Rearrangements of 5-Isoxazolylhydrazines: 1-Amino- and 4-Aminopyrazolin-5-ones

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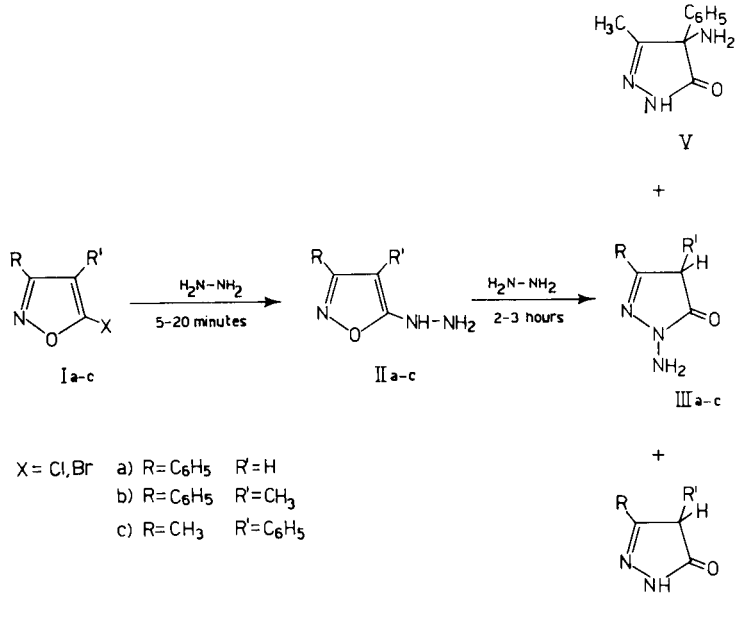
5-Isoxazolylhydrazines rearranged to 1-aminopyrazolin-5-ones on heating. Under the same conditions, 5-(3-methyl-4-phenylisoxazolyl)hydrazine also gave 3-methyl-4-amino-4-phenylpyrazolin-5-one. The structures of aminopyrazolones were assigned on the basis of spectroscopic properties and chemical behavior.

In a previous paper (1), we reported that 5-haloisoxazoles (Ia-c) heated with anhydrous hydrazine for a short period gave 5-isoxazolylhydrazines (IIa-c) in 70-90% yield. In a short communication (2), we have described that prolonged heating led to rearrangement of compounds IIa-c to 1-aminopyrazolin-5-ones (IIIa-c). In addition under these circumstances, small amounts of the corresponding pyrazolones (IVa-c) were obtained. Furthermore when R = CH_3 and R' = C_6H_5, we isolated 3-methyl-4-amino-4-phenylpyrazolin-5-one (V). Increased yields V of this compound were obtained when the reaction was carried out with hydrazine hydrate.

The hydrazines (IIa-c) were the intermediates in the reaction since they gave the same products, in the same ratios, under the same conditions.

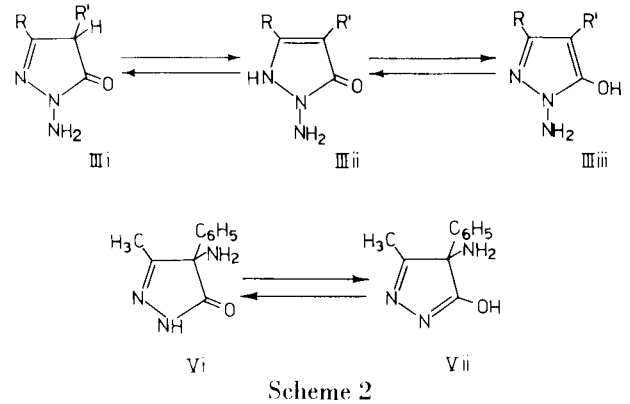
The structures of compounds IIIa-c and V were established by their spectroscopic properties and chemical behavior. The ir spectra show bands in the region 3450-3100 cm^{-1} attributable to imino and/or amino groups. In chloroform solution, strong bands near 1700 cm^{-1} (for compounds IIIa-c) and 1740 cm^{-1} (for compound V) can be attributed to the stretching vibrations of CO groups which are present. In the spectra of IIIa and V, this band is still present in the solid state whereas in the spectra of



Ia-c IIa-c IIIa-c V IVa-c

Scheme 1

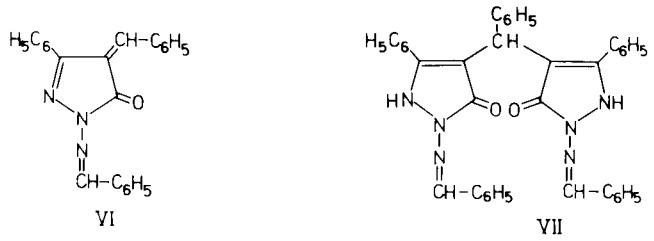
IIIb and IIIc, broad absorption bands between 2800 and 2100 cm^{-1} support the presence of bonded OH groups. This evidence indicated tautomeric behavior of compounds IIIb,c.



