane

INTRODUCTION

Organic phosphorus compounds are one of the most important groups of modern pesticides (*1, 2*). The widespread use of these compounds is due to their high insecticidal and ascaricidal activity, the broad spectrum and rapidity of action on pests, their low solubility in biological media, their decomposition to products nontoxic to humans and animals, their relatively rapid metabolism in the organisms of animals and the absence of an ability to be deposited in them, the systemic action of a number of toxicants, and their low rate of use per unit treated area. The discovery of the mechanism of action of organophosphorus compounds made it possible to develop the fundamental principles of the directed synthesis of new substances and to establish the cause of their relative action on an organism (*3*−*6*). It was realized that, on the basis of suitable logic, organic molecules incorporating phosphorus may be designed such that they may be used as effective pesticides (*1*).

Keeping this in view, the present paper deals with synthesis, characterization, and antifungal activity of different organophosphorus derivatives containing isatin-3-hydrazones.

MATERIALS AND METHODS

The reactions of *O,O*-diethylchlorophosphate/thiophosphate were carried out under an inert atmosphere and anhydrous conditions. Special precautions were taken to exclude moisture from the apparatus and chemicals as the starting materials (*O,O*-diethylchlorophosphate or *O,O*-diethylchlorothiophosphate), and reactions were susceptible to hydrolysis. A glass apparatus with interchangeable joints was used throughout the work. The solvents were purified and dried using the method described in the literature (*7*). *O,O*-Diethylchlorophosphate and *O,O*-diethylchlorothiophosphate were prepared according to the reported method (*8*). Hydrazones were prepared as described (*9*).

For antifungal activity, all compounds were tested against all test fungi by the food poison technique (*10*) at three concentrations (10, 100, and 1000 mg/L). For this, the desired amount of chemical was dissolved in 0.5 mL of acetone and mixed with the culture medium on the basis of the volume of the medium in each Petri plate (about 80 mm in diameter). Oatmeal-agar medium were used for all test fungi. In controls, the same amount of medium containing the requisite amount of solvent was poured in place of test chemicals. A mycelial disk (5 mm in diameter) obtained from the periphery of 2-week-old cultures was taken and transferred to the center of each Petri plate. Plates were incubated for 7 days at 28 ± 2 °C. Each treatment was repeated 3 times, and the inhibition was recorded relative to percent mycelial inhibition, calculated using the formula

$$(d_c - d_t)/d_c \times 100$$

where d_c is the average diameter of the mycelial colony of the control and d_t is the average diameter of the mycelial colony of the treatment.

The minimum inhibitory concentrations (MICs) of the most active *O,O*-diethylchlorophosphate/thiophosphate derivatives were determined. Three concentrations, 1000, 2000, and 3000 mg/L, of each tested compound with respect to the culture medium were prepared. The fungistatic/fungicidal nature of the active chemicals was determined in three replicates using the test fungi following the reported procedure (*11*).

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10.1021/jf801975z CCC: $40.75
Published on Web 10/28/2008

Reactions of *O*,*O*-Diethylchlorophosphate/Thiophosphate with Isatin-3-(benzoic/4-chloro benzoic/4-nitro benzoic acid or phenoxy acetic/4-chloro phenoxy acetic/4-nitro phenoxy acetic acid) Hydrazone. A mixture of *O*,*O*-diethylchlorophosphate/thiophosphate (0.001 mol) and the appropriate substituted benzoic acid/phenoxy acetic acid hydrazone (0.001 mol) was refluxed in ethanol (~25 mL) in the presence of pyridine (5 mL) for 18−25 h. The reaction mixture was cooled and poured in ice, and the product, thus obtained, was filtered and recrystallized from acetone.

Reactions of *O*,*O*-Diethylchlorophosphate/Thiophosphate with Isatin-3-(2-hydroxy/4-hydroxy benzoic acid or 2-hydroxy/4-hydroxy phenoxy acetic acid) Hydrazone. A mixture of *O*,*O*-diethylchlorophosphate/thiophosphate (0.002 mol) was added to a solution of appropriate hydrazone (0.001 mol) in ethanol (~25 mL) in the presence of pyridine (5 mL), and the mixture was refluxed for 12−15 h. The reaction mixture was then cooled and poured in ice. The product, thus obtained, was filtered and recrystallized from acetone.

Compounds Reported in This Paper Are Listed below. *Compound* **Ia.** Dark brown solid. Yield (%): 66. Decomposition temperature (°C): 248−246. Found (calcd) (%): C, 56.68 (56.86); H, 4.88 (5.02); N, 10.35 (10.47). IR (cm^{-1}): 1610, 1560 ($\nu_{C=N}$), 1030 (ν_{P-O-C}), 1265 ($\nu_{P=O}$). ^1H NMR (δ): 7.58−7.70 (m, 9H, phenyl ring), 8.12 (s, 1H, N−H), 3.58 (q, 4H CH_2), 1.25 (t, 6H, CH_3). ^{13}C NMR (δ): 131.0, 130.8, 129.8, 129.0, 128.5, 124.5, 120.5 (phenyl ring), 160.0 (amide C), 163.8 (imine C), 58.5 (CH_2), 15.5 (CH_3).

