Perkin-Elmer 137 IR spectrophotometer. NMR spectra were obtained with a Jeol C-60H spectrometer at 60 MHz (Ib, IIb, and V) and a Perkin-Elmer spectrometer at 90 MHz (III) (Me_4Si as internal reference). Mass spectra were recorded on a Jeol JMS-10SG-2 mass spectrometer. Elemental analyses were carried out by the Kurt Eder service (Genève, Suisse) and satisfactory microanalysis results (C, H, and N) were obtained for all products.

***trans*-1,3-Bis(4,5-dimethoxy-2-nitrophenyl)-5,6-dimethoxyindane (Ib).** To a suspension of 1,3-bis(3,4-dimethoxyphenyl)-5,6-dimethoxyindane (Ia) (5 g, 0.011 mol) in acetic anhydride (100 mL) was added dropwise nitric acid (65%) (2.5 mL), while the mixture was stirred vigorously for 15 min, at 0 °C. The reaction mixture was quenched with crushed ice and the precipitate collected; it was washed with water and dried to give a yellow solid, Ib, 2 g (33.3 %). An analytical sample was recrystallized from ethanol to yield yellow crystals: mp 192 °C; NMR ($CDCl_3$) δ 2.77 (t, J = 7.5 Hz, 2 H, C_2–H), 3.80, 3.85, and 4.00 (3s, 18 H, 6 OCH_3), 5.27 (t, J = 7.5 Hz, 2 H, $C_{1,3}$–H), 6.52, 6.65, and 7.60 (3s, 6 H, aromatic H). This compound had molecular weight by mass spectroscopy m/e 540.

(4,5-Dimethoxy-1,2-phenylene)bis[(2-nitro-4,5-dimethoxyphenyl)methanone] (IIb) and 1,4-bis(4,5-dimethoxy-2-nitrophenyl)-7-hydroxy-6-methoxy-3*H*-2-benzopyran-3-one (III). To a solution of 1,3-bis(4,5-dimethoxy-2-nitrophenyl)-5,6-dimethoxyindane (Ib) (2 g, 0.0037 mol) in acetic acid (10 mL) was added dropwise an aqueous acetic acid solution of $Na_2Cr_2O_7$ (1 g-atom of oxygen/L) (80 mL). The mixture was refluxed for 1 h and then allowed to stand for 2 h at room temperature. Addition of water to the solution gave a precipitate which was filtered, washed until neutral, dried, and chromatographically separated into two products over a column of silica gel (200 g) with 15% of water by using a solvent system consisting of 7 parts ethyl acetate to 3 parts petroleum ether as eluent. The first product was IIb, sparingly soluble in ethanol (0.55 g, 26.7% yield): mp 194–195 °C (recrystallized from acetic acid); IR 1653 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.90 and 4.00 (2s, 18 H, 6 OCH_3), 7.00, 7.02, and 7.42 (3s, 6 H, aromatic H). Compound IIb had molecular weight by mass spectroscopy m/e 556. To the second product (orange solid, sensible to light) is assigned structure III; it is more soluble in ethanol than IIb (0.15 g, 7.3% yield): mp 239–240 °C (recrystallized from ethanol); IR 3440 (OH), 1720 (C=O) cm^{-1}; NMR (pyridine-d_5) δ 3.70, 3.72, 3.76, 3.80, and 3.85 (5s, 15 H, 5 OCH_3), 4.65 (br s, 1 H, exchangeable with deuterium oxide, OH), 6.75, 7.00, 7.18, 7.60, 7.80, and 8.40 (6s, 6 H, aromatic H). The mass spectrum was in agreement with the structure of 1,4-diphenyl-3*H*-2-benzopyran-3-one derivative.

1,4-Bis(2-nitro-4,5-dimethoxyphenyl)-6,7-dimethoxyphthalazine (V). To a suspension of (4,5-dimethoxy-1,2-phenylene)bis[(2-nitro-4,5-dimethoxyphenyl)methanone] (IIb) (0.5 g, 0.000 89 mol) in ethanol (300 mL) was added hydrazine hydrate (85%) (1 mL). The mixture was refluxed for 10 h. After the mixture was cooled, the resulting solid material was filtered, washed, dried, and then recrystallized repeatedly from ethanol yielding 0.32 g (64.4%) of V as yellow crystals: mp 169–170 °C; NMR ($CDCl_3$) δ 3.86, 4.05, and 4.10 (3s, 18 H, 6 OCH_3), 6.77, 7.15, and 7.87 (3s, 6 H, aromatic H). This compound had molecular weight by mass spectroscopy m/e 552.

Registry No. Ia, 90047-39-5; Ib, 90047-40-8; IIb, 90047-41-9; III, 90047-42-0; V, 90047-43-1.