Scheme 2

The amphoteric properties of IIIa and V and their reactivity with diazomethane (see below) suggest tautomeric behavior for these compounds also.

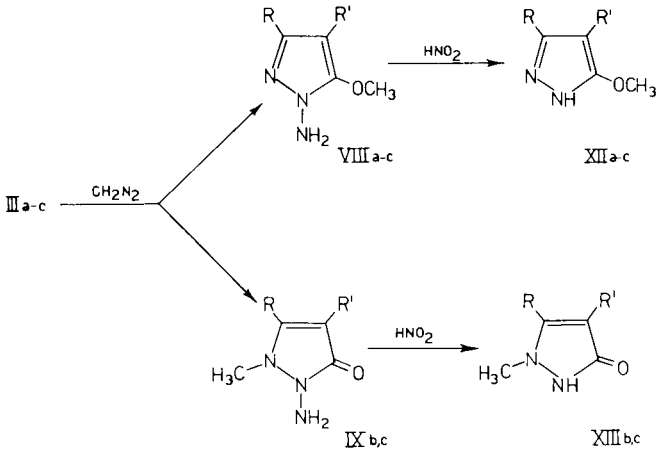
Compounds IIIb,c and V reacted with benzaldehyde to yield the corresponding benzal derivatives, whose ir spectra do not show the presence of the amino vibrational modes. As for compound IIIa, we isolated both compounds VI and VII in different ratios depending upon the reaction conditions: this type of reaction is characteristic of 2-pyrazolin-5-ones unsubstituted at 4-position (3).



Scheme 3

As would be expected both compounds IIIa-c and V reacted with diazomethane; generally we isolated the *N*-methyl (IXb,c and XI) and the *O*-methyl (VIIIa-c and X) derivatives whose ratios depended on the substituents.

The assignment of the pyrazolone structure for compounds IIIa-c was based on the deamination of the methyl derivatives (VIIIa-c) or (IXb,c) with nitrous acid to give the corresponding pyrazoles (XIIa-c) and pyrazolones (XIIIb,c) respectively. This reaction (4) supported the *N*-aminopyrazolone structure for compounds IIIa-c and enabled us, in the case of the *N*-methylpyrazolones (XIIIb, c), to establish which nitrogen atom was linked with the amino group. The correct structure for compounds XIIIb, c was established as follows. In the literature (5) was reported compound XIVc whose structure was based on



