Synthesis and Herbicidal Activity of Some Novel Cyanoguanidines and Related Cyanoisothioureas

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A series of *N''*-cyano-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidines is reported. Preparation via several routes is described including the following: (a) condensation of primary amines with *N'*-cyano-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)-*S*-methylisothioureas; (b) condensation of 1,2,3,4-tetrahydro-1-naphthylamine with *N-tert*-butyl-*N'*-cyano-*S*-methylisothiourea; (c) condensation of *N*-cyano-*O*-phenylisourea with 1,2,3,4-tetrahydro-1-naphthylamine; (d) reaction of sodium dicyanamide with 1,2,3,4-tetrahydro-1-naphthylamine hydrochloride to give *N'*-cyano-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine. Significant herbicidal activity is described for some of the cyanoguanidines and their corresponding cyanoisothiourea precursors. Those compounds with methoxyl substitution on the aromatic nucleus demonstrate significant activity with the methoxyl group in the 7-position and no activity with the methoxyl group in the 6-position.

Cyanoguanidines have been reported as H_2-receptor antagonists (Durant et al., 1976), as antihypertension agents (Petersen, 1977), as animal growth promoters (Dunbar and Maruyama, 1987), and as plant growth regulators (Speltz et al., 1984). Only recently has a class of herbicidal cyanoguanidines been described: *N*-(substituted benzyl)-*N''*-cyanoguanidines (Arotin et al., 1987).

Cyanoisothioureas have been reported as ulcer inhibitors (Shimamura et al., 1987; Morishita Pharmaceutical Co., Ltd., 1982; Hirata et al., 1978) and as fungicides (Chiyomaru et al., 1975; Kawada et al., 1975). None have been reported to have proven herbicidal activity.

We now report the synthesis and herbicidal activities of a novel class of cyanoguanidines, consisting of *N''*-cyano-*N*-substituted-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidines and their cyanoisothiourea precursors.

EXPERIMENTAL SECTION

Synthetic Methods. General Procedures. ^{1}H NMR spectra were obtained on a Varian EM360 spectrometer with tetramethylsilane as an internal standard. ^{13}C NMR spectra were obtained on a JEOL FX-90Q spectrometer. Infrared spectra were obtained on a Beckman AccuLab 4 spectrophotometer. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Combustion analyses were performed by Steven Konopnicki, Analytical Laboratories, Midland Division, Dow Chemical Co.

***N'*-Cyano-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)-*S*-methylisothiourea (2).** To a stirred solution of 73.1 g (0.5 mol) of dimethyl cyanodithioiminocarbonate in 200 mL of ethanol was slowly added a solution of 73.6 g (0.5 mol) of 1,2,3,4-tetrahydro-1-naphthylamine in 75 mL of ethanol, keeping the temperature of the reaction mixture between 3 and 5 °C by means of an ice–salt bath. After the addition, which required about 10 min, the reaction mixture was stirred for 30 min at 0–2 °C and then allowed to remain at room temperature for 3 h. The product crystallized as a white solid, mp 143–144 °C, weighing 103.5 g (84% yield): ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 1.96 (m, 4 H), 2.60 (s, 3 H), 2.79 (m, 2 H), 5.28 (m, 1 H), 7.21 (m, 4 H), 8.61 (m, 1 H). Anal. Calcd for $C_{13}H_{15}N_3S$: C, 63.64; H, 6.16; N, 17.13. Found: C, 63.70; H, 6.01; N, 17.26.

***N''*-Cyano-*N*-methyl-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1a).** A solution of 12.3 g (50 mmol) of **2** and 20 mL (ca. 0.2 mol) of 33% ethanolic methylamine in 200 mL of ethanol was heated at reflux with stirring for 22 h. The solvent and excess methylamine were then removed by evaporation in vacuo, leaving the crude product as a glassy, amorphous solid. Crystallization from a mixture of isopropyl acetate, methylcyclohexane, and 2-propanol gave 7.03 g (62% yield) of white, crystalline solid: mp 169–170 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 1.84 (m, 4 H), 2.76 (m, 2 H), 2.88 (d, 3 H), 5.05 (m, 1 H), 6.14 (m, 2 H), 7.21 (m, 4 H). Anal. Calcd for $C_{13}H_{16}N_4$: C, 68.39; H, 7.07; N, 24.54. Found: C, 68.20; H, 7.01; N, 24.66.

***N''*-Cyano-*N*-ethyl-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1b).** A solution of 6.13 g (25 mmol) of **2** and 10 mL (ca. 0.18 mol) of 70% aqueous ethylamine in 90 mL of ethanol was heated at reflux with stirring for 20 h. The reaction mixture was cooled in a refrigerator to give 2.44 g (40% yield) of white, crystalline solid: mp 152–153.5 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 1.20 (t, 3 H), 1.94 (m, 4 H), 2.80 (m, 2 H), 3.31 (m, 2 H), 5.06 (m, 1 H), 6.43 (m, 2 H), 7.18 (m, 4 H). Anal. Calcd for $C_{14}H_{18}N_4$: C, 69.39; H, 7.49; N, 23.12. Found: C, 69.50; H, 7.54; N, 23.18.

***N''*-Cyano-*N*-(*n*-propyl)-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1c).** A solution of 12.3 g (50 mmol) of **2** and 16 mL (ca. 0.20 mol) of *n*-propylamine in 100 mL of acetonitrile was heated at reflux with stirring for 20 h. The reaction mixture was then cooled in a refrigerator to give 7.06 g of white, crystalline solid, mp 130.5–131.5 °C. Concentration of the mother liquor gave 1.57 g of additional product, mp 130–130.5 °C, bringing the total yield to 8.63 g (67%): ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 0.92 (t, 3 H), 1.49 (m, 2 H), 1.87 (m, 4 H), 2.77 (m, 2 H), 3.23 (m, 2 H), 5.06 (m, 1 H), 6.50 (m, 2 H), 7.20 (m, 4 H). Anal. Calcd for $C_{15}H_{20}N_4$: C, 70.28; H, 7.86; N, 21.86. Found: C, 70.30; H, 7.83; N, 21.81.