Compound **Ib.** Brown solid. Yield (%): 56. Decomposition temperature (°C): 230−227. Found (calcd) (%): C, 52.32 (52.36); H, 4.30 (4.39); N, 9.49 (9.64). IR (cm^{-1}): 1620, 1565 ($\nu_{C=N}$), 1040 (ν_{P-O-C}), 1270 ($\nu_{P=O}$). ^1H NMR (δ): 7.60−7.78 (m, 8H, phenyl ring), 8.15 (s, 1H, N−H), 3.56 (q, 4H, CH_2), 1.18 (t, 6H, CH_3). ^{13}C NMR (δ): 135.8, 131.0, 130.2, 129.7, 129.0, 124.0, 120.5 (phenyl ring), 161.2 (amide C), 164.0 (imine C), 58.3 (CH_2), 14.8 (CH_3).

Compound **Ic.** Dark brown solid. Yield (%): 69. Decomposition temperature (°C): 220−216. Found (calcd) (%): C, 51.06 (51.13); H, 4.25 (4.29); N, 12.48 (12.55). IR (cm^{-1}): 1615, 1570 ($\nu_{C=N}$), 1050 (ν_{P-O-C}), 1260 ($\nu_{P=O}$). ^1H NMR (δ): 7.62−7.82 (m, 8H, phenyl ring), 8.00 (s, 1H, N−H), 3.58 (q, 4H, CH_2), 1.20 (t, 6H, CH_3). ^{13}C NMR (δ): 150.5, 130.0, 129.6, 129.0, 124.2, 123.8, 120.8 (phenyl ring), 160.8 (amide C), 165.2 (imine C), 58.6 (CH_2), 14.6 (CH_3).

Compound **Id.** Blackish brown solid. Yield (%): 58. Decomposition temperature (°C): 207−204. Found (calcd) (%): C, 54.58 (54.67); H, 4.80 (4.83); N, 10.02 (10.07). IR (cm^{-1}): 1610, 1565 ($\nu_{C=N}$), 1055 (ν_{P-O-C}), 720 ($\nu_{P=S}$). ^1H NMR (δ): 7.50−7.70 (m, 9H, phenyl ring), 7.92 (s, 1H, N−H); 3.60 (q, 4H, CH_2) 1.28 (t, 6H, CH_3). ^{13}C NMR (δ): 130.0, 129.7, 128.5, 127.8, 127.2, 123.8, 119.8 (phenyl ring), 159.6 (amide C), 162.7 (imine C), 56.8 (CH_2), 14.8 (CH_3).

Compound **Ie.** Grey solid. Yield (%): 64. Decomposition temperature (°C): 198−195. Found (calcd) (%): C, 50.29 (50.50); H, 4.18 (4.22); N, 9.25 (9.30). IR (cm^{-1}): 1615, 1560 ($\nu_{C=N}$), 1050 (ν_{P-O-C}), 715 ($\nu_{P=S}$). ^1H NMR (δ): 7.60−7.82 (m, 8H, phenyl ring), 8.10 (s, 1H, N−H), 3.62 (q, 4H, CH_2), 1.30 (t, 6H, CH_3). ^{13}C NMR (δ): 134.2, 130.2, 129.0, 128.5, 128.0, 122.8, 119.8 (phenyl ring), 159.8 (amide C), 163.2 (imine C), 57.6 (CH_2), 14.3 (CH_3).

Compound **If.** Green solid. Yield (%): 63. Decomposition temperature (°C): 236−232. Found (calcd) (%): C, 49.18 (49.35); H, 4.08 (4.14); N, 11.98 (12.12). IR (cm^{-1}): 1610, 1575 ($\nu_{C=N}$), 1055 (ν_{P-O-C}), 710 ($\nu_{P=S}$). ^1H NMR (δ): 7.65−7.85 (m, 8H, phenyl ring), 8.12 (s, 1H, N−H), 3.60 (q, 4H, CH_2), 1.28 (t, 6H, CH_3). ^{13}C NMR (δ): 133.8, 128.8, 128.0, 127.8, 126.2, 120.6, 116.9 (phenyl ring), 159.7 (amide C), 162.9 (imine C), 57.2 (CH_2), 14.5 (CH_3).

Compound **Ig.** Brown solid. Yield (%): 60. Decomposition temperature (°C): 215−212. Found (calcd) (%): C, 49.78 (49.1); H, 5.17 (5.28); N, 7.48 (7.59). IR (cm^{-1}): 1630, 1570 ($\nu_{C=N}$), 1040 (ν_{P-O-C}), 1270 ($\nu_{P=O}$). ^1H NMR (δ): 7.65−7.85 (m, 8H, phenyl ring), 8.10 (s, 1H, N−H), 3.60 (q, 8H, CH_2), 1.20 (t, 12H, CH_3). ^{13}C NMR (δ): 158.2, 138.6, 131.2, 130.2, 129.0, 124.2, 123.1, 120.2, 115.8 (phenyl ring), 160.8 (amide C), 164.0 (imine C), 58.2 (CH_2), 14.2 (CH_3).