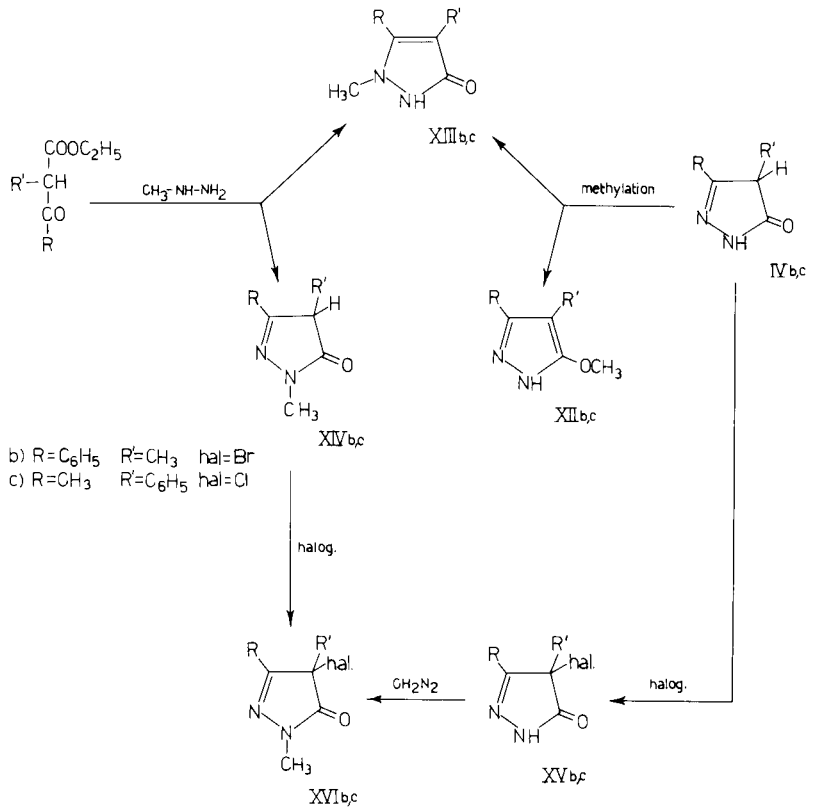
Scheme 4

the assumption that the β-ketoesters with methylhydrazine give 2-pyrazolin-5-ones only. Repetition of this reaction gave, in contrast to the original report, a mixture of isomers XIII and XIV, therefore the problem of their structures was still unsolved.

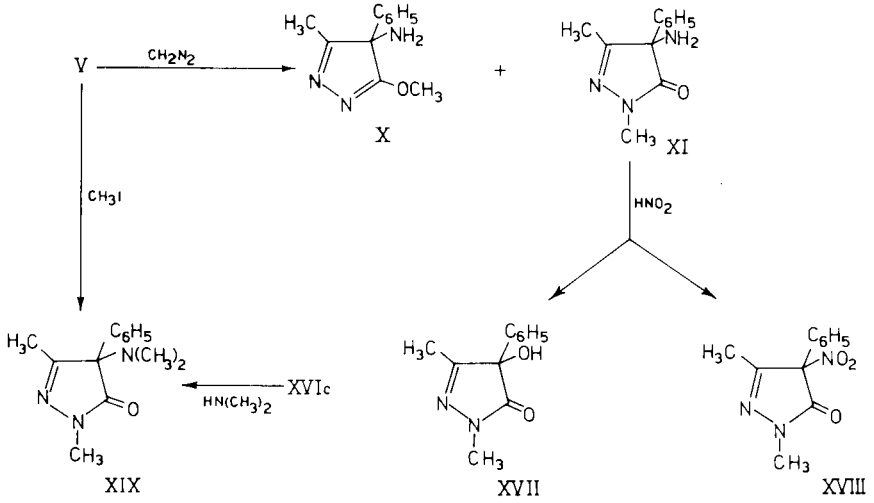
We established the structure of compounds XIVb,c since they gave the corresponding 4-halo derivatives (XVIb,c) when treated with halogens. This behavior is consistent with the structure of 2-pyrazolin-5-ones, since the 4-pyrazolin-3-ones cannot be halogenated at the 4-position. Compounds XVIb,c were obtained also by methylation of the halopyrazolones (XVb,c) with diazomethane. Consequently, isomers XIIIb,c were assigned the structure of 1-methylpyrazolin-3-ones. Methylation of the pyrazolones (IVb,c) with methyl iodide led to *N*-methyl derivatives XIIIb,c mainly, whereas methylation with diazomethane led to the methoxy derivatives (XIIb, c).

The structure of 1-amino-3-phenylpyrazolin-5-one for compound IIIa followed from the reaction with benzaldehyde. The nmr spectrum of compound IIIa in DMSO-d_6 is consistent with the assigned structure. It shows a multiplet centered at about δ 7.5 ppm and a singlet at δ 5.76 ppm (in the ratio 5:1) attributable to the phenyl group and to a proton at the 4-position. The latter signal disappears on deuteration with deuterium oxide. To explain this behavior, we must assume that in solution only a small amount of the form IIIi (for compound IIIa) is present.

In order to establish the structure of compound V, we did not consider the reaction of compound X with nitrous acid because of the low stability of the 4*H*-pyrazole system especially in acidic medium (6). By contrast, the *N*-methylpyrazolone (XI) with nitrous acid yielded the 4-