***N''*-Cyano-*N*-isopropyl-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1d).** A solution of 30 g (0.122 mol) of **2** and 40 mL (ca. 0.47 mol) of isopropylamine in 300 mL of acetonitrile was heated at reflux with stirring for 154 h. The solvent and excess isopropylamine were removed by evaporation in vacuo, leaving the crude product as a tacky, white solid. One recrystallization from isopropyl acetate and a second from a mixture of isopropyl acetate and 2-propanol gave 5.13 g (16% yield) of white, crystalline solid: mp 170.5–172.5 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 1.20 (d, 6 H), 1.90 (m, 4 H), 2.78 (m, 2 H), 4.04 (m, 1 H), 5.09 (m, 1 H), 6.16 (d, 1 H), 6.71 (d, 1 H), 7.20 (m, 4 H). Anal. Calcd for $C_{15}H_{20}N_4$: C, 70.28; H, 7.86; N, 21.86. Found: C, 70.20; H, 7.70; N, 21.76.

***N''*-Cyano-*N*-cyclopropyl-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1e).** A solution of 24.6 g (0.1 mol) of **2** and 25 g (0.438 mol) of cyclopropylamine in 250 mL of ethanol was heated at reflux with stirring for 120 h. The solvent was removed by evaporation in vacuo. The residual oil was crystallized from a mixture of isopropyl acetate and ethanol to give the partially purified product as a white solid. Recrystallization from isopropyl acetate–ethanol gave 7.75 g (31% yield) of the pure product as a white, crystalline solid: mp 170.5–171.5 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 0.72 (m, 4 H), 1.90 (m, 4 H), 2.52 (m, 1 H), 2.75 (m, 3 H), 4.97 (m, 1 H), 6.46 (m, 1 H), 7.09 (m, 4 H). Anal.

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Calcd for $C_{15}H_{18}N_4$: C, 70.84; H, 7.13; N, 22.03. Found: C, 70.60; H, 7.06; N, 22.07.

N-Allyl-N″-cyano-N′-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1f). A solution of 24.6 g (0.1 mol) of **2** and 38 mL (ca. 0.51 mol) of allylamine in 400 mL of ethanol was heated at reflux for 87 h. The solvent was removed by evaporation in vacuo, leaving a pale yellow semisolid, which was recrystallized from isopropyl acetate to give 11 g (43% yield) of white, crystalline solid: mp 130–132 °C; ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 1.77 (m, 4 H), 2.64 (m, 2 H), 3.74 (m, 2 H), 4.99 (m, 3 H), 5.67 (m, 1 H), 6.37 (m, 2 H), 6.97 (m, 4 H). Anal. Calcd for $C_{15}H_{18}N_4$: C, 70.84; H, 7.13; N, 22.03. Found: C, 70.83; H, 7.15; N, 22.14.

N-(n-Butyl)-N″-cyano-N′-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1g). A solution of 12.3 g (50 mmol) of **2** and 20 mL (ca. 0.20 mol) of *n*-butylamine in 100 mL of acetonitrile was heated at reflux with stirring for 100 h. The solvent was then removed by evaporation in vacuo. The residual oil was dissolved in methylene chloride, and the solution was washed with 3 × 80 mL portions of 3 N HCl and then dried (Na_2SO_4). Filtration and concentration in vacuo left 9.73 g (72% yield) of the pure product as a pale yellow, viscous oil: ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 0.61–2.25 (br m, 12 H), 2.79 (m, 2 H), 3.27 (m, 2 H), 5.06 (m, 1 H), 6.24 (m, 1 H), 7.16 (m, 4 H). Anal. Calcd for $C_{16}H_{22}N_4$: C, 71.07; H, 8.20; N, 20.72. Found: C, 70.80; H, 8.28; N, 20.63.

N″-Cyano-N-isobutyl-N′-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1h). By the same procedure for the preparation of **1g**, this compound was prepared as a pale yellow, viscous oil in 86% yield: ^{1}H NMR ($CDCl_3$/DMSO-d_6) δ 0.91 (d, 6 H), 1.88 (m, 5 H), 2.77 (m, 2 H), 3.10 (m, 2 H), 5.08 (m, 1 H), 6.48 (m, 2 H), 7.20 (m, 4 H). Anal. Calcd for $C_{16}H_{22}N_4$: C, 71.07; H, 8.20; N, 20.72. Found: C, 70.48; H, 8.05; N, 20.63.

N″-Cyano-N-[2-(dimethylamino)ethyl]-N′-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1i). A solution of 16 g (65.2 mmol) of **2** and 11.5 g (0.13 mol) of *N,N*-dimethylethylenediamine in 125 mL of acetonitrile was heated at reflux with stirring for 50 h. The mixture was then cooled in a refrigerator to give the crude product as a white, crystalline solid, mp 149.5–153.5 °C. Recrystallization from ethanol gave 11 g (59% yield) of the pure product as a white, crystalline solid: mp 154.5–155.5 °C; ^{1}H NMR (DMSO-d_6) δ 1.82 (m, 4 H), 2.00 (s, 6 H), 2.32 (m, 2 H), 2.73 (m, 2 H), 3.27 (m, 3 H), 4.89 (m, 1 H), 6.88 (m, 1 H), 7.17 (s, 4 H). Anal. Calcd for $C_{16}H_{23}N_5$: C, 67.33; H, 8.12; N, 24.54. Found: C, 67.20; H, 8.06; N, 24.63.