Compound **Ih.** Yellow solid. Yield (%): 60. Decomposition temperature (°C): 182−180. Found (calcd) (%): C, 47.07 (47.18); H, 4.88 (4.99); N, 7.15 (7.18). IR (cm^{-1}): 1625, 1560 ($\nu_{C=N}$), 1035 (ν_{P-O-C}), 730 ($\nu_{P=S}$). ^1H NMR (δ): 7.60−7.82 (m, 8H, phenyl ring), 8.0 (s, 1H, N−H), 3.56 (q, 8H, CH_2), 1.18 (t, 12H, CH_3). ^{13}C NMR (δ): 157.8, 136.2, 130.0, 129.7, 128.5, 122.8, 121.6, 118.2, 115.0 (phenyl ring), 159.8 (amide C), 163.2 (imine C), 57.6 (CH_2), 14.0 (CH_3).

Compound **Ii.** Yellow solid. Yield (%): 52. Decomposition temperature (°C): 238−234. Found (calcd) (%): C, 51.35 (51.40); H, 5.32 (5.44); N, 7.78 (7.82). IR (cm^{-1}): 1625, 1560 ($\nu_{C=N}$), 1150 (ν_{P-O-C}, phenolic), 1030 (ν_{P-O-C}, alkyl), 1280 ($\nu_{P=O}$). ^1H NMR (δ): 6.80−7.70 (m, 8H, phenyl ring), 8.0 (s, 1H, N−H), 3.50 (q, 8H, CH_2), 1.15 (t, 12H, CH_3). ^{13}C NMR (δ): 157.2, 138.7, 131.0, 130.8, 130.4, 129.2, 124.1, 123.0, 121.2, 120.0, 118.4, 115.6 (phenyl ring), 158.8 (amide C), 162.6 (imine C), 58.2 (CH_2), 14.3 (CH_3).

Compound **Ij.** Light brown solid. Yield (%): 60. Decomposition temperature (°C): 260−257. Found (calcd) (%): C, 48.42 (48.50); H, 5.08 (5.13); N, 7.30 (7.38). IR (cm^{-1}): 1620, 1550 ($\nu_{C=N}$), 1150 (ν_{P-O-C}, phenolic), 1020 (ν_{P-O-C}, alkyl), 710 ($\nu_{P=S}$). ^1H NMR (δ): 6.78−7.75 (m, 8H, phenyl ring), 7.95 (s, 1H, N−H); 3.48 (q, 8H, CH_2) 1.12 (t, 12H, CH_3). ^{13}C NMR (δ): 156.5, 138.0, 130.0, 129.9, 129.2, 128.2 123.0, 122.7, 120.8, 119.5, 117.2, 115.0 (phenyl ring), 158.0 (amide C), 160.4 (imine C), 58.0 (CH_2), 14.0 (CH_3).

Compound **IIa.** Dirty yellow solid. Yield (%): 62. Decomposition temperature (°C): 258−255. Found (calcd) (%): C, 55.62 (55.69); H, 5.08 (5.14); N, 9.58 (9.74). IR (cm^{-1}): 1600, 1550 ($\nu_{C=N}$), 1260 (ν_{C-O-C}), 1030 (ν_{P-O-C}), 1275 ($\nu_{P=O}$). ^1H NMR (δ): 6.70−7.60 (m, 9H, phenyl ring), 8.0 (s, 1H, N−H), 4.0 (s, 2H), 3.55 (q, 4H, CH_2), 1.22 (t, 6H, CH_3). ^{13}C NMR (δ): 160.0, 138.0, 130.5, 129.8, 128.7, 123.2, 120.9, 120.5, 114.0 (phenyl ring), 161.8 (amide C), 164.5 (imine C), 67.3, 56.8 (CH_2), 14.0 (CH_3).

Compound **IIb.** Yellow solid. Yield (%): 58. Decomposition temperature (°C): 280−276. Found (calcd) (%): C, 51.48 (51.57); H, 4.37 (4.54); N, 8.98 (9.02). IR (cm^{-1}): 1610, 1555 ($\nu_{C=N}$), 1265 (ν_{C-O-C}), 1040 (ν_{P-O-C}), 1270 ($\nu_{P=O}$). ^1H NMR (δ): 6.75−7.80 (m, 8H, phenyl ring), 8.12 (s, 1H, N−H), 4.10 (s, 2H), 3.60 (q, 4H, CH_2), 1.24 (t, 6H, CH_3). ^{13}C NMR (δ): 160.0, 138.5, 131.2, 130.0, 129.8, 129.5, 126.0, 124.2, 123.1, 115.2 (phenyl ring), 162.5 (amide C), 165.2 (imine C), 67.5, 57.2 (CH_2), 14.4 (CH_3).

