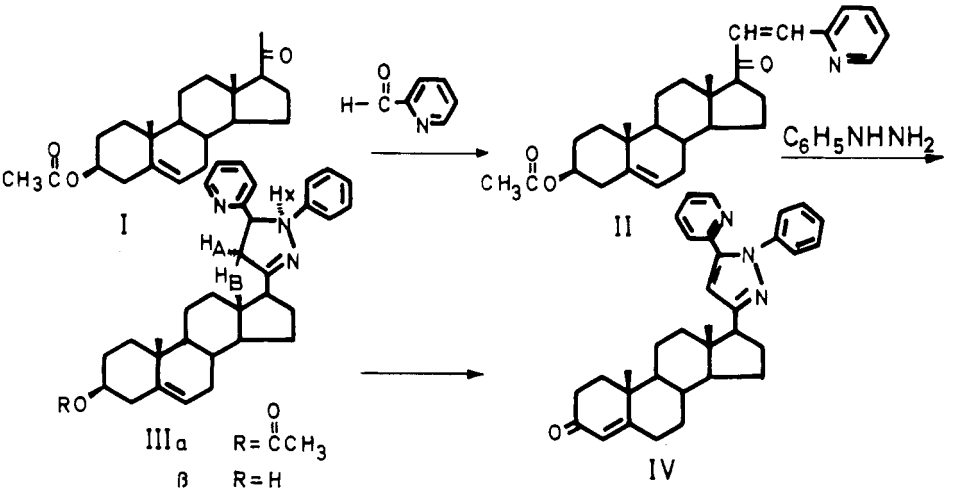
Scheme I



for 24 h. Then water was added and extracted several times with chloroform. After evaporation of the solvent the residue was acetylated with pyridine–acetic anhydride; yield 7.5 g; mp 132–134 °C (acetone–water); IR V_{max} 1730 cm^{-1}; 1240 cm^{-1} (CH_3CO); 1610 cm^{-1} (C=C).

3β-Acetoxy-5-pregneno[20,21-c]-1′-phenyl-5′-(2-pyridinyl)pyrazoline (III). To a solution of II (4.7 g) in ethanol (100 mL) containing hydrochloric acid (3 mL), phenylhydrazine (1.2 g) is added. The resultant solution is refluxed for 24 h. Then water was added and neutralized with ammonium hydroxide. The precipitate was collected by filtration, dried, and acetylated with pyridine–acetic anhydride at room temperature. Then the usual work up and column chromatography from silica gel (eluent chloroform) gave 4.0 g of III. Recrystallization from methanol gives mp 115–117 °C; IR V_{max} 1730 cm^{-1}; 1250 cm^{-1} (CH_3CO).

3-Oxo-4-pregneno[20,21-c]-1′-phenyl-5′-(2-pyridinyl)-pyrazole (IV). Pyrazoline (III) (1.5 g) was dissolved in 200 mL of methanol containing 2 g of sodium hydroxide. The mixture was refluxed for 1.5 h. The reaction mixture was poured into water and the precipitate, collected by filtration, was washed several times with water and dried to yield IIIβ (1.3 g).

To a solution of IIIβ (0.5 g) in 7 mL of cyclohexanone, 20 mL of dry dioxane and 20 mL of dry toluene was distilled slowly as a solution of aluminum isopropylate (0.8 g) in dry toluene (6 mL) was added. Distillation was continued for 2 h as 15 mL of toluene was added and 30 mL of distillate was collected. Then the mixture was refluxed for 4 h and left to stand at room temperature overnight. The mixture was filtered to remove the precipitate containing the aluminum. The filtrate was distilled, extracted with chloroform, and evaporated. The volatile constituents were removed by steam distillation. The residue was extracted with chloroform and evaporated. Column chromatography from silica gel (eluent chloroform:methanol, 98:2) gave pyrazole IV (1.15 g), which was recrystallized from chloroform–methanol; mp 249–251 °C; IR V_{max} 1670 cm^{-1}; 1615 cm^{-1} (C=C).

Registry No. I, 1778-02-5; (*E*)-II, 110027-50-4; (*Z*)-II, 110027-56-0; (*E*)-II·AcOH, 110027-51-5; (*Z*)-II·AcOH, 110027-57-1; IIIa, 110027-52-6; IIIa·AcOH, 110027-53-7; IIIb, 110027-54-8; IV, 110027-55-9; pyridine-2-carboxaldehyde, 1121-60-4.