Scheme 5

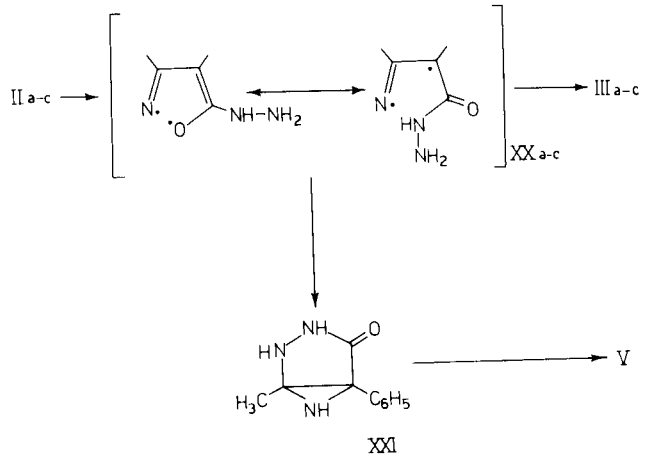


Scheme 6

hydroxypyrazolone (XVII) (7) and 4-nitro-3-methyl-4-phenylpyrazolin-5-one (XVIII), which was also obtained from the pyrazolone (XIVc) with nitric acid. Further supporting evidence of the structure of compound V was obtained from the reaction with methyl iodide, from which we isolated 4-dimethylamino-1,3-dimethyl-4-phenylpyrazolin-5-one (XIX). This compound was also prepared from the chloropyrazolone (XVIc) with dimethylamine.

From our preliminary study we found also that 5-isoxazolylhydrazines rearrange to aminopyrazolones when

they were heated without hydrazine in an inert solvent. On the basis of what is reported in the literature (8), we could assume that the rearrangement pathway would afford the pyrazolones (IIIa-c) *via* the radical intermediate (XXa-c) and the pyrazolone (V) *via* the bicyclic compound (XXI).



XXI

Scheme 7

Research is now under way in our laboratory in order to elucidate the rearrangement mechanism and to establish the factors which govern the reaction.

EXPERIMENTAL

All melting points are uncorrected. The ir, uv, and nmr spectra were recorded on Perkin Elmer 457, Cary Model 14 and Hitachi-Perkin Elmer R20 B spectrometers, respectively.

1-Amino-3-phenylpyrazolin-5-one (IIIa).

A mixture of 10 g. (0.056 mole) of 3-phenyl-5-chloroisoxazole (Ia) (or 5-(3-phenylisoxazolyl)hydrazine (IIa)) and 53 ml. (1.66 moles) of anhydrous hydrazine was heated at 105-110° with vigorous stirring for 2 hours. The resulting solution was concentrated *in vacuo* to a small volume. The reaction mixture was mixed with water (100 ml.) and extracted with ether. The aqueous layer was acidified to *p*H 6 with concentrated hydrochloric acid to afford 5.4 g. (yield 55%) of crude IIIa (m.p. 138-140° dec.) which held a small amount of 3-phenylpyrazolin-5-one (IVa). An analytical sample (m.p. 159-160° dec.) which became colored on long standing in air, was obtained by recrystallization from benzene:ethanol (1:1) and twice from benzene; ir (chloroform) ν max 3350 (NH), 1710 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 253 nm (4.18); nmr (DMSO-d_6) δ 5.75 (s, 1H, CH), 7.22-7.76 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 62.00; H, 5.30; N, 23.82.

1-Amino-3-phenyl-4-methylpyrazolin-5-one (IIIb).

A mixture of 10 g. (0.052 mole) of 3-phenyl-4-methyl-5-chloroisoxazole (Ib) (or 5-(3-phenyl-4-methylisoxazolyl)hydrazine (IIb)) and 50 ml. (1.56 moles) of anhydrous hydrazine was heated at 90-100° with vigorous stirring for 3 hours. The resulting solution was concentrated *in vacuo* to a small volume. The reaction mixture was mixed with water (150 ml.) and extracted with ether. The aqueous layer was acidified to *p*H 6 with concentrated hydrochloric acid to afford 6.2 g. (yield 63%) of crude IIIb (m.p. 128-132° dec.) which was contaminated with a small amount of 3-phenyl-4-methylpyrazolin-5-one (IVb). An analytical sample (m.p. 144-145° dec.) was obtained by repeated recrystallizations from water (charcoal); ir (chloroform) ν max 3350 (NH), 1710 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 250 nm (4.12); nmr (DMSO-d_6) δ 2.00 (s, 3H, CH_3), 7.29-7.72 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.35; H, 5.88; N, 22.29.

Compound IIIb with benzaldehyde gave a benzylideneamino derivative, m.p. 93-96° from ethanol:water (1:1).

Anal. Calcd. for $C_{17}H_{15}N_3O{\cdot}H_2O$: C, 69.14; H, 5.80; N, 14.23. Found: C, 69.17; H, 5.56; N, 14.53.

1-Amino-3-methyl-4-phenylpyrazolin-5-one (IIIc) and 3-Methyl-4-amino-4-phenylpyrazolin-5-one (V).