Compound **IIc.** Yellow solid. Yield (%): 55. Decomposition temperature (°C): 252−250. Found (calcd) (%): C, 50.28 (50.43); H, 4.37 (4.44); N, 11.72 (11.76). IR (cm^{-1}): 1615, 1550 ($\nu_{C=N}$), 1260 (ν_{C-O-C}), 1035 (ν_{P-O-C}), 1272 ($\nu_{P=O}$). ^1H NMR (δ): 6.82−7.80 (m, 8H, phenyl ring), 8.10 (s, 1H, N−H), 4.05 (s, 2H), 3.58 (q, 4H, CH_2), 1.22 (t, 6H, CH_3). ^{13}C NMR (δ): 159.8, 137.2, 130.8, 129.8, 129.0, 128.7, 125.2, 122.8, 121.2, 114.0 (phenyl ring), 161.8 (amide C), 164.0 (imine C), 67.0, 57.0 (CH_2), 14.2 (CH_3).

Compound **IId.** Yellow solid. Yield (%): 62. Decomposition temperature (°C): 215−212. Found (calcd) (%): C, 53.55 (53.69); H, 4.78 (4.96); N, 9.28 (9.39). IR (cm^{-1}): 1610, 1560 ($\nu_{C=N}$), 1255 (ν_{C-O-C}), 1025 (ν_{P-O-C}), 720 ($\nu_{P=S}$). ^1H NMR (δ): 6.58−7.70 (m, 9H, phenyl ring), 7.95 (s, 1H, N−H); 4.0 (s, 2H), 3.5 (q, 4H, CH_2), 1.20 (t, 6H, CH_3). ^{13}C NMR (δ): 159.0, 136.8, 129.2, 128.3, 125.8, 122.0, 119.2 118.2, 112.6 (phenyl ring), 160.0 (amide C), 163.2 (imine C), 66.8, 55.2 (CH_2), 13.6 (CH_3).

Compound **IIe.** Brown solid. Yield (%): 65. Decomposition temperature (°C): 242−240. Found (calcd) (%): C, 49.76 (49.85); H, 4.32 (4.39); N, 8.56 (8.72). IR (cm^{-1}): 1600, 1550 ($\nu_{C=N}$), 1260 (ν_{C-O-C}), 1035 (ν_{P-O-C}), 715 ($\nu_{P=S}$). ^1H NMR (δ): 6.72−7.70 (m, 8H, phenyl ring), 8.10 (s, 1H, N−H); 4.0 (s, 2H), 3.55 (q, 4H, CH_2) 1.22 (t, 6H, CH_3). ^{13}C NMR (δ): 159.2, 136.8, 130.1, 129.5, 128.2, 127.3, 125.2, 121.0, 120.5, 114.0 (phenyl ring), 160.2 (amide C), 164.0 (imine C), 66.8, 57.0 (CH_2), 14.0 (CH_3).

Compound **IIf.** Dark brown solid. Yield (%): 64. Decomposition temperature (°C): 262−258. Found (calcd) (%): C, 48.70 (48.78); H, 4.26 (4.30); N, 11.35 (11.38). IR (cm^{-1}): 1610, 1540 ($\nu_{C=N}$), 1250 (ν_{C-O-C}), 1030 (ν_{P-O-C}), 725 ($\nu_{P=S}$). ^1H NMR (δ): 6.80−7.75 (m, 8H, phenyl ring), 8.05 (s, 1H, N−H), 4.0 (s, 2H), 3.52 (q, 4H, CH_2), 1.20 (t, 6H, CH_3). ^{13}C NMR (δ): 158.6, 136.2, 129.8, 128.2, 127.8, 127.5, 124.0, 120.6, 119.5, 113.8 (phenyl ring), 160.2 (amide C), 163.2 (imine C), 65.2, 56.8 (CH_2), 14.0 (CH_3).

Compound **IIg.** Brown solid. Yield (%): 68. Decomposition temperature (°C): 205−202. Found (calcd) (%): C, 49.28 (49.40); H, 5.25 (5.36); N, 7.08 (7.20). IR (cm^{-1}): 1610, 1560 ($\nu_{C=N}$), 1250 (ν_{C-O-C}), 1150 (ν_{P-O-C}, phenolic), 1035 (ν_{P-O-C}, alkyl), 1265 ($\nu_{P=O}$). ^1H NMR