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2-Pyrazinyl-2-arylalkanenitriles

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A series of new 2-alkyl-2-(3,4-dialkylphenyl)-2-pyrazineacetonitriles (3) was prepared from readily available starting materials by a simple, efficient, two-step sequence. The products are potential herbicides.

Compounds of the type **2** and **3** have been reported in the patent literature (*1*, *2*) to possess sedative and anticonvulsive activity. Pyrazineacetonitriles (**3**) (Scheme I) were prepared in our lab for testing as herbicides.

2-Substituted acetonitriles were reacted at room temperature with 2-chloropyrazine under basic conditions (NaOH) in dimethyl sulfoxide (DMSO) (*3*, *4*) to afford **2** in high yields. Syntheses of these compounds previously reported (*1*) used drastic conditions ($NaNH_2$/toluene, reflux or liquor ammonia/dioxane) and the yields were lower (27–80%) than ours (70–90%). Compounds **2** with base (see Table I) and the appropriate alkyl halide gave **3** in fair to very good yields, usually by simple workup. Thus, quenching of the reaction mixture with water

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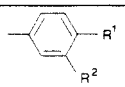
Table I. Physical Properties and NMR Data of Compounds 3

compd	yield, %	mp, °C, or bp, °C/mmHg	recryst solvent	^{1}H NMR chem shifts[a] for R^3 group[b]
3a	82[c]	155–157/0.6		2.6 (m, 2 H), 1.4 (m, 4 H), 0.8 (m, 3 H)
3b	72[c]	77–78	MeOH[n]	4.1 (CH_2–S, dd, 2H, J = 15 Hz)
3c	78[c]	94–96	MeOH	7.0 (ap. s, 4 H), 3.8 (dd, 2 H, CH_2), 2.2 (s, CH_3)
3d	52[c]	178–179	DMF/H_2O	8.2 (d, 2 H),[r] 7.2 (d, 2 H),[r] 4.1 (ap. s, 2 H, CH_2) (in DMSO-d_6)
3e	49[c]	192–193	DMF/H_2O	6.7 (d, enolic H, J = 1.5 Hz)
3f	80[d]	87–89	MeOH/hexane	2.8 (m, 4 H)
3g	62[e]	76–79	*f*, *g*	3.7 (dd, 2 H, J = 17 Hz)
3h	24[h]	oil	*f*, *m*	5.7 (dd, 2 H, J = 15 Hz)
3i	63[i]	97–99	MeOH[f]	4.1 (dd, 2 H, J = 14 Hz)
3j	34[j]	91–93	MeOH/CH_2Cl_2	2.7 (m, 4 H)
3k	70[i]	95–97	MeOH	6.9 (AA'BB', 4 H, J = 4 Hz), 3.8 (dd, 2 H, J = 14 Hz), 3.8 (s, 3 H)
3l	77[c]	108–109	MeOH	3.8 (dd, 2 H, J = 14 Hz)
3m	66[c]	138–139	MeOH	3.8 (dd, 2 H, J = 14 Hz), 2.3 (s, 6 H)
3n	69[c]	113–115	MeOH	3.8 (dd, 2 H, J = 13 Hz)
3o	69[c]	86–87	MeOH	4.0–3.4 (m, 3 H), 2.3 (s, 3 H)
3p	61[k]	89–91	MeOH	2.2 (s, 3 H)
3q	76[k]	~130/0.1	oil	6.5–5.2 (m, CH=CH_2), 3.4 (t, CH_2)
3r	79	111–113	MeOH	3.7 (2 H, CH_2–CO_2Et), 4.2 (q, CH_2CH_3), 1.2 (t, CH_2CH_3)
3s	74[c]	205–207/0.4	oil	3.8 (CH_2–Ph, covered by adjacent peaks)
3t	77	172–174	MeOH	9.9 (br s, 1 H), 3.9 (q, J = 16 Hz)
3u	61	*l*		10.9 (br s, 1 H), 3.3–2.3 (m, 4 H)