A mixture of 10 g. (0.052 mole) of 3-methyl-4-phenyl-5-chloroisoxazole (Ic) (or 5-(3-methyl-4-phenylisoxazolyl)hydrazine (IIc)) and 50 ml. (1.56 moles) of anhydrous hydrazine was heated at 90-100° with vigorous stirring for 2 hours. The resulting solution was concentrated *in vacuo* to a small volume. The reaction mixture was mixed with water (100 ml.) and refrigerated for 15 hours to give 1.2 g. (12%) of crystalline crude V (m.p. 142-145°) which was contaminated with a small amount of 3-methyl-4-phenylpyrazolin-5-one (IVc). An analytical sample (m.p. 154-156°) was obtained by repeated recrystallizations from benzene; ir (chloroform) ν max 3450, 3390, 3300 (NH, NH_2), 1740 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 252 nm (3.64); nmr (DMSO-d_6) δ 1.76 (s, 3H, CH_3), 2.55 (deuterium oxide-exchangeable broad s, 2H, NH_2), 7.31 (s, 5H, C_6H_5), 10.94 (deuterium oxide-exchangeable broad s, 1H, NH) ppm.

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.76; H, 5.73; N, 22.30.

Compound V with benzaldehyde gave a benzylideneamino derivative, m.p. 164-166° from ligroin (75-120° b.p.).

Anal. Calcd. for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.55; H, 5.49; N, 14.87.

The mother liquors of V were acidified to *p*H 6 with concentrated hydrochloric acid to afford 4.2 g. (43%) of IIIc which after two recrystallizations from water (charcoal) melted at 177-178° dec.); ir (carbon tetrachloride) ν max 3390 (NH), 1685 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 263 nm (4.08); nmr (DMSO-d_6) δ 2.18 (s, 3H, CH_3), 7.08-7.55 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.45; H, 5.74; N, 22.27.

Compound IIIc with benzaldehyde gave a benzylideneamino derivative, m.p. 92-95° from cyclohexane.

Anal. Calcd. for $C_{17}H_{15}N_3O{\cdot}H_2O$: C, 69.14; H, 5.80; N, 14.23. Found: C, 69.38; H, 5.76; N, 14.10.

When the above experiment was repeated using hydrazine hydrate (78 ml.) the yields of V and IIIc were 5 g. (51%) and 3.2 g. (33%) respectively.

1-Benzylideneamino-3-phenyl-4-benzylidenepyrazolin-5-one (VI).

To 1 g. (0.0057 mole) of IIIa in 10 ml. of glacial acetic acid was added 1.21 g. (0.0114 mole) of benzaldehyde. The reaction mixture was refluxed for 1 hour. After cooling, the crude product (1.3 g., 65%) was filtered, dried *in vacuo* and recrystallized from ethyl acetate to give compound (VI) as red crystals, m.p. 220-222°; ir (nujol) ν max 1690 (CO) cm^{-1}.

Anal. Calcd. for $C_{23}H_{17}N_3O$: C, 78.61; H, 4.88; N, 11.96. Found: C, 78.27; H, 4.85; N, 11.79.

Bis(1-benzylideneamino-3-phenylpyrazolin-5-one-4-)phenylmethane (VII).

The procedure used was the same for the preparation of VI using methanol as solvent. After cooling, the crude VII (yield 81%) was collected by filtration and recrystallized by dissolving in the least amount of chloroform and adding petroleum ether (b.p. 40-70°); m.p. 162-163°. Compound VII became colored on long standing in air.

Anal. Calcd. for $C_{39}H_{30}N_6O_2$: C, 76.22; H, 4.89; N, 13.68. Found: C, 76.30; H, 4.96; N, 13.49.

General Procedure for Methylation of IIIa-c and V with Diazomethane.

To compounds IIIa-c and V (0.014 mole) was dissolved in a minimum amount of methanol:ether (1:1) was added 0.028 mole of diazomethane in ether. After 24 hours the solvent was rotary evaporated and the oily residue was dried over phosphorus pentoxide *in vacuo*. Compound VIIIa was purified as described below. The resulting residue from compounds IIIb,c and V was dissolved in the minimum amount of ethanol and chromatographed on a 17 x 300 mm silica gel column. Elution was carried out first with ether, until the eluate did not leave a residue by evaporation, then with ethanol.

1-Amino-3-phenyl-5-methoxypyrazole (VIIIa).

The dried residue from compound IIIa was purified by repeated recrystallizations from ethanol, m.p. 158-160° dec., yield 1.4 g. (53%); ir (nujol) ν max 3270, 3150 (NH_2) cm^{-1}; uv (methanol) λ max (log ϵ) 251 nm (4.22); nmr (DMSO-d_6) δ 3.89 (s, 3H, OCH_3), 5.94 (deuterium oxide-exchangeable s, 2H, NH_2), 6.09 (s, 1H, CH) 7.28-7.82 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.81; H, 5.90; N, 22.16.