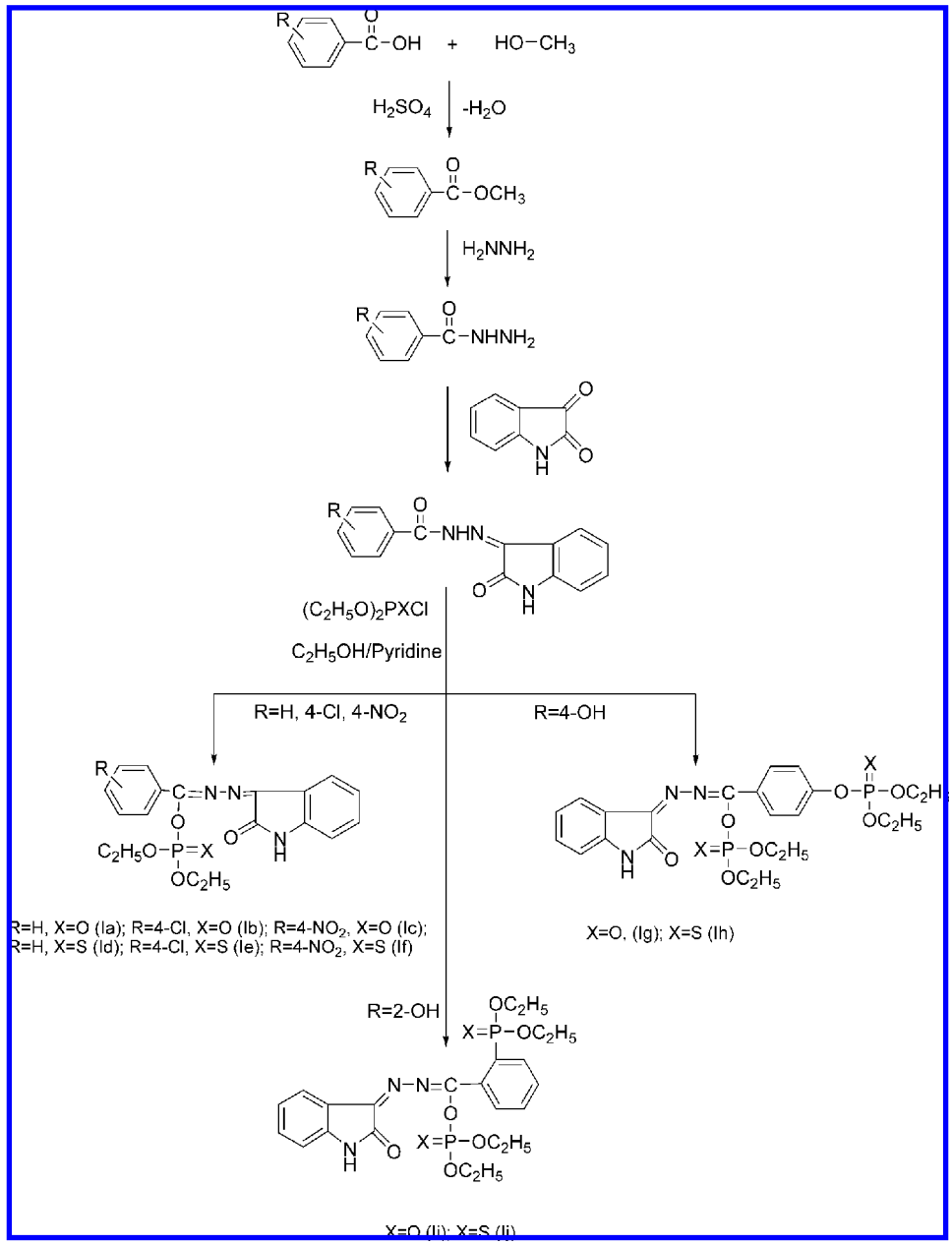

Figure 1. Synthetic route of organophosphorus derivatives containing isatin-3-(substituted benzoic acid hydrazone).

(δ): 6.8−7.5 (m, 8H, phenyl ring), 8.1 (s, 1H, N−H), 4.12 (s, 2H), 3.50 (q, 8H, CH_2), 1.20 (t, 12H, CH_3). ^{13}C NMR (δ): 161.5, 136.8, 130.0, 129.8, 127.8, 123.5, 122.4, 119.8, 115.0 (phenyl ring), 160.1 (amide C), 164.2 (imine C), 67.1, 58.0 (CH_2), 13.6 (CH_3).

Compound **IIh.** Dark brown solid. Yield (%): 61. Decomposition temperature (°C): 194−192. Found (calcd) (%): C, 46.76 (46.83); H, 5.05 (5.08); N, 6.74 (6.83). IR (cm^{-1}): 1600, 1555 ($\nu_{C=N}$), 1245 (ν_{C-O-C}), 1140 (ν_{P-O-C}, phenolic), 1030 (ν_{P-O-C}, alkyl), 720 ($\nu_{P=S}$). ^{1}H NMR (δ): 6.7−7.4 (m, 8H, phenyl ring), 8.0 (s, 1H, N−H), 4.08 (s, 2H), 3.45 (q, 8H, CH_2), 1.15 (t, 12H, CH_3). ^{13}C NMR (δ): 160.2, 135.2, 129.8, 128.9, 126.7, 122.6, 121.2, 118.5, 114.8 (phenyl ring), 158.9 (amide C), 163.8 (imine C), 67.0, 57.2 (CH_2), 13.4 (CH_3).

Compound **IIi.** Yellowish brown solid. Yield (%): 65. Decomposition temperature (°C): 212−210. Found (calcd) (%): C, 50.72 (5.80); H, 5.45 (5.51); N, 7.35 (7.40). IR (cm^{-1}): 1620, 1555 ($\nu_{C=N}$), 1260 (ν_{C-O-C}), 1160 (ν_{P-O-C}, phenolic), 1030 (ν_{P-O-C}, alkyl), 1260 ($\nu_{P=O}$). ^{1}H NMR (δ): 6.72−7.68 (m, 8H, phenyl ring), 8.15 (s, 1H, N−H), 4.10 (s, 2H), 3.45 (q, 8H, CH_2), 1.18 (t, 12H, CH_3). ^{13}C NMR (δ): 158.0, 137.8, 130.8, 130.1, 129.7, 128.6, 124.0, 122.0, 120.8, 118.0, 115.2 (phenyl ring), 159.8 (amide C), 163.1 (imine C), 67.0, 57.2 (CH_2), 13.0 (CH_3).