N″-Cyano-N-[2-(diethylamino)ethyl]-N′-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (1j). A solution of 16.2 g (66 mmol) of **2** and 11.5 g (0.132 mol) of *N,N*-diethylethylenediamine in 125 mL of acetonitrile was heated at reflux with stirring for 64 h. The mixture was then cooled in a refrigerator to give 9.8 g (47% yield) of the pure product as a white, crystalline solid: mp 114–114.5 °C; ^{1}H NMR (DMSO-d_6) δ 0.99 (t, 6 H), 2.00 (m, 4 H), 2.62 (m, 8 H), 3.42 (m, 3 H), 5.11 (m, 1 H), 7.20 (m, 4 H). Anal. Calcd for $C_{18}H_{27}N_5$: C, 68.97; H, 8.68; N, 22.35. Found: C, 68.90; H, 8.81; N, 22.38.

N′-Cyano-N-(6-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)-S-methylisothiourea (7a). To a stirred solution of 11 g (62 mmol) of 6-methoxy-1,2,3,4-tetrahydro-1-naphthylamine (Sarges et al., 1973) in 100 mL of ethanol at 0 °C was added 10 g (68 mmol) of dimethyl cyanodithioiminocarbonate over a period of 30 min. The mixture was then stirred at room temperature for 16 h, after which it was cooled in a refrigerator to give 9.7 g (57% yield) of white, crystalline solid: mp 147–148 °C; ^{1}H NMR ($CDCl_3$) δ 1.84 (m, 4 H), 2.48 (s, 3 H), 2.70 (m, 2 H), 3.74 (s, 3 H), 4.99 (m, 1 H), 5.96 (m, 1 H), 6.47–7.27 (br m, 3 H). Anal. Calcd for $C_{14}H_{17}N_3OS$: C, 61.06; H, 6.22; N, 15.26. Found: C, 61.20; H, 6.27; N, 15.32.

N″-Cyano-N-ethyl-N′-(6-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (3a). A solution of 5.5 g (20 mmol) of **7a** and 10 mL (ca. 0.18 mol) of 70% aqueous ethylamine in 100 mL of ethanol was heated at reflux for 13 h. The solvent was then removed by evaporation in vacuo, and the residual oil was chromatographed on a silica gel column, eluting with ethyl acetate. The solvent was removed by evaporation in vacuo, and the residual oil was crystallized from toluene to give 1.7 g (31% yield) of white, crystalline solid: mp 139–140 °C; ^{1}H NMR ($CDCl_3$) δ 1.14 (t, 3 H), 1.83 (m, 4 H), 2.70 (m, 2 H), 3.19 (m, 2 H) 3.76 (s, 3 H), 4.99 (m, 2 H), 5.66 (m, 1 H), 6.49–7.36 (br m, 3 H). Anal. Calcd for $C_{15}H_{20}N_4O$: C, 66.15; H, 7.40; N, 20.58. Found: C, 66.30; H, 7.30; N, 20.69.

1-(Hydroxyimino)-7-methoxy-1,2,3,4-tetrahydronaphthalene (5b). To a mixture of 100 g (0.57 mol) of 7-methoxy-1-tetralone and 60 g (0.86 mol) of hydroxylamine hydrochloride in 500 mL of ethanol was added a solution of 100 g of sodium acetate in 200 mL of hot water. The mixture was heated on a steam bath for 30 min, and enough water was added to the hot solution to cause turbidity. Cooling gave the crude, solid product, which was recrystallized from ethanol (Darco) to give 88 g (81% yield) of the pure product as off-white crystals: mp 88–90 °C; ^{1}H NMR ($CDCl_3$) δ 1.82 (m, 2 H), 2.70 (m, 4 H), 3.76 (s, 3 H), 6.63–7.50 (br m, 3 H), 9.11 (m, 1 H). Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.03; H, 6.93; N, 7.35.

7-Methoxy-1,2,3,4-tetrahydro-1-naphthylamine Hydrochloride (6b). To a suspension of 3 g of 5% Pd/C in 200 mL of glacial acetic acid was added 78 g (0.41 mol) of **5b**. The mixture was hydrogenated with shaking in a Parr apparatus at room temperature (40 psi). Shaking and periodic recharging of the reactor with hydrogen to 40 psi were continued for 15 h. Subsequently, the catalyst was removed by filtration, and the acetic acid was removed by evaporation in vacuo. The residue was dissolved in CH_2Cl_2, and the solution was washed with 20% aqueous NaOH. The organic phase was then extracted with 20% HCl, and the acidic extract was made basic by the addition of 20% aqueous NaOH. This was followed by extraction with CH_2Cl_2, drying of the organic extract (Na_2SO_4), filtration, and concentration in vacuo. The residual amine was diluted with an equal volume of ethanol, and the solution was treated with concentrated HCl to give 45 g (52% yield) of the pure product as a white, crystalline solid: mp 249–250 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 2 H), 1.77 (m, 4 H), 2.66 (m, 2 H), 3.77 (m, 4 H), 6.80 (m, 3 H). Anal. Calcd for $C_{11}H_{16}ClNO$: C, 61.82; H, 7.55; N, 6.56. Found: C, 62.00; H, 7.58; N, 6.55.

N′-Cyano-N-(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)-S-methylisothiourea (7b). This compound was prepared by the method used for the preparation of **7a**. The product was obtained in 72% yield as colorless plates (ethanol): mp 131–132 °C; ^{1}H NMR ($CDCl_3$) δ 1.84 (m, 4 H), 2.84 (s, 3 H), 2.65 (m, 2 H), 3.73 (s, 3 H), 5.03 (m, 1 H), 6.21 (m, 1 H), 6.89 (m, 3 H). Anal. Calcd for $C_{14}H_{17}N_3OS$: C, 61.06; H, 6.22; N, 15.26. Found: C, 61.20; H, 6.22; N, 15.31.