1-Amino-3-phenyl-4-methyl-5-methoxypyrazole (VIIIb) and 1-Amino-2,4-dimethyl-3-phenyl-pyrazolin-5-one (IXb).

The crude product (VIIIb) was obtained by evaporation of ethereal eluate and purified by recrystallization from ligroin (75-120° b.p.): m.p. 98-99°, yield 1 g. (35%); ir (nujol) ν max 3300, 3190 (NH_2) cm^{-1}; uv (methanol) λ max (log ϵ) 248 nm (4.13); nmr (deuteriochloroform) δ 2.11 (s, 3H, CH_3), 3.97 (s, 3H, OCH_3), 4.98 (deuterium oxide-exchangeable s, 2H, NH_2), 7.2-7.7 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 65.28; H, 6.50; N, 20.96.

The crude product (IXb) was obtained by evaporation of ethanolic eluate and purified by recrystallization from benzene: m.p. 155-157°, yield 1.1 g. (39%); ir (nujol) ν max 3320, 3200 (NH_2), 1665 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 246 nm (4.05); nmr (deuteriochloroform) δ 1.88 (s, 3H, CH_3), 3.05 (s, 3H, NCH_3), 4.73 (deuterium oxide-exchangeable s, 2H, NH_2), 7.25-7.53 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 65.19; H, 6.55; N, 20.71.

1-Amino-3-methyl-4-phenyl-5-methoxypyrazole (VIIIc) and 1-Amino-2,3-dimethyl-4-phenylpyrazolin-5-one (IXc).

The crude product (VIIIc) was obtained by evaporation of ethereal eluate and purified by recrystallization from ligroin (75-120° b.p.): m.p. 94-95°, yield 0.95 g. (33%); ir (nujol) ν max 3280, 3180 (NH_2) cm^{-1}; uv (methanol) λ max (log ϵ) 245 nm (4.05); nmr (deuteriochloroform) δ 2.20 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 4.89 (deuterium oxide exchangeable broad s, 2H, NH_2), 7.22-7.40 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 64.70; H, 6.45; N, 20.40.

The crude product (IXc) was obtained by evaporation of ethereal eluate and purified by recrystallization from benzene: ligroin (75-120° b.p.) (1:1): m.p. 143-144° dec., yield 1.4 g. (49%); ir (carbon tetrachloride) ν max 3350, 3160 (NH_2), 1660 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 275 nm (4.09); nmr (deuteriochloroform) δ 2.20 (s, 3H, CH_3), 3.29 (s, 3H, NCH_3), 7.10-7.47 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O \cdot H_2O$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.48; H, 6.67; N, 19.10.

1,3-Dimethyl-4-amino-4-phenylpyrazolin-5-one (XI) and 3-Methyl-4-phenyl-4-amino-5-methoxy-(4*H*)pyrazole (X).

The crude product (XI) was obtained by evaporation of ethereal eluate and purified by sublimation (0.06 mm) at 50°: m.p. 71-72°, yield 1.9 g. (67%); ir (nujol) ν max 3350, 3280 (NH_2) 1710 (CO) cm^{-1}; uv (methanol) λ max (log ϵ) 257 nm (3.63); nmr (deuteriochloroform) δ 1.83 (deuterium oxide-exchangeable broad s, 2H, NH_2), 1.94 (s, 3H, CH_3), 3.38 (s, 3H, NCH_3), 7.35 (s, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 65.32; H, 6.56; N, 20.53.

The crude product (X) was obtained by evaporation of ethanolic eluate and purified by sublimation (0.06 mm) at 70°: m.p. 125-126°, yield 0.32 g. (11%); ir (nujol) ν max 3320, 3260 (NH_2) cm^{-1}; uv (methanol) λ max (log ϵ) 247 nm (3.56); nmr (DMSO-d_6) δ 1.78 (s, 3H, CH_3), 2.68 (deuterium oxide-exchangeable broad band, 2H, NH_2), 3.83 (s, 3H, OCH_3), 7.28 (d, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 64.90; H, 6.47; N, 20.57.

Deamination of Compound (VIIIa): 3-Phenyl-5-methoxypyrazole (XIIa).

To a stirred solution of compound VIIIa (0.001 mole) in glacial acetic acid was added with ice cooling a solution of sodium nitrite (0.001 mole) in the minimum amount of water. The reaction mixture was diluted with water and the suspended solid was filtered and recrystallized from water: m.p. 105-106° (lit. 106-106.5° (9)).