[a] The spectra were recorded on a Varian EM 360 L (60 MHz) instrument, for solutions in deuteriochloroform (tetramethylsilane as the internal standard) unless otherwise stated. [b] Peaks due to aromatic protons are not included, since they always come together with all other aromatic peaks, making assignment impossible. In all cases, however, integration showed the expected number of aromatic protons. [c] Conditions: 50% aqueous NaOH (5 mL), DMSO (10 mL), **2** (20 mmol), at 60–70 °C for 3–4 h. [d] Conditions: *t*-BuOH (4 mL), 30% NaOH (1 drop) in *t*-BuOH, **2** (2 mmol), at 60 °C for 6 h. [e] In anhydrous DMSO (4 mL) and powdered NaOH (see ref *3*). [f] Purified by column chromatography on silica gel. [g] The obtained oil crystallized upon standing. [h] In NaH (60% oil dispersion, 6-fold excess)/toluene, reflux. Incomplete reaction after 2 days. [i] In NaH (60% oil dispersion)/DMF, overnight stirring (see ref *5*). [j] In excess Na/absolute EtOH, reflux, 3 days. [k] Conditions: 50% aqueous NaOH (4 mL), DMSO (20 mL), **2** (20 mmol), at 60–70 °C for 4–5 h. [l] The solid was extremely hydroscopic and was characterized only by its NMR spectra (see Tables I and II). [m] The necessary alkyl halide, chloromethyl-1-benzotriazole, was prepared as described in ref *6*. [n] For the preparation of the necessary alkyl halide, see ref *7*. [o] Product was first distilled (bp 180–185 °C/0.4 mmHg) and then it crystallized on standing. [p] Conditions: **2d** (50 mmol) in DMSO (150 mL)/50% aqueous NaOH (2 mL). [q] The product was obtained on hydrolysis (NaOH) of **3r** in water (20 min). [r] J = 8 Hz. [s] s, 3 H.

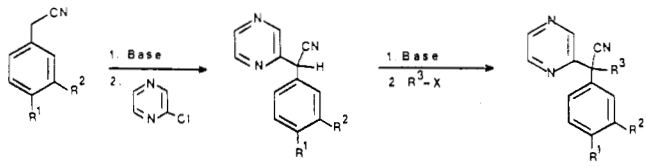
Table II. ^{13}C NMR Chemical Shifts for Compounds 3[a]

compd	pyrazinyl group		R^1	R^2	)C(	CN	R^3
3b	152.2, 143.8, 143.1	136.6, 128.8, 127.0, 126.3			53.8	119.6	134.8, 131.4, 128.6, 128.5, 44.2
3c	153.8, 144.2, 143.7, 143.3	136.8, 128.7, 128.2, 126.9			53.7	120.2	137.8, 131.4, 130.2, 44.2 (CH_2), 20.8 (CH_3)
3d[b]	144.7, 144.3, 143.2[b]	137.4, 129.4, 128.8, 126.9			53.7	*b*	147.0, 131.8, 123.2[b]
3f	151.9, 144.1, 143.8, 143.3	135.8, 129.1, 128.7, 125.8			50.9	119.0[c]	117.6 (–CN),[c] 33.9, 13.6
3g	150.9, 144.8, 144.4, 143.3	135.2, 129.6, 128.9, 126.1			49.2	118.4	115.5 (–CN), 28.6
3h	151.5, 144.6, 143.2	134.9, 129.2, 127.4, 126.7			52.6	118.9	145.4, 133.5, 127.4, 123.8, 119.8, 109.4, 54.4
3i	153.7, 143.9, 143.5, 143.2	137.7, 128.8, 128.2, 126.6			52.1	120.2	155.0, 149.0, 135.9, 124.2, 121.9, 46.0
3j	153.6, 143.6, 143.4	140.0[d]			52.1	120.3	40.4,[c] 31.7
3k	153.6, 144.1, 143.7, 143.3	137.6, 128.7, 128.2, 126.8			53.8	120.2	158.7, 131.3, 126.4, 113.4, 54.9, 43.7
3l	153.9, 144.1, 143.6, 143.2	138.0, 134.7, 130.3, 127.9	20.7		53.3	120.2	134.8, 129.4, 127.1, 126.7, 44.5 (CH_2)
3m	154.0, 144.1, 143.5, 143.2	138.0, 134.9, 130.2, 128.7	20.7		53.4	120.3	136.7, 131.6, 129.4, 126.8, 44.2 (CH_2), 20.7
3o	154.2, 144.3, 143.6, 143.3	159.6, 130.0, 128.8, 114.3	55.3		53.2	120.5	136.9, 131.7, 130.0., 128.2, 44.5, 20.9
3p	155.0, 143.4, 143.2, 142.9	149.2, 148.9, 131.0, 118.4, 111.1, 109.5	55.8	55.7	46.6	121.8	26.4
3q	153.7, 144.5, 143.6, 143.4	149.1, 148.8, 129.5, 118.3, 111.1, 109.7	55.8	55.7	51.7	119.8	131.25, 120.6, 42.8
3r	153.3, 144.0, 143.7, 143.0	149.3, 149.1, 129.3, 118.6, 111.3, 109.4	55.9	55.8	48.0	120.3	168.4 (–CO_2–), 61.0, 43.0 (–CH_2), 13.8
3u	153.8, 143.8, 143.5, 143.4	149.4, 149.2, 128.9, 118.9, 111.4, 109.5	55.8	55.8	51.1	120.1	176.7 (–CO_2H), 38.4, 30.2