N″-Cyano-N-ethyl-N′-(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (3b). This compound was prepared from **7b** by the method used for the preparation of **3a**. The product was obtained in 50% yield as a white crystalline solid: mp 130–131 °C; ^{1}H NMR ($CDCl_3$) δ 1.20 (t, 3 H), 1.87 (m, 4 H), 2.73 (m, 2 H), 3.23 (m, 2 H), 3.80 (s, 3 H), 5.00 (m, 2 H), 5.59 (m, 1 H), 7.00 (m, 3 H). Anal. Calcd for $C_{15}H_{20}N_4O$: C, 66.15; H, 7.40; N, 20.58. Found: C, 66.40; H, 7.31; N, 20.33.

6,7-Dimethoxy-1-(hydroxyimino)-1,2,3,4-tetrahydronaphthalene (5c). This compound was prepared in 53% yield from 6,7-dimethoxy-1-tetralone (Schrötter et al., 1981) by the method used for the preparation of **5b**. The product was obtained as off-white crystals: mp 160–161 °C; ^{1}H NMR ($CDCl_3$) δ 1.87 (m, 2 H), 2.76 (m, 4 H), 3.91 (s, 6 H), 6.63 (s, 1 H), 7.47 (s, 1 H), 9.24 (br m, 1 H). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.12; H, 6.85; N, 6.34.

6,7-Dimethoxy-1,2,3,4-tetrahydro-1-naphthylamine (6c). This compound was prepared from **5c** in 91% yield by the method used for the preparation of **6b**, except that the product was not isolated as the hydrochloride. The crude, free amine was a pale yellow oil and was used in the next step without purification: ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 2 H), 1.71 (m, 4 H), 2.71 (m, 2 H), 3.87 (m, 7 H), 6.55 (s, 1 H), 6.96 (s, 1 H).

N′-Cyano-N-(6,7-dimethoxy-1,2,3,4-tetrahydro-1-naphthalenyl)-S-methylisothiourea (7c). This compound was prepared from **6b** in 94% yield by the method used for the preparation of **7a** to give the pure product as a white, crystalline solid: mp 180–181 °C; ^{1}H NMR ($CDCl_3$) δ 1.87 (m, 4 H), 2.53 (s, 3 H), 2.65 (m, 2 H), 3.88 (s, 6 H), 5.03 (m, 1 H), 6.16 (m, 1 H), 6.69 (s, 1 H), 6.79 (s, 1 H). Anal. Calcd for $C_{15}H_{19}N_3O_2S$: C, 58.99; H, 6.27; N, 13.76; S, 10.50. Found: C, 59.00; H, 6.12; N, 13.98; S, 10.60.

N''-Cyano-N-ethyl-N'-(6,7-dimethoxy-1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (3c). This compound was prepared from **7c** in 61% yield by the method used for the preparation of **3a** (37 h reflux) to give the pure product as a white, crystalline solid: mp 167–168 °C; ^{1}H NMR ($CDCl_3$) δ 1.20 (t, 3 H), 1.90 (m, 4 H), 2.72 (m, 2 H), 3.22 (m, 2 H), 3.88 (s, 6 H), 4.98 (m, 2 H), 5.59 (m, 1 H), 6.60 (s, 1 H), 6.70 (s, 1 H). Anal. Calcd for $C_{16}H_{22}N_4O_2$: C, 63.55; H, 7.33; N, 18.53. Found: C, 63.70; H, 7.38; N, 18.45.

N'-Cyano-N-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (8). *Method A.* A solution of 18.4 g (0.1 mol) of 1,2,3,4-tetrahydro-1-naphthylamine hydrochloride and 8.9 g (0.1 mol) of sodium dicyanamide in 220 mL of water was heated at 95 °C (steam bath) for 21 h, during which a viscous oil separated from the hot solution. The mixture was cooled and extracted with CH_2Cl_2. The extract was dried (Na_2SO_4), filtered, and concentrated in vacuo, leaving the crude product as a pale yellow gum. The latter was crystallized from isopropyl acetate to give an off-white, crystalline solid, mp 153.5–156.5 °C. Recrystallization from aqueous ethanol gave 3.87 g (18% yield) of white, crystalline solid, mp 157–158 °C. Anal. Calcd for $C_{12}H_{14}N_4$: C, 67.26; H, 6.59; N, 26.15. Found: C, 67.00; H, 6.57; N, 26.16.

Method B. A mixture of 1.3 g (8.1 mmol) of *N*-cyano-*O*-phenylisourea (Grigat and Pütter, 1966) and 1.2 g (8.2 mmol) of 1,2,3,4-tetrahydro-1-naphthylamine in 5 mL of $CHCl_3$ was heated at reflux. Disappearance of the isourea was monitored by TLC analysis. After 30 h the thick solution was treated with 5 mL of toluene and allowed to stand at room temperature. This resulted in crystallization of the desired product. The supernatant solution was withdrawn, and the solid was washed with toluene and dried. This gave 0.91 g of white, crystalline product, mp 153–155 °C. The mother liquor was concentrated to give an additional 0.38 g of product: total yield 1.29 g (74%); IR (KBr) 3375, 2933, 2170, 1631, 1555, 1162 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.80 (m, 1 H), 2.72 (m, 2 H), 3.40 and 6.58 (3 H, N*H* and NH_2), 4.85 (m, 1 H), 7.16 (br m, 4 H); ^{13}C NMR (DMSO-d_6) δ 19.56, 28.61, 29.69, 48.65, 118.21, 125.91, 127.04, 128.24, 128.83, 136.74, 137.07, 160.69. Anal. Calcd for $C_{12}H_{14}N_4$: C, 67.26; H, 6.59; N, 26.15. Found: C, 67.50; H, 6.65; N, 26.23.