Reaction of Ethyl-α-benzoylpropionate with Methylhydrazine.

A mixture of 2 g. (0.0097 mole) of ethyl-α-benzoylpropionate and 0.66 g. (0.0143 mole) of methylhydrazine was heated at 180° for 4 hours. After the excess methylhydrazine was evaporated *in vacuo*, the gummy residual mixture of XIIIb and XIVb crystallized (1.8 g., 99%) by rubbing after treating with 2.5 ml. of ether.

Compound XIIIb was recovered by repeated recrystallizations from benzene; m.p. 190-192°; uv (methanol) λ max (log ϵ) 242 nm (4.05); nmr (deuteriochloroform) δ 1.92 (s, 3H, CH_3), 3.60 (s, 3H, NCH_3), 7.22-7.50 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.47; H, 6.65; N, 14.69.

The mother liquor of the first recrystallization of XIIIb was concentrated and the crude compound XIVb crystallized, m.p. 110-125°. An analytical sample of XIVb was obtained by washing crude product with hot ether and recrystallization from a very small amount of benzene, m.p. 128-129°; uv (methanol) λ max (log ϵ) 250 nm (4.13); nmr (DMSO-d_6) δ 2.03 (s, 3H, CH_3), 3.57 (s, 3H, NCH_3), 7.30-7.72 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.44; H, 6.61; N, 14.53.

Compound XIIIb was also obtained as follows: (a) By deamination of compound IXb as described for compound XIIa and recrystallization from ethanol:water (1:1), m.p. 189-191°; (b) Compound IVb (0.01 mole) and methyl iodide (0.02 mole) were added to sodium methoxide prepared from 0.01 mole of sodium and 10 ml. of methanol. This solution was refluxed for 45 minutes and the solvent was evaporated to dryness *in vacuo*. The resultant residue treated with 1*N* sodium hydroxide afforded a clear solution which, by acidification (*p*H 5) with concentrated hydrochoric acid, precipitated compound XIIIb (yield 28%).

Reaction of Ethyl-α-phenylacetoacetate and Methylhydrazine.

To 2 g. (0.0097 mole) of ethyl-α-phenylacetoacetate cooled in an ice bath was added 0.45 g. (0.0097 mole) of methylhydrazine. The ice bath was then removed and the mixture was heated at 180° for 1 hour. After cooling the oily mixture was dissolved in the minimum amount of boiling ethanol. The solution was allowed to stand in the refrigerator and compound XIIIc (0.11 g., 6%) was collected by filtration and recrystallized from ethanol: m.p. 250-252°; uv (methanol) λ max (log ε) 256 nm (4.09); nmr (DMSO-d_6) δ 2.26 (s, 3H, CH_3), 3.59 (s, 3H, NCH_3), 7.22-7.44 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.40; H, 6.68; N, 15.06.

Compound XIVc (1.3 g., 71%) was obtained from the mother liquor of (XIIIc) by dilution with water and recrystallization from ethanol:water (1:1): m.p. 179-180° (lit. 179-180° (5)).

Compound XIIIc was also obtained as follows: (a) By deamination of compound IXc as described for compound XIIa; (b) By methylation of compound IVc as described for compound XIIIb. In this case, the undissolved residue after treatment with 1*N* sodium hydroxide was filtered and identified as XIIc. The mother liquor was acidified (*p*H 5) with concentrated hydrochloric acid to afford compound XIIIc (yield 40%).

General Procedure for the Preparation of 5-Methoxypyrazoles (XIIb,c).

To compounds IVb,c (0.01 mole) suspended in 100 ml. of ether was added 0.02 mole of diazomethane in ether. After 12 hours, a clear solution was obtained; evaporation of this solution gave a residue which solidified by washing with 1*N* sodium hydroxide and water. The crude compounds XIIb,c were crystallized from ligroin (75-120° b.p.).

3-Phenyl-4-methyl-5-methoxypyrazole (XIIb).

This compound was obtained from IVb; m.p. 116-117°, yield 75%; ir (nujol) ν max 3175 (NH) cm^{-1}; uv (methanol) λ max (log ε) 250 nm (4.16); nmr (deuteriochloroform) δ 2.02 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 7.38 (d, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.39; H, 6.47; N, 14.71.

Compound XIIb was also obtained by deamination of compound VIIIb as described for compound XIIa and recrystallization from ligroin (75-120° b.p.); m.p. 114-116.5°.

3-Methyl-4-phenyl-5-methoxypyrazole (XIIc).