[a] The spectra were recorded on a JEOL FX-100 (25 MHz, FT mode) spectrometer. Deuteriochloroform (δ = 77.0) was the solvent, unless otherwise stated. The chemical shifts were expressed in parts per million (ppm) relative to the deuterium signal of the solvent. [b] The solubility of this compound in DMSO-d_6 (δ = 39.5) is very low; therefore some of the peaks are missing in the noise. [c] Assignments can be reversed. [d] Signals at 128.9, 128.1, 126.2, and 126.0 correspond to both aromatic nuclei; some peaks overlap.

most often precipitated the product; otherwise extraction with chloroform was used. Column chromatography was necessary in only the cases of **3g**, **3h**, and **3l**. The products were characterized by ^{1}H (60 MHz) and ^{13}C (25 MHz) NMR spectroscopy. Satisfactory elemental analyses and/or high-resolution mass spectra were obtained for all compounds, except for **3u**, which, due to its extreme hydroscopicity, was characterized only by its ^{1}H and ^{13}C NMR spectra. The proton NMR spectra of all compounds showed a doublet (δ ~9.0, 1 H, J = 1 Hz), and a multiplet (δ ~8.8, 2 H) due to the pyrazinyl group, and also a multiplet (δ ~7.0–8.0) due to the protons of the aromatic nucleus bearing R^1 and R^2. These latter signals frequently over-

Scheme I



1 2 3

1a, $R^1 = R^2 = H$ **2a**, $R^1 = R^2 = H$
1b, $R^1 = CH_3$, $R^2 = H$ **2b**, $R^1 = CH_3$, $R^2 = H$
1c, $R^1 = OCH_3$, $R^2 = H$ **2c**, $R^1 = OCH_3$, $R^2 = H$
1d, $R^1 = R^2 = OCH_3$ **2d**, $R^1 = R^2 = OCH_3$

3a, $R^1 = R^2 = H$, $R^3 = (CH_2)_3CH_3$
3b, $R^1 = R^2 = H$, $R^3 = CH_2-S-Ph$
3c, $R^1 = R^2 = H$, $R^3 = CH_2-C_6H_4-(4-CH_3)$
3d, $R^1 = R^2 = H$, $R^3 = CH_2-C_6H_4-(4-NO_2)$
3e, $R^1 = R^2 = H$, $R^3 = CH_2COPh$
3f, $R^1 = R^2 = H$, $R^3 = (CH_2)_2-CN$
3g, $R^1 = R^2 = H$, $R^3 = CH_2CN$
3h, $R^1 = R^2 = H$, $R^3 = CH_2$-benzotriazol-1-yl
3i, $R^1 = R^2 = H$, $R^3 = CH_2$-2-pyridinyl
3j, $R^1 = R^2 = H$, $R^3 = (CH_2)_2Ph$
3k, $R^1 = R^2$, H, $R^3 = CH_2-C_6H_4-(4-OMe)$
3l, $R^1 = CH_3$, $R^2 = H$, $R^3 = CH_2Ph$
3m, $R^1 = CH_3$, $R^2 = H$, $R^3 = CH_2-C_6H_4-(4-CH_3)$
3n, $R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_2Ph$
3o, $R^1 = OCH_3$, $R^2 = H$, $R^3 = CH_2-C_6H_4-(4-CH_3)$
3p, $R^1 = R^2 = OCH_3$, $R^3 = CH_3$
3q, $R^1 = R^2 = OCH_3$, $R^3 = CH_2-CH=CH_2$
3r, $R^1 = R^2 = OCH_3$, $R^3 = CH_2CO_2Et$
3s, $R^1 = R^2 = OCH_3$, $R^3 = CH_2Ph$
3t, $R^1 = R^2 = OCH_3$, $R^3 = CH_2CO_2H$
3u, $R^1 = R^2 = OCH_3$, $R^3 = CH_2CH_2CO_2H$

lapped with peaks due to aromatic protons of R^3 (Table I). In all cases where $R^1 = CH_3$, the protons appeared at $\delta \sim 2.2$, whereas the methoxy protons, for R^1 or R^2 = OMe, resonated at 4.0 ppm.

