+8.08°, was hydrogenated over Raney nickel as previously reported.[8] Rectification of the crude product afforded (+)-(*S*)-3-methylhexane (77% yield): bp 91°, $n^{20}D$ 1.3894, d^{25}_4 0.6826, $[\alpha]^{25}D$ +8.67° (lit.[33] bp 91–93°, $n^{20}D$ 1.3894, $d^{19.9}_4$ 0.6898). By an analogous procedure (+)-(*S*)-5-methyl-1-heptyne, $[\alpha]^{20}D$ +14.81°, was reduced to (+)-(*S*)-3-methylheptane (78% yield), bp 118–119°, $n^{25}D$ 1.3966, d^{25}_4 0.7020, $[\alpha]^{25}D$ +9.34° (lit.[3] bp 118–119°, $n^{25}D$ 1.3965). (+)-(*S*)-7-Methyl-1-nonyne, $[\alpha]^{20}D$ +9.65°, in ethyl ether, was hydrogenated over Raney nickel at 80° and 100 atm of hydrogen pressure. By distillation over sodium, (+)-(*S*)-3-methylnonane having bp 168°, $n^{20}D$ 1.4126, $[\alpha]^{25}D$ +9.34° [lit.[26] bp 80° (39 mm), $n^{24}D$ 1.4110, d^{25}_4 0.730] (80% yield) was obtained.

(+)-(*S*)-4-Methylhexan-2-one, (+)-(*S*)-5-Methylheptan-2-one, and (+)-(*S*)-6-Methyloctan-2-one (by Catalytic Hydration of Corresponding 1-Alkynes).—(+)-(*S*)-4-Methyl-1-hexyne, $[\alpha]^{20}D$ +8.26°, was treated in 60% acetic acid with aqueous sulfuric acid in the presence of mercuric sulfate, as described in the literature[23] (70–75° for 6 hr). The crude product was distilled and (+)-(*S*)-4-methylhexan-2-one, bp 139–140°, $n^{25}D$ 1.4059, $[\alpha]^{18}D$ +6.13° (lit.[21] bp 140°, $n^{25}D$ 1.4061), was obtained (50% yield). By an analogous procedure with a reaction temperature of 80–85°, (+)-(*S*)-5-methyl-1-heptyne, $[\alpha]^{20}D$ +14.81°, was converted to (+)-(*S*)-5-methylheptan-2-one, bp 166–167°, $n^{25}D$ 1.4154, $[\alpha]^{25}D$ +9.30 (lit.[21] bp 167°, $n^{25}D$ 1.4154) (71% yield). (+)-(*S*)-6-Methyl-1-octyne, $[\alpha]^{20}D$ +10.44°, was treated, with vigorous stirring (100° for 14 hr) under the above conditions; (+)-(*S*)-6-methyloctan-2-one was recovered, having bp 186°, $n^{25}D$ 1.4209, $[\alpha]^{25}D$ +7.91° (lit.[21] bp 186°, $n^{25}D$ 1.4205) (58% yield).

(33) B. C. Easton and M. K. Hargreaves, *J. Chem. Soc.*, 1417 (1959).

Acknowledgments.—We are grateful to Professor P. Pino for his interest and helpful advice. We are also indebted to Dr. Elena Belgodere of the Institute of Organic Chemistry of Florence University for the ultraviolet determinations.

Some Reactions of 3-Hydroxy-1-phenylpyrazole

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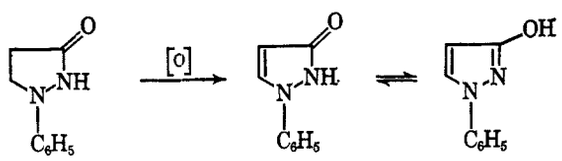
The oxidation products of 1-phenyl-3-pyrazolidone and 4-methyl-1-phenyl-3-pyrazolidone were examined to determine their structure and reactivity. Their infrared, ultraviolet, and nuclear magnetic resonance spectra indicate that they exist chiefly as 3-hydroxypyrazoles rather than as 3-pyrazolones. 3-Hydroxy-1-phenylpyrazole underwent electrophilic substitution in the 4 position, O alkylation, and acetylation. The appropriate derivatives underwent Claisen and Fries rearrangements. 3-Hydroxy-4-methyl-1-phenylpyrazole was reduced to 1-cyclohexyl-3-hydroxy-4-methylpyrazole. These reactions are discussed with regard to the known chemistry of phenol and 1-phenylpyrazole.