Compound **IIj.** Brown solid. Yield (%): 58. Decomposition temperature (°C): 185−182. Found (calcd) (%): C, 48.02 (48.07); H, 5.15 (5.21); N, 7.01 (7.01). IR (cm^{-1}): 1625, 1550 ($\nu_{C=N}$), 1255 (ν_{C-O-C}), 1150 (ν_{P-O-C}, phenolic), 1025 (ν_{P-O-C}, alkyl), 710 ($\nu_{P=S}$). ^{1}H NMR (δ): 6.70−7.60 (m, 8H, phenyl ring), 8.08 (s, 1H, N−H), 4.0 (s, 2H), 3.40 (q, 8H, CH_2), 1.15 (t, 12H, CH_3). ^{13}C NMR (δ): 157.6, 136.2, 129.8, 129.0, 128.3, 126.8, 122.5, 121.6, 119.9, 119.5, 118.0, 115.0 (phenyl ring), 159.0 (amide C), 162.0 (imine C), 66.8, 57.0 (CH_2), 12.8 (CH_3).

RESULTS AND DISCUSSION

Reactions of *O*,*O*-diethylchlorophosphate/thiophosphate with isatin-3-(substituted benzoic acid/phenoxy acetic acid hydrazones) have been carried out in ethanol in the presence of pyridine, and a variety of organophosphorus derivatives have been isolated according to **Figures 1** and **2**. The methods used for the preparation and isolation of these compounds gave materials of good purity as supported by their analyses and thin-layer chromatography (TLC). The organophosphorus derivatives

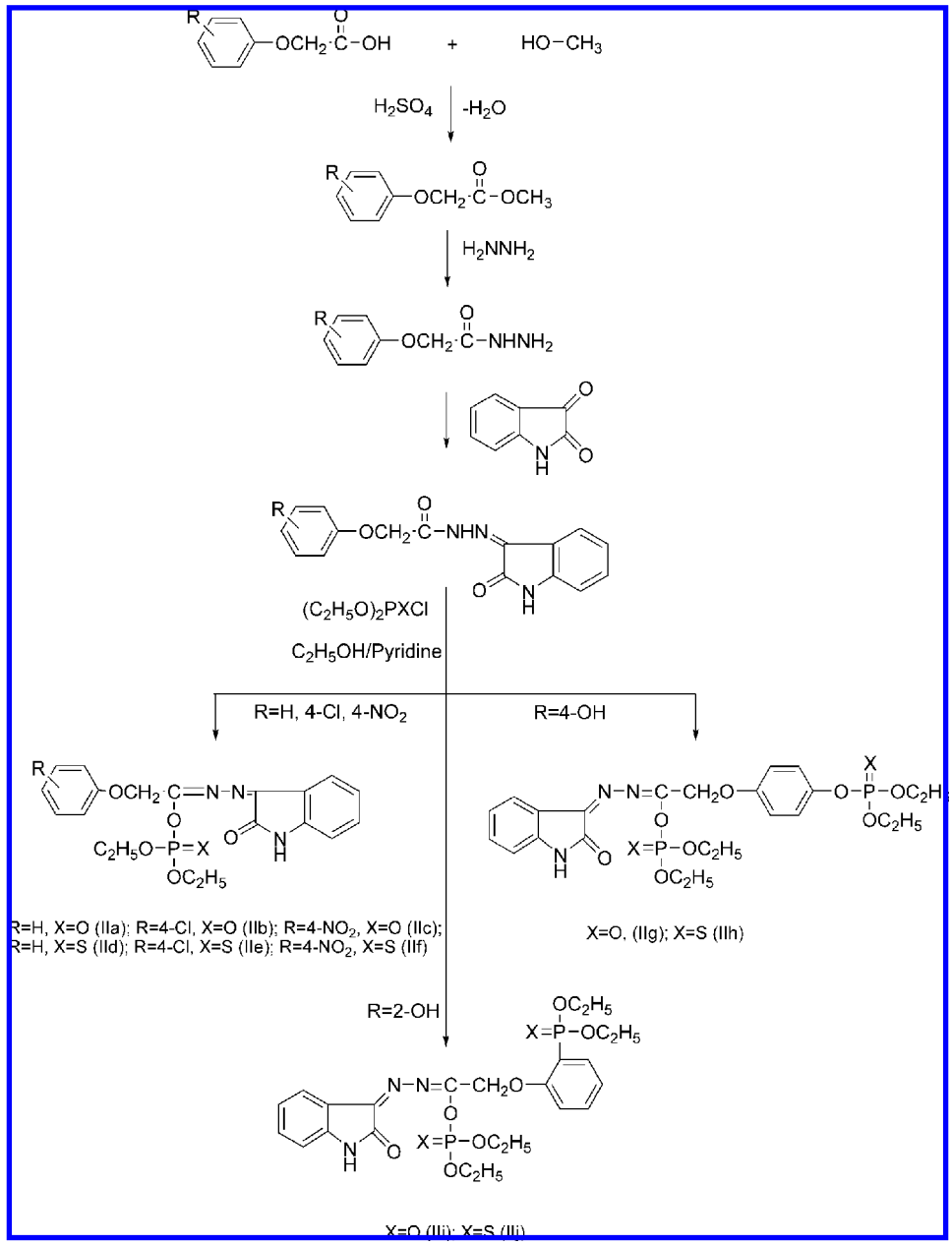

Figure 2. Synthetic route of organophosphorus derivatives containing isatin-3-(substituted phenoxyacetic acid hydrazone).