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Syntheses of 1,3-Disubstituted 4-Arylidenepyrazolin-5-ones and the Keto and Enol Forms of 4,4′-Arylidenebis(1,3-disubstituted pyrazolin-5-ones)

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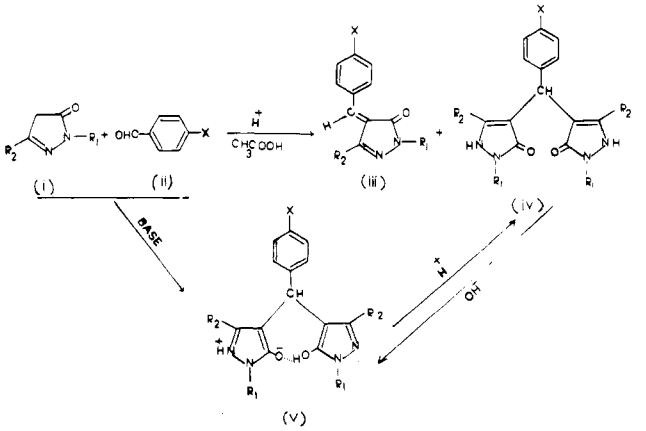
A number of 1,3-disubstituted 4-arylidenepyrazolin-5-ones and keto and enol forms of 4,4′-arylidenebis(1,3-disubstituted pyrazolin-5-ones) have been synthesized as possible antifungal agents by condensing 1,3-disubstituted pyrazolin-5-ones with aromatic aldehydes in acidic and basic media. The compounds were characterized by UV, IR, NMR, and elemental analysis.

The syntheses and therapeutical studies of pyrazolones and their derivatives were undertaken by several groups of workers (*1–5*). We wish to report some important compounds of this class (Scheme I).

Scheme I



Experimental Section

Melting points are uncorrected. All the elemental analyses were carried out on Coleman C, H, and N analyzers; the analytical values for C, H, and N were within ±0.4% of the calculated values. The IR spectra were recorded on Perkin-Elmer (Models 257 and 720) spectrometers in Nujol. Qualitative UV spectra were recorded on a Beckman spectrometer in methanol. The NMR spectra were recorded on a Varian-A-60D spectrometer in $CDCl_3$ and the chemical shifts are reported in

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Table I. 1,3-Disubstituted 4-Arylidenepyrazolin-5-ones (III) and the Keto (IV) and Enol (V) Forms of 4,4′-Arylidenebis(1,3-disubstituted pyrazolin-5-ones)

		III			IV		V	
R_1	R_2	X	mp, °C	yield, %	mp, °C	yield, %	mp, °C	yield, %
CH_2Ph	Me	OMe	157	20	193–195	30	175–177	20
CH_2Ph	Me	NO_2	170–172	12	225–226	55	185–187	35
CH_2Ph	Me	H	36–37	15	188	60	179–180	15
CH_2Ph	Me	NMe_2	178–80	80				
2-benzothiazolyl	Me	OMe	187–188	69				
2-benzothiazolyl	Me	NO_2	198–200	58				
2-benzothiazolyl	Me	H	210–212	65				
2-benzothiazolyl	Me	NMe_2	270–272	83				

ppm. Me_4Si was used as an internal standard. The notations employed in IR and NMR observations have their usual meanings.

1,3-Disubstituted Pyrazolin-5-ones. 1-Benzyl-3-methylpyrazolin-5-one was prepared by the method of Buck and Jenkins (*6*) and 1-(2-benzothiazolyl)-3-methylpyrazolin-5-one was prepared by the method of Efros and Devidenkov (*7*).

4-(p-Methoxybenzylidene)-1-benzyl-3-methylpyrazolin-5-one (III) and 4,4′-(p-Methoxybenzylidene)bis(1-benzyl-3-methylpyrazolin-5-one) (IV). A mixture of 1.88 g (0.01 mol) of 1-benzyl-3-methylpyrazolin-5-one and 1.63 g (0.12 mol) of *p*-methoxybenzaldehyde was dissolved in 10–15 mL of glacial acetic acid in a flask. The reaction mixture was heated for 15 min and left overnight at room temperature. A small amount of water was added until turbidity appeared; the mixture was allowed to stand, and the orange crystals of 4-(*p*-methoxybenzylidene)-1-benzyl-3-methylpyrazolin-5-one (III) separated and were filtered, dried, and recrystallized from benzene: yield 0.62 g (20%); mp 157 °C; UV λ_{max} 214 nm; IR 1675 (s, C=O), 1605 (s, C=N), 1560 (m), 1520 (w), 1330 (w), 1280 (s), 1240 (w), 1130 (w), 1080 (w), 1040 (m), 1020 (m), 860 (m) cm^{-1}; NMR δ 2.18 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 4.92 (s, 2 H, CH_2), 6.90–8.60 (m, 10 H, 9 Ar–H and 1 olefinic proton).

To the filtrate water was added. 4,4′-(*p*-Methoxybenzylidene)bis(1-benzyl-3-methylpyrazolin-5-one) (IV) separated and was filtered, dried, and recrystallized from methanol as a colorless solid: yield 0.74 g (30%); mp 193–195 °C; UV λ_{max} 220 nm; IR 2500 and 1760 (b, NH--O), 1600 (s, C=N), 1520 (m), 1350 (w), 1310 (w), 1280 (w), 1250 (w), 1170 (m), 1090 (w), 1030 (m), 950 (m), 820 (m) cm^{-1}.