This compound was prepared from IVc; m.p. 153-155°, yield 70%; ir (nujol) ν max 3160 (NH) cm^{-1}; uv (methanol) λ max (log ε) 252.5 nm (4.13); nmr (deuteriochloroform) δ 2.26 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 7.20-7.43 (m, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.33; H, 6.44; N, 14.72.

Compound XIIc was also obtained by deamination of compound VIIIc as described for compound XIIa and recrystallization from water:methanol (1:2).

1,4-Dimethyl-3-phenyl-4-bromopyrazolin-5-one (XVIb).

Method A.

This compound was prepared following the method of Carpino (10) from 0.2 g. (0.001 mole) of XIVb and 0.07 ml. (0.0013 mole) of bromine. The crude product, 0.15 g. (56%), was recrystallized from ethanol, m.p. 116-119°; ir (nujol) ν max 1715 (CO) cm^{-1}.

Anal. Calcd. for $C_{11}H_{11}N_2OBr$: C, 49.44; H, 4.12; N, 10.49; Br, 29.96. Found: C, 49.56; H, 4.27; N, 10.17; Br, 30.15.

Method B.

To a solution of XVb (1 mole) in a minimum amount of methanol:ether (1:1) was added ethereal diazomethane (2 moles). After 24 hours the solvents were removed *in vacuo* and the crude product XVIb was purified from methanol.

1,3-Dimethyl-4-phenyl-4-chloropyrazolin-5-one (XVIc).

This compound was obtained as described above for XVIb from compound XIVc and chlorine, yield 85%, following method A and from compound XVc and diazomethane, yield 78%, following method B; b.p. 95° at 0.1 mm; ir (nujol) ν max 1720 (CO) cm^{-1}.

Anal. Calcd. for $C_{11}H_{11}N_2OCl$: C, 59.32; H, 4.94; N, 12.58; Cl, 15.95. Found: C, 59.25; H, 5.07; N, 12.62; Cl, 16.12.

Reaction of 1,3-Dimethyl-4-phenyl-4-aminopyrazolin-5-one (XI) with Nitrous Acid.

To a solution of XI (2 g., 0.0098 mole) in 50 ml. of 1*N* hydrochloric acid, 1.353 g. of sodium nitrite (0.0196 mole) dissolved in a minimum amount of water was added under stirring and cooling. The oily precipitate crystallized after cooling for 2 hours in the refrigerator.

This crude product (1.9 g., 83%) was identified as 1,3-dimethyl-4-phenyl-4-nitropyrazolin-5-one (XVIII) and tlc analysis (95% chloroform, 5% methanol v/v) showed the presence of a small quantity of 1,3-dimethyl-4-phenyl-4-hydroxypyrazolin-5-one (XVII) (7).

The solid was purified by dissolving in a minimum amount of ethanol and adding water, m.p. 81-83° dec.; ir (nujol) ν max 1720 (CO) cm^{-1}.

Anal. Calcd. for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.85; H, 4.80; N, 18.17.

The same product was obtained by reaction of XIVc with nitric acid (d = 1.40).

1,3-Dimethyl-4-phenyl-4-dimethylaminopyrazolin-5-one (XIX).

Method A.

Compound V (1 g., 0.0052 mole) and methyl iodide (2.3 g., 0.016 mole) were added to sodium methoxide prepared from 0.25 g. (0.011 mole) of sodium and 10 ml. of methanol. The solution was refluxed for 1 hour and the solvent removed *in vacuo*. The oily residue crystallized by trituration with cold water. The solid product was filtered, dried, and purified by two sublimations (0.06 mm at 60°); m.p. 118-120°, yield 0.6 g. (50%); ir (nujol) ν max 1700 (CO) cm^{-1}; nmr (deuteriochloroform) δ 1.92 (s, 3H, CH_3), 2.33 (s, 6H, $N(CH_3)_2$), 3.36 (s, 3H, NCH_3), 7.34 (d, 5H, C_6H_5) ppm.

Anal. Calcd. for $C_{13}H_{17}N_3O$: C, 67.51; H, 7.41; N, 18.17. Found: C, 67.31; H, 7.42; N, 18.00.

Method B.

An excess of dimethylamine was added to a solution of XVIc (0.5 g., 0.0022 mole) in the minimum volume of benzene and the reaction mixture was allowed to stand overnight. Dimethylammonium chloride was filtered off and the mother liquor eva-

porated *in vacuo*. The residue was purified by sublimation at 60° (0.06 mm).

The product (yield 95%) was identical (ir and nmr spectra) with material prepared by method A.

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