are found to be soluble in chloroform, dimethylsulfoxide, tetrahydrofuran, and dimethylformamide. All of these compounds are yellow or brown in color.

Infrared Spectra. The infrared spectra of hydrazones show bands at ca. 3200−3100 cm^{-1}, which may be due to ν_{N-H} vibration. The hydrazones also show bands at 1640−1685, 1490−1515, 1270−1285, 600−660, and 530−570 cm^{-1}, which may be assigned (*9*) to amide-I (C═O), amide-II ν (C−N) plus δ (N−H), amide-III δ (N−H), amide-IV θ (C═O), and amide-VI π (C═O) vibrations, respectively. In organophosphorus derivatives, these bands disappear, providing evidence for enolization and formation of the bond through enolic oxygen. New bands appear at ca. 1560 cm^{-1} (newly formed C═N), 1290−1330 cm^{-1} ($\nu_{C=O}$), and 1040 cm^{-1} (ν_{N-N}) in these derivatives, which further supported enolization of the keto group. The spectra of hydrazones also show two bands at 3280 and 1700 cm^{-1}, assignable (*9*) to ν_{N-H} and $\nu_{C=O}$ vibrations of the isatin ring. In organophosphorus derivatives, both the bands remain almost at the same position, indicating non-involvement of the groups in the bond formation. The spectra of phenoxy acetic acid hydrazones show a band at ca. 1260 cm^{-1}, which may be assigned to ν_{C-O-C} vibration (aryl alkyl ether). In organophosphorus derivatives, these band remain at the same position, indicating non-involvement of these groups in bond formation. The hydrazone shows a weak band at 1600−1630 cm^{-1}, which can be assigned (*9*) to the $\nu_{C=N}$ vibration (azomethine linkage). This band remains almost at the same position in organophosphorus derivatives, ruling out the possibility of bond formation between organophosphorus and azomethine nitrogen.

The spectra of isatin-3-(2-hydroxy/4-hydroxy benzoic acid hydrazone) and isatin-3-(2-hydroxy/4-hydroxy phenoxy acetic acid hydrazone) show a band in the 3350−3390 cm^{-1} region, which may be assigned to ν_{O-H}. In organophosphorus derivatives, this band disappears, indicating deprotonation of the phenolic −OH group. The formation of the bond between phosphorus and phenolic −OH is confirmed by the presence of a strong band at 1160 cm^{-1}, assignable to ν_{P-O-C} phenolic.

In addition, all organophosphorus derivatives obtained by *O*,*O*-diethylchlorophosphate show a band at 1025−1055 and

Table 1. Fungitoxic Screening Data of Organophosphorus Derivatives Containing Isatin-3-(hydrazones)

	percent mycelial inhibition								
	Colletotrichum falcatum			*Fusarium oxysporum*			*Curvularia pallescence*		
compound	10 ppm	100 ppm	1000 ppm	10 ppm	100 ppm	1000 ppm	10 ppm	100 ppm	1000 ppm
Ia	40.3	49.4	60.8	41.2	50.4	61.8	40.4	49.2	59.8
Ib	56.8	64.2	69.6	54.2	67.8	72.6	51.6	62.4	71.2
Ic	30.2	40.1	54.2	29.4	39.6	56.2	26.8	38.6	51.8
Id	58.2	65.1	70.8	55.2	69.2	74.2	55.7	65.8	73.5
Ie	60.5	72.4	88.6	68.6	78.2	85.8	61.6	71.6	85.8
If	39.8	46.2	58.2	40.0	47.2	58.2	36.2	45.6	57.2
Ig	52.3	62.4	69.2	52.6	58.0	71.5	51.8	51.7	67.8
Ih	58.2	68.2	87.0	57.1	68.2	82.4	56.0	66.2	81.4
Ii	51.5	59.9	68.8	49.8	56.2	66.5	47.7	56.7	65.6
Ij	57.6	67.2	86.6	55.2	66.5	82.8	54.2	64.2	80.5
IIa	51.2	61.6	70.2	50.0	59.2	69.6	50.1	58.2	68.8
IIb	64.8	71.6	80.2	61.8	74.2	85.6	60.9	71.8	82.6
IIc	38.6	48.6	60.2	37.2	45.8	61.5	34.0	42.8	55.6
IId	56.2	67.0	75.2	54.0	69.1	76.8	52.6	62.7	74.2
IIe	80.5	90.2	100.0	80.0	89.2	100.0	78.2	84.8	100.0
IIf	48.2	56.2	68.4	44.6	52.6	67.8	40.6	52.8	65.6
IIg	61.5	70.2	80.6	60.2	69.2	78.6	62.8	70.0	76.4
IIh	75.1	86.2	100.0	70.2	82.6	100.0	68.6	80.5	100.0
IIi	60.2	67.4	78.2	58.6	64.0	74.2	57.2	64.6	71.2
IIj	72.5	81.2	95.6	71.6	80.0	92.8	72.8	79.9	93.8

1250−1280 cm^{-1}, assignable (*3*) to ν_{P-O-C} alkyl and $\nu_{P=O}$ vibrations, respectively. Organophosphorus derivatives derived by *O*,*O*-diethylchlorothiophosphate show bands at 700−730 cm^{-1}, assignable to $\nu_{P=S}$vibration.