The oxidation product (**1**) of 1-phenyl-3-pyrazolidinone (**2**) was prepared by Harries and Loth[1] in 1896. Few reactions of **1** are reported in the literature.



2 **1a** **1b**

The infrared spectrum of **1** in the crystalline state and of **1** and 1-phenyl-5-methyl-3-methoxypyrazole (**3**) in chloroform solution were reported recently.[2] These authors concluded that **1** exists chiefly in the enol form, 3-hydroxy-1-phenylpyrazole (**1b**). Katritzky and Maine[3] have concluded that both 3-hydroxy-1,5-dimethylpyrazole and 3-hydroxy-5-methyl-1-phenylpyrazole exist in the enol form in nonpolar solvents and in the solid state. In aqueous media comparable amounts of keto and enol forms exist.[3]

Results and Discussion

Compound **1** was alkylated with dimethyl sulfate in dilute aqueous base. The resulting liquid product was identified as 3-methoxy-1-phenylpyrazole (**4**) by its nmr spectrum (Table I). The infrared spectra ($CHCl_3$) between 1800 and 1450 cm^{-1} and the ultraviolet spectra (EtOH) (Table IV) of **1** and **4** were nearly the same. The spectral data for **1** and the other 3-hydroxy-1-phenylpyrazoles reported herein support the conclusions of the earlier authors.[2,3] These materials were not examined in aqueous media.

The action of dilute nitric acid on **1** gave a yellow solid, 3-hydroxy-4-nitro-1-phenylpyrazole (**7**) identified by its spectral characteristics. The nitro group may be reduced by the action of sodium dithionate. The product is 4-amino-3-hydroxy-1-phenylpyrazole (**8**), which is sensitive to acids. The procedure used is a modification of that used to prepare *o*-aminophenol from *o*-nitrophenol.[4]

Bromination of 3-hydroxy-1-phenylpyrazole was accomplished both in carbon tetrachloride and in chloroform with bromine at room temperature. The reaction was rapid and gave a high yield of 4-bromo-3-hydroxy-1-phenylpyrazole (**9**). Chlorination of **1** by sulfuryl chloride in chloroform gave a high yield of a white solid, 4-chloro-3-hydroxy-1-phenylpyrazole (**10**). Its infrared and nmr spectra were very similar to those of **9**.

The facile electrophilic attack at the 4 position of **1** is consistent with the reported chemistry of 1-phenylpyrazole, which undergoes initial electrophilic substitution at the 4 position on the pyrazole ring.[5] Lynch and co-workers have discussed the nitration and bromination of this system.[5b]

Compound **1** was found to couple in the 4 position with phenyldiazonium chloride to give a yellow azo compound (**11**). 3-Hydroxy-1-phenylpyrazole under-

(1) C. Harries and G. Loth, *Ber.*, **29**, 513 (1896).

(2) V. G. Vinokurov, V. S. Troitskaya, I. I. Grandberg, and Yu. A. Pentin, *Zh. Obshch. Khim.*, **33**, 2597 (1963).

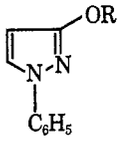
(3) A. R. Katritzky and F. W. Maine, *Tetrahedron*, **20**, 315 (1964).

(4) L. F. Hewitt and H. King, *J. Chem. Soc.*, 822 (1926).

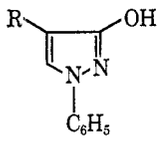
(5) (a) E. G. Brain and I. L. Finar, *ibid.*, 2435 (1958); (b) M. A. Khan, B. M. Lynch, and Y. Hung, *Can. J. Chem.*, **41**, 1540 (1963); (c) B. M. Lynch and Y. Hung, *ibid.*, **42**, 1605 (1964), and references cited therein.