Registry No. **2a**, 1080-87-1; **2b**, 1082-48-0; **2c**, 1084-83-9; **2d**, 1088-67-1; **3a**, 109929-53-5; **3b**, 109929-54-6; **3c**, 109929-55-7; **3d**, 109929-56-8; **3e**, 109929-57-9; **3f**, 4422-44-0; **3g**, 4190-80-1; **3h**, 109929-58-0; **3l**, 109929-59-1; **3j**, 109929-60-4; **3k**, 109929-61-5; **3l**, 109929-62-6; **3m**, 109929-63-7; **3n**, 109929-64-8; **3o**, 109929-65-9; **3p**, 109929-66-0; **3q**, 109929-67-1; **3r**, 109929-68-2; **3s**, 109929-69-3; **3t**, 109929-70-6; **3u**, 109929-71-7; $Me(CH_2)_3Br$, 109-65-9; $Br(CH_2)SPh$, 35572-08-8; $4\text{-}MeC_6H_4CH_2Br$, 104-81-4; $4\text{-}NO_2C_6H_4CH_2Br$, 100-11-8; $BrCH_2COPh$, 70-11-1; $Br(CH_2)_2CN$, 2417-90-5; $BrCH_2CN$, 590-17-0; $Br(CH_2)_2Ph$, 103-63-9; $4\text{-}MeOC_6H_4CH_2Br$, 2746-25-0; $PhCH_2Br$, 100-39-0; MeBr, 74-83-9; $CH_2=CHCH_2Br$, 106-95-6; $MeCO_2Et$, 105-36-2; $Br(CH_2)_2CO_2H$, 590-92-1; 1-(chloromethyl)benzotriazole, 54187-96-1; 2-(bromomethyl)pyridine, 55401-97-3.

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Heterocycles. 14. Synthesis of 5*H*-Indenopyrimidines

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1-Indanone (I) was reacted with aryl aldehydes (II) to give the corresponding 2-arylidene-1-indanones (III). Condensation of the chalcones III with guanidine revealed the formation of the corresponding 5*H*-2-amino-4-arylidenopyrimidines (V). The structures of all products were substantiated by chemical and spectroscopic methods.

Various aromatic and heterocyclic aldehydes (IIa-k) were reacted with 1-indenone to give the corresponding 2-arylidene-1-indenones (IIIa-k) (Scheme I). The structures of these products were evident from the infrared (*1*, *2*), electronic (*3*, *4-7*), NMR spectra (*8*), and chemical analyses (Tables I and II). The infrared spectra of IIIa show absorption bands at 1625 and 1695 cm^{-1} attributed to $\nu_{C=C}$ and C=O, respectively. The chalcones (III a-k) were condensed with guanidine to yield the corresponding 5*H*-2-amino-4-arylindenopyrimidines (Va-k) (*3*, *9*, *10*) (Scheme I). The structures of these products were substantiated by spectroscopy (*3*, *8*) (Tables I and II). The IR spectrum of Va shows absorptions at 1600 cm^{-1} (C=C), 1640 cm^{-1} (C=N), and 3140, 3280, and 3460 cm^{-1} (NH_2).

Chemical evidence can be also adduced in favor of the structure of compounds V. Thus acetylation of Vf,h leads to the formation of the corresponding acetylamido derivatives (VIf,h) (Scheme I) (*3*, *9*). Their structures were established from their infrared (*11*), electronic (*12*), and mass spectra (Table I). The IR spectrum of VIf shows absorptions at 1720 cm^{-1} (C=O) and 3400 cm^{-1} (NH).

Treatment of the 2-aminopyrimidines (Vf,h,j) with nitrous acid revealed the formation of the corresponding 2(1*H*)-pyrimidinones (VIIf,h,j) (Scheme I). The lactam form of these products was inferred from their infrared (*9*), electronic and mass spectra (Table I). The IR spectrum of VIIf revealed absorptions at 1640 cm^{-1} (C=O) and 2990 and 3080 cm^{-1} (NH).

Experimental Section

Melting points were measured using a Bock-Monoscope (thermal microscope) and are uncorrected. Electronic and infrared spectra were run on Cary 17 and Perkin-Elmer 580B, respectively. The ^1H NMR and the mass spectra were measured with Varian T60A and Varian MAT 311A, respectively. Microanalyses were determined by A. Bernhardt Microanalytical Laboratory, GFR.

0021-9568/87/1732-0481$01.50/0