N'-Cyano-N-(2,3-dihydro-1*H*-indan-1-yl)guanidine (10). A mixture of 5.2 g (32 mmol) of *N*-cyano-*O*-phenylisourea and 4.8 g (36 mmol) of 1-aminoindan in a 25-mL flask was immersed in an oil bath preheated to 220 °C and stirred at this temperature for 20 min. The resulting melt was allowed to cool briefly and treated with 5 mL of toluene to prevent it from solidifying. The viscous liquid was then chromatographed on a silica gel column, eluting initially with toluene and then with toluene–ethyl acetate mixtures with gradual increases in the ethyl acetate content. This gave 4.12 g (63% yield) of the desired product: mp 175.5–176 °C (cyclohexane–isopropyl acetate); ^{13}C NMR (DMSO-d_6) δ 29.59, 33.27, 55.86, 118.11, 123.90, 124.61, 126.39, 127.70, 142.86, 143.13, 161.07. Anal. Calcd for $C_{11}H_{12}N_4$: C, 65.98; H, 6.04; N, 27.98. Found: C, 66.80; H, 6.10; N, 27.49.

***N*-*tert*-Butyl-N''-cyano-N'-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (11).** A solution of 5 g (29 mmol) of *N*-*tert*-butyl-*N'*-cyano-*S*-methylisothiourea (Tilley and Ramuz, 1980) and 5 g (34 mmol) of 1,2,3,4-tetrahydro-1-naphthylamine in 100 mL of acetonitrile was heated at reflux for 2 weeks. The solvent was then removed in vacuo, and the residue was taken up in CH_2Cl_2 and washed with 3 N HCl. Drying (Na_2SO_4), filtration, and concentration in vacuo left an oil, which was purified by column chromatography (silica gel), eluting with ethyl acetate. The resulting crude product was crystallized from hexane–diethyl ether to give 6.2 g (78% yield) of white, crystalline solid: mp 123–126 °C; ^{1}H NMR ($CDCl_3$–DMSO-d_6) δ 1.30 (s, 9 H), 1.86 (m, 4 H), 2.74 (m, 3 H), 4.94 (m, 2 H), 7.14 (s, 4 H). Anal. Calcd for $C_{16}H_{22}N_4$: C, 71.07; H, 8.20; N, 20.73. Found: C, 71.10; H, 8.21; N, 20.80.

N'-Cyano-2,2-dimethyl-N-(1,2,3,4-tetrahydro-1-naphthalenyl)hydrazinecarboximidamide (13). A solution of 24.5 g (0.1 mol) of **2** and 30 mL (ca. 0.4 mol) of *N,N*-dimethylhydrazine in 200 mL of ethanol was heated at reflux with stirring for 66 h. The mixture was cooled in an ice bath to give the crude product as a white solid. Recrystallization from isopropyl acetate gave 7.5 g (29% yield) of white crystals: mp 210–212.5 °C; ^{1}H NMR (DMSO-d_6) δ 1.76 (m, 4 H), 2.44 (s, 6 H), 2.65 (m, 2 H), 3.28 (d, 1 H, J = 2 Hz), 4.82 (m, 1 H), 7.03 (m, 5 H). Anal. Calcd for $C_{14}H_{19}N_5$: C, 65.34; H, 7.44; N, 27.22. Found: C, 65.40; H, 7.49; N, 27.01.

N''-Cyano-N-piperidino-N'-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (14). This compound was prepared in 30% yield by the same method used for the preparation of **13**, using a reflux period of 138 h. This gave the pure product as a white, crystalline solid: mp 220–221 °C; ^{1}H NMR (DMSO-d_6) δ 1.56 (m, 10 H), 2.70 (m, 6 H), 3.27 (s, 1 H), 4.84 (m, 1 H), 7.10 (m, 5 H). Anal. Calcd for $C_{17}H_{23}N_5$: C, 68.65; H, 7.80; N, 23.55. Found: C, 68.60; H, 7.77; N, 23.55.

Biological Test Methods. Pre- and postemergence herbicide evaluations were conducted on all target compounds from this series. Technical compound was dissolved in a mixture of 50% acetone/50% aqueous 0.1% Tween-20 surfactant. A serial dilution was performed to achieve a range of test concentrations (generally 4 kg/ha to 0.125). The solution was thoroughly agitated and sprayed directly onto a sandy loam soil surface preseeded with the desired test species for preemergence application, or onto the foliage for postemergent applications. All applications were made with a hand-held syringe modified to discharge the solution through a flat fan nozzle. The volume of application was approximately 400 L/ha.

Test species included in these evaluations were yellow foxtail (*Setaria lutescens*), barnyard grass (*Echinochloa crus-galli*), velvetleaf (*Abutilon theophrasti*), morning glory (*Ipomoea hederaceae*), and cotton (*Gossypium spp.*). Postemergence applications were made when the test species were 2–8 cm in height and generally had one to three true leaves. Following applications, the plants were returned to a glasshouse where they received regular watering and nutrient additions.

Evaluations were conducted 2 weeks after application by visual comparison of treated plants and controls. GR_{50} concentrations, or concentrations of chemical expected to reduce plant growth by 50%, were determined by interpolation of control ratings plotted against the log of the test concentration.