Enolic Form of 4,4′-(p-Methoxybenzylidene)bis(1-benzyl-3-methylpyrazolin-5-one) (V). A mixture of 1.88 g (0.01 mol) of 1-benzyl-3-methylpyrazolin-5-one and 1.63 g (0.012 mol) of *p*-methoxybenzaldehyde was dissolved in 40 mL of 95% ethanol; 5–6 drops of piperidine were added and the reaction mixture was kept at 60 °C for 15–20 min and then at room temperature for 1 week. Colorless crystals separated and were recrystallized from ethanol: yield 0.48 g (20%); mp 185–187 °C; UV λ_{max} 218 nm; IR 2770, 2560 and 2460 (vw, $^+$NH), 1590 (s, C=N), 1560 (m), 1510 (m), 1340 (w), 1310 (m), 1280 (m), 1170 (m), 1110 (m), 1150 (w), 975 (m), 870 (w), 850 (w), 750 (m), 730 (s), 710 (m) cm^{-1}.

With a similar procedure as above various 1,3-disubstituted 4-arylidenepyrazolin-5-ones and 4,4′-arylidenebis(1,3-disubstituted pyrazolin-5-ones) in the keto and enol forms were prepared as detailed in Table I. Compounds IV were isomerized into V by refluxing alcoholic solutions of IV in the presence of 5–6 drops of piperidine at 100 °C for 4–5 h. The enolic compounds (V) were isomerized into the keto (IV) by boiling in glacial acetic acid.

4-(p-Methoxybenzylidene)-1-(2-benzothiazolyl)-3-methylpyrazolin-5-one (III). A mixture of 2.31 g (0.01 mol) of 1-(2-benzothiazolyl)-3-methylpyrazolin-5-one and 1.63 g (0.012 mol) of *p*-methoxybenzaldehyde was dissolved in 10–15 mL of glacial acetic acid. The reaction mixture was refluxed on an oil bath at 100 °C for 3–4 h and left overnight; orange crystals separated and were filtered, dried, and recrystallized from ethanol: yield 2.40 g (69%); mp 187–188 °C; UV λ_{max} 228 and 282 nm; IR 1675 (s, C=O), 1575 (s, C=N), 1540 (w), 1360 (m), 1300 (m), 1260 (s), 1155 (s), 980 (m), 890 (w), 810 (w), 740 (m), cm^{-1}; NMR δ 2.37 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.8–8.53 (m, 9 H, 8 ArH and 1 olefinic proton).

Similarly various 4-arylidene-1-(2-benzothiazolyl)-3-methylpyrazolin-5-ones were synthesized (Table I). When the condensation of 1-benzyl-3-methylpyrazolin-5-one with *p*-(dimethylamino)benzaldehyde was attempted under acidic or basic conditions, 4-[*p*-(dimethylamino)benzylidene]-1-benyl-3-methylpyrazolin-5-one (III) was obtained as the single product and corresponding bis keto (IV) and bis enol (V) compounds were not formed at all. The condensations of 1-(2-benzothiazolyl)-3-methylpyrazolin-5-one with aromatic aldehydes also resulted in the formation of single products (III) in acidic as well as basic media.

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Registry No. I (R_1 = CH_2Ph, R_2 = Me), 946-23-6; I (R_1 = 2-benzothiazolyl, R_2 = Me), 17304-62-0; II (X = OMe), 123-11-5; II (X = NO_2), 555-16-8; II (X = H), 100-52-7; II (X = NMe_2), 100-10-7; III (R_1 = CH_2Ph, R_2 = Me, X = OMe), 89936-49-2; III (R_1 = CH_2Ph, R_2 = Me, X = NO_2), 89936-50-5; III (R_1 = CH_2Ph, R_2 = Me, X = H), 89936-51-6; III (R_1 = CH_2Ph, R_2 = Me, X = NMe_2), 89936-52-7; III (R_1 = 2-benzothiazolyl, R_2 = Me, X = OMe), 89936-53-8; III (R_1 = 2-benzothiazolyl, R_2 = Me, X = NO_2), 89936-54-9; III (R_1 = 2-benzothiazolyl, R_2 = Me, X = H), 89936-55-0; III (R_1 = 2-benzothiazolyl, R_2 = Me, X = NMe_2), 89936-56-1; IV (R_1 = CH_2Ph, R_2 = Me, X = OMe), 89936-57-2; IV (R_1 = CH_2Ph, R_2 = Me, X = NO_2), 89936-58-3; IV (R_1 = CH_2Ph, R_2 = Me, X = H), 89936-59-4; V (R_1 = CH_2Ph, R_2 = Me, X = OMe), 89936-60-7; V (R_1 = CH_2Ph, R_2 = Me, X = NO_2), 89936-61-8; V (R_1 = CH_2Ph, R_2 = Me, X = H), 89936-62-9.

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