^{1}H NMR Spectra. The proton magnetic resonance spectra of hydrazones and their corresponding organophosphorus derivatives have been recorded in DMSO-d_6. The following conclusions can be derived by comparing the spectra of hydrazones with their corresponding organophosphorus derivatives: (a) A signal because of the −NH appears at ca. δ 5.6−5.9, which disappears completely in corresponding organophosphorus derivatives, indicating enolization of the hydrazones. (b) The signal because of the −NH group of the isatin ring at appear ca. δ 8.0 in the spectra of hydrazones and their corresponding organophosphorus derivatives. (c) The signals because of the ethoxy group appear at ca. δ 3.5 (quartet, because of the CH_2 group) and at ca. δ 1.2 (triplet, because of the CH_3 group). (d) Isatin-3-(benzoic acid/phenoxy acetic acid hydrazones) and their corresponding organophosphorus derivatives show a multiplet for the aromatic ring at ca. δ 7.50−7.80.

^{13}C NMR Spectra. The ^{13}C NMR spectra of organophosphorus compounds were recorded in DMSO-d_6. Different signals, appearing for these compounds, are already given in the Materials and Methods. For the *O*,*O*-diethyl group, two signals appear at ca. δ 58.0 (CH_2) and δ 15.0 (CH_3). For amide carbon, a signal appears at ca. δ 160.0, while for imine carbon, a signal appears at ca. δ 163.0. For the phenyl ring, a number of signals appear.

Antifungal Activity. The organophosphorus derivatives containing isatin-3-hydrazones show (**Table 1**) a promising result in inhibiting the mycelial growth of all test fungi. There is significant alteration in antifungal activity with the change in the nature of the organic group attached to the *O*,*O*-diethylchlorophosphate/thiophosphate moiety. The compounds containing isatin-3-(substituted phenoxy acetic acid hydrazones) are found to be more active than compounds containing isatin-3-(substituted benzoic acid hydrazones). Organophosphorus compounds containing isatin-3-(4-dichloro phenoxy acetic acid hydrazone) (**IIe**) and the compound containing two molecules of *O*,*O*-diethylchlorophosphate attached to isatin-3-(4-hydroxy phenoxy acetic acid) hydrazone (**IIh**) are proven to be more active than some prevalent commercial synthetic fungicides. These two compounds show inhibition of 100% for all of the test fungi at 1000 mg/L concentration.

Table 2. Efficacy of Organophosphorus Derivatives Compared to Synthetic Fungicides against Sugarcane Pathogens

common name of fungicide/ chemical	trade name	MIC (ppm) against		
		C. falcatum	*F. oxysporum*	*C. pallescence*
carbendazim	Bavistin	4000	3000	4000
copper oxychloride	Blitox 50	4000	3000	2000
mancozeb	Dithane M-45	4000	3000	4000
thiophanate methyl	Topsin M	4000	4000	4000
IIe		1000	1000	1000
IIh		1000	1000	1000

The MICs of the most active *O*,*O*-diethyl chlorothiophosphate derivatives were determined. Three concentrations, 1000, 2000, and 3000 mg/L, of each test compound with respect to culture medium were prepared. The fungistatic/fungicidal nature of active chemicals was determined in three replicates using the test fungi, following the procedure of Garbour and Houston (*11*). This was performed by observing if revival of growth of inhibition mycelial disks occurred following transfer to a chemical-free medium.

The two derivatives, namely, *O*,*O*-diethylchlorothiophosphate derivatives containing isatin-3-(2,4-chlorophenoxyacetic acid hydrazone) (**IIe**) and the compound containing two molecules of *O*,*O*-diethylchlorophosphate attached to isatin-3-(4-hydroxy phenoxy acetic acid) hydrazone (**IIh**) showed superiority over the commercial fungicides Bavistin, Bitox-50, Topsin M, and Dithione M-45 during the present study. These compounds are 2−4 times more active than the tested commercial fungicides (**Table 2**), which are being used in sugarcane fungal disease management.

ACKNOWLEDGMENT

We are thankful to Dr. G. P. Rao, Sugarcane Research Station, Kunraghat, Gorakhpur, India, for helpful discussion and suggestions.

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Received for review July 11, 2008. Revised manuscript received September 8, 2008. Accepted September 9, 2008. S.K.S. is thankful to University Grants Commission, New Delhi, India, for financial assistance.

JF801975Z