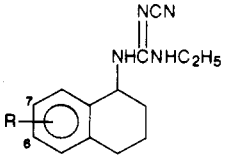
Hill reaction rates were determined by monitoring oxygen evolution with a Clark-type O_2 electrode. The reaction contained 100 mM sorbitol, 50 mM Tricine (pH 8.0), 5 mM $MgCl_2$, 2 mM ferricyanide, and chloroplasts (10 μg of Chl/mL) in a final volume of 1 mL. Oxygen evolution was monitored at 25 °C on a strip chart recorder, and rates were calculated from a linear portion of the recording. Chloroplasts were isolated from spinach by a method similar to that described previously (Gerwick et al., 1977).

RESULTS AND DISCUSSION

Chemical Studies. The (tetrahydronaphthalenyl)-cyanoguanidines **1**, with two exceptions, were prepared by the reaction of an *N'*-cyano-*N*-(tetrahydro-1-naphthalenyl)-*S*-methylisothiourea (**2**) with the appropriate amine in refluxing ethanol or acetonitrile (Scheme I).

The basicity of the reacting amine is important in the displacement of the methyl mercaptide group from **2**. Attempts to displace the mercaptide group with aromatic amines and ammonia failed. Likewise, sterically hindered amines such as *tert*-butylamine failed to react.

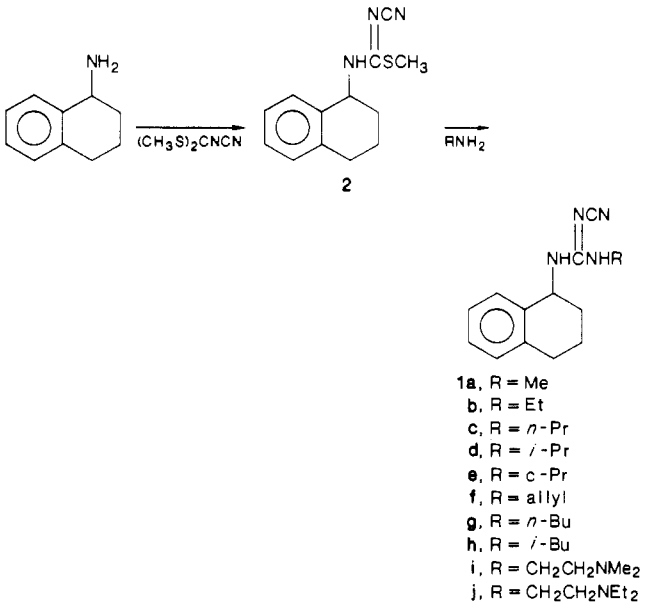
Preparation of ring-substituted cyanoguanidines **3** necessitated synthesis of the corresponding ring-substituted *N'*-cyano-*N*-(substituted 1,2,3,4-tetrahydro-1-naphthalenyl)-*S*-methylisothioureas (Scheme II).



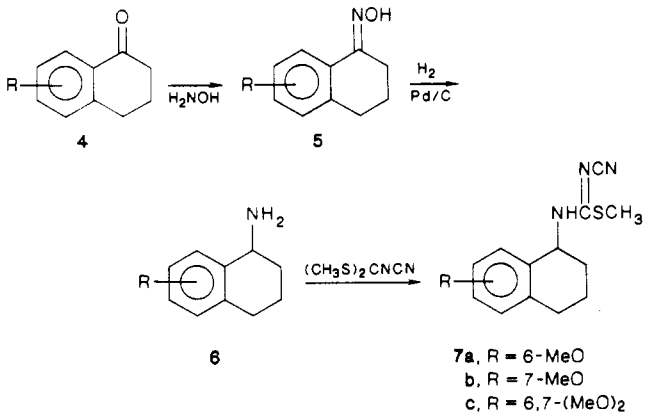
3a, R = 6-MeO
b, R = 7-MeO
c, R = 6,7-(MeO)$_2$

N'-Cyano-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)-guanidine (**8**) was initially prepared by the reaction of 1,2,3,4-tetrahydronaphthylamine hydrochloride and so-

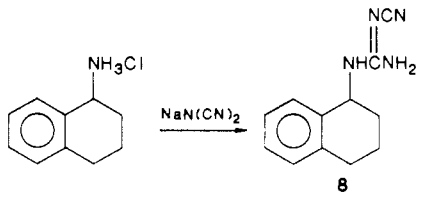
Scheme I



Scheme II

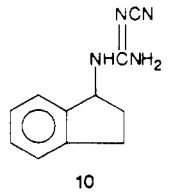


Scheme III



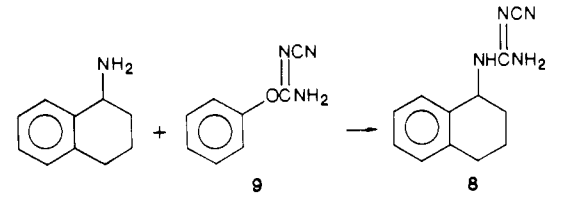
dium dicyanamide in aqueous solution at 95–100 °C in a yield of only 18% (Scheme III). A preferred method for the preparation of **8** involved the reaction of *N*-cyano-*O*-phenylisourea (**9**) (Grigat and Pütter, 1965) with 1,2,3,4-tetrahydro-1-naphthylamine (Scheme IV).

N'-Cyano-*N*-1-indanylguanidine (**10**) was also prepared in like manner.



N-tert-Butyl-*N''*-cyano-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidine (**11**) could not be prepared according to Scheme I but was successfully prepared in 78% yield by the reaction of *N-tert*-butyl-*N'*-cyano-*S*-methyl-

Scheme IV



Scheme V

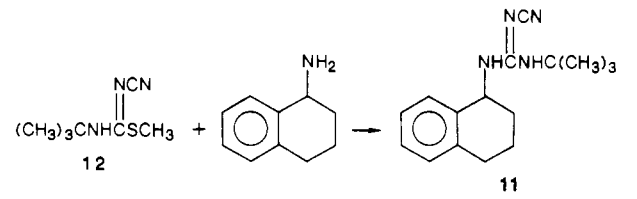
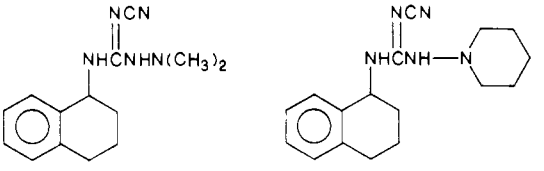


Table I

treatment	Hill reactn rate, μmol O_2 mg Chl h	% inhibn
control	150	
2 μM monuron	30	80
1 μM atrazine	21	86
100 μM **1b**	140	7

isothiourea (**12**) (Tilley and Ramuz, 1980) with 1,2,3,4-tetrahydro-1-naphthylamine in refluxing acetonitrile over a period of 2 weeks (Scheme V).

Two *N''*-cyano-*N*-(dialkylamino)-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)guanidines were prepared according to Scheme I, with in one case *unsym*-dimethylhydrazine to give *N'*-cyano-2,2-dimethyl-*N*-(1,2,3,4-tetrahydro-1-naphthalenyl)hydrazinecarboximidamide (**13**) and in the other case 1-aminopiperidine to give *N''*-cyano-*N*-1-piperidinyl-*N'*-(1,2,3,4-tetrahydro-1-naphthalenyl)-guanidine (**14**).

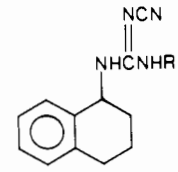


Biological Evaluation. The *N*-(alkylamino)-*N*-cyanoguanidines were found to be effective pre- and postemergent herbicides. These compounds were generally more efficacious when foliarly applied, as in postemergence applications, than in preemergence applications. Furthermore, broadleaf weeds demonstrated greater sensitivity than grass weeds.

The onset of symptoms following foliar application is moderately rapid with chlorosis apparent on treated leaves 1–2 days after application. The chlorosis is followed by severe necrosis, desiccation, and ultimately plant death. This symptomology is similar to that observed with compounds affecting photosynthetic or mitochondrial electron transport. When a representative compound was evaluated for inhibition of the Hill reaction, however, no significant activity was observed (Table I). Under these same assay conditions the well-known photosynthetic inhibitors atrazine and monuron were highly effective (Table I). The inhibition of mitochondrial electron transport was not evaluated in this investigation.

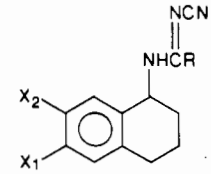
Considerable variation in the length and branching of the aminoalkyl substitution appears to have only a modest effect on activity (Table II). This effect appears to be very species dependent. For example, the *N*-butyl substitution

Table II



		GR_{50} concentration, kg/ha									
		preemergence					postemergence				
compd	R	*Gossi-pium*	*Eschino-chloa*	*Setaria*	*Abutilon*	*Ipomoea*	*Gossi-pium*	*Eschino-chloa*	*Setaria*	*Abutilon*	*Ipomoea*
8	H	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
1a	Me	4.0	>4.0	0.9	0.6	>4.0	0.4	2.0	0.4	0.12	2.0
1b	Et	3.0	1.5	1.4	0.6	1.5	1.0	0.4	1.5	0.1	3.0
1c	*n*-Pr	3.0	2.0	3.0	0.6	1.5	0.5	>2.0	>2.0	0.1	1.0
1f	allyl	3.0	3.0	1.5	9.8	3.5					
1d	*i*-Pr	1.0	1.0	0.7	0.5	>4.0	1.0	>4.0	>4.0	0.5	>4.0
1e	c-Pr	>4.0	0.8	2.0	0.7	5.0	0.5	1.5	3.0	0.2	3.0
1g	*n*-Bu	1.5	1.5	1.5	0.25	3.0	0.12	0.4	0.5	0.06	1.0
1l	*t*-Bu	>4.0	1.5	1.5	0.4	>4.0	>4.0	3.0	1.0	0.06	>4.0
1h	*i*-Bu	>4.0	3.0	3.0	0.7	>4.0	0.2	>2.0	>2.0	0.12	1.0
1i	$Me_2NCH_2CH_2$	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
1j	$Et_2NCH_2CH_2$	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
13	Me_2N	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
14	1-piperidinyl	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0

Table III



				GR_{50} concentration, kg/ha									
				preemergence					postemergence				
compd	R	X_1	X_2	*Gossi-pium*	*Eschino-chloa*	*Setaria*	*Abutilon*	*Ipomoea*	*Gossi-pium*	*Eschino-chloa*	*Setaria*	*Abutilon*	*Ipomoea*
7b	SMe	H	OMe	2.0	0.7	0.3	0.7	0.13	0.05	0.3	0.5	0.03	0.07
7a	SMe	OMe	H	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
2	SMe	H	H	3.0	2.5	2.0	1.3	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
7c	SMe	OMe	OMe	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
3b	NHEt	H	OMe	4.0	0.7	0.7	0.2	2.0	0.6	0.3	0.3	0.03	0.5
3a	NHEt	OMe	H	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0
1b	NHEt	H	H	3.0	1.5	1.4	0.6	1.5	1.0	0.4	1.5	0.1	3.0
3c	NHEt	OMe	OMe	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0	>4.0

resulted in the greatest levels of activity on *Abutilon* while the greatest activity on *Setaria* was displayed by the *N*-methyl derivatives. The apparent flexibility in *N*-alkyl substitution could provide an important handle for fine-tuning subtle changes in spectrum with these series. Cotton, the crop included in these comparative evaluations, was sensitive to all the *N*-alkyl-substituted compounds.

While a number of *N*-alkyl substitutions appear feasible within this series and results only in modest fluctuations in activity, the larger *N*-alkylamino substitutions have either very low activity or are completely inactive (Table II).

The methylcyanoisothioureas were generally similar in levels of activity to the corresponding cyanoguanidines (Table III). Activity levels in both series are quite dependent on position of substitution of the aromatic ring. Introduction of a methoxyl group in the 7-position results in a significant activity enhancement relative to the corresponding unsubstituted compounds (Table III). Quite surprisingly, introduction of a methoxyl group in the 6-position completely eliminates activity, even if an additional methoxyl group is present in the 7-position. Compound **3b** demonstrates selectivity to cotton in pre- and postemergence applications (Table III). This compound is quite effective on several important weed species in cotton including *Abutilon*.

Registry No. **1a**, 111448-77-2; **1b**, 111448-75-0; **1c**, 111758-76-0; **1d**, 111448-76-1; **1e**, 111758-80-6; **1f**, 111484-42-5; **1g**, 111758-77-1; **1h**, 111758-78-2; **1i**, 119999-65-4; **1j**, 119999-66-5; **2**, 111448-74-9; **3a**, 119999-68-7; **3b**, 111758-81-7; **3c**, 119999-71-2; **5b**, 20175-97-7; **5c**, 52401-41-9; **6b**, 111758-82-8; **6c**, 119999-69-8; **7a**, 119999-67-6; **7b**, 111758-75-9; **7c**, 119999-70-1; **8**, 110685-23-9; **10**, 119999-72-3; **11**, 111758-79-3; **13**, 120057-54-7; **14**, 119999-73-4; dimethyl cyanodithioiminocarbonate, 22122-48-1; 1,2,3,4-tetrahydro-1-naphthylamine, 2217-40-5; ethylamine, 75-04-7; *n*-propylamine, 107-10-8; isopropylamine, 75-31-0; cyclopropylamine, 765-30-0; allylamine, 107-11-9; *n*-butylamine, 109-73-9; *N,N*-dimethylethylenediamine, 108-00-9; *N,N*-diethylethylenediamine, 100-36-7; 6-methoxy-1,2,3,4-tetrahydro-1-naphthylamine, 52373-02-1; 7-methoxy-1-tetralone, 6836-19-7; hydroxylamine hydrochloride, 5470-11-1; 6,7-dimethoxy-1-tetralone, 13575-75-2; 1,2,3,4-tetrahydro-1-naphthylamine, 3459-02-7; *N*-cyano-*O*-phenylisourea, 3277-47-2; 1-aminoindan, 34698-41-4; *N*-*tert*-butyl-*N'*-cyano-*S*-methylisothiourea, 60573-21-9; *N,N*-dimethylhydrazine, 57-14-7.

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Effect of pH on the Volatiles of Hydrolyzed Protein Insect Baits

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Four volatile concentrates were prepared from acidic corn protein hydrolysate and from basified hydrolysate, under atmospheric and vacuum conditions. Examination by capillary gas chromatography/mass spectrometry revealed that both the atmospheric and vacuum concentrates prepared from acidic hydrolysate were qualitatively very similar, with phenylacetaldehyde and several other aromatic oxygenated compounds predominating. In contrast, nitrogenous compounds were the major components of the two basic concentrates. These were primarily alkyl-substituted pyrazines in the atmospheric concentrate, but in the vacuum concentrate a group of 3-methylbutylamine-derived imines predominated. Some attraction was shown for all four concentrates in field bioassays with *Dacus dorsalis*, *Ceratitis capitata*, and *Dacus cucurbitae*, but with one exception (basified atmospheric concentrate vs *D. dorsalis*), none were as attractive as basified protein hydrolysate itself. No attractancy could be demonstrated for the four major imines.

Hydrolyzed protein products from various protein sources have been used as baits for certain insects (Steiner, 1952; Hagen et al., 1976; van Emden and Hagen, 1976; Miller and Haarer, 1981). Such insects, which include the green lace wing (*Chrysopa carnea*), the onion fly (*Hylemya antigua* Meigen), the seedcorn fly (*Hylemya platura* Meigen), and several fruit flies, including the Mediterranean fruit fly (*Ceratitis capitata* Wiedemann), the oriental fruit fly (*Dacus dorsalis* Hendel), and several *Anastrepha* species, are thought to be attracted to these baits by the volatile compounds associated with the baits. Hagen et al. (1976) have proposed that these protein preparations are related in composition to the "honeydew" produced by aphids, which in nature can apparently supply a suitable diet for both the adult and larval stages of certain insects.

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The usefulness of hydrolysate baits prepared from corn gluten protein in large-scale programs to combat insect pests has been demonstrated in several Mediterranean fruit fly eradication projects. Suppression efforts in the 1980–1982 California Mediterranean fruit fly infestation included both aerial and ground spraying of commercial hydrolyzed corn protein bait Staley Protein Bait No. 7 (PIB-7) combined with malathion (Jackson and Lee, 1985).

Several papers reporting the identities of volatile compounds associated with PIB-7 have recently appeared. Morton and Bateman (1981) in Australia have identified 39 compounds in two different hydrolyzed protein preparations, a yeast hydrolysate (NBS) and PIB-7. Buttery et al. (1983) in this laboratory have reported the identities of some additional components. A second paper from this laboratory (Matsumoto et al., 1985) presented some preliminary results from the present study. Reports on the identification of volatiles from other hydrolyzed protein sources include those by Manley and Fagerson (1970a,b), Markh and Vinnikova (1973), and Withycombe et al. (1978). Bateman and Morton (1981) have also reported that raising the pH of their standard yeast protein hydrolysate mixture (NBS) significantly increased the attractiveness of their bait for the Queensland fruit fly