TABLE I

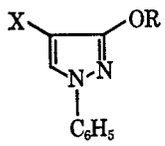
PEAK POSITIONS OF DERIVATIVES OF 1-PHENYLPYRAZOLE[a]



Compd	OR	4-H ($J_{4,5}$, cps)	5-H	Solvent
1	OH, −0.24	4.11 (3.0)	1.75	DMSO
6	$OCOCH_3$, 7.69	3.64 (2.7)	2.16	$CDCl_3$
4	OCH_3, 6.05	4.14 (2.5)	2.33	$CDCl_3$
14	OCH_2, 5.22; $=CH_2$, 4.62; CH, 3.63	4.08 (2.9)	2.31	$CDCl_3$



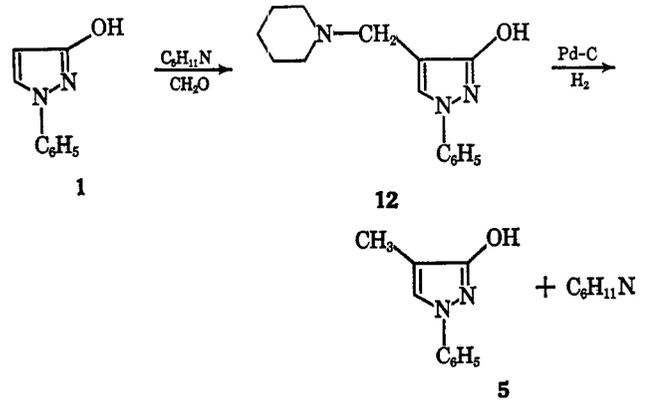
Compd	R	5-H	OH	Solvent
5	CH_3, 8.08	2.01	0.25	DMSO
7	NO_2	0.64	−2.11	DMSO
8	NH_2, 4.46	2.51	4.46	DMSO
9	Br	1.47	−0.99	DMSO
10	Cl	1.45	−1.01	DMSO
11	$C_6H_5N{=}N$, 2.50–2.90	1.60	0.28	$CDCl_3$
12	$CH_2NC_5H_{10}$	1.88	4.40	DMSO
12	CH_2, 6.35; NC_5H_{10}, 8.50, 7.52	...	...	Pyridine
13[b]	CH_3, 8.04; CH, 6.23; C_6H_{11}, 8.00–8.50	3.03	−1.62	$CDCl_3$
15	CH_2, 6.71; $=CH_2$, 4.83; CH, 4.00	2.55	−1.11	$CDCl_3$



Compd	OR	X	5-H	Solvent
17	OH, −1.11	$COCH_3$, 7.57	1.12	DMSO
18	OCH_3, 5.92	$COCH_3$, 7.52	1.77	$CDCl_3$

[a] Peak positions are expressed in parts per million relative to an internal tetramethylsilane standard, which is given an arbitrary position of 10 (τ scale). In all spectra, the phenyl protons appear as a multiplet, 2.10–2.80. [b] Cyclohexane protons are given under R.

goes a Mannich reaction with formaldehyde and piperidine to give 3-hydroxy-1-phenyl-4-piperidino methylpyrazole (**12**). Compound **12** was reduced with

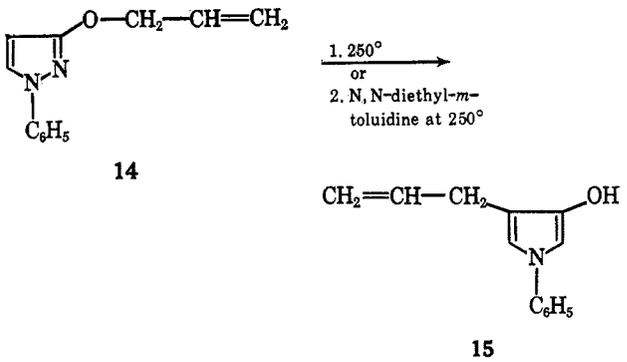


palladium on charcoal in ethanol. One equivalent of hydrogen was used. The product was identical with 3-hydroxy-4-methyl-1-phenylpyrazole (**5**).

Further reduction of 3-hydroxy-4-methyl-1-phenylpyrazole (**5**) was accomplished with rhodium on alumina as catalyst in glacial acetic acid. Approximately 1.5 moles of hydrogen were taken up and a 53% yield of 1-cyclohexyl-3-hydroxy-4-methylpyrazole (**13**) was produced. The bands at 1590 and 1490 cm^{-1} in the spectrum of **5**, which were believed to be due to the benzene ring, were absent in the spectrum of **15**. However, the C=N stretching frequency at 1600 cm^{-1} was present in the spectra of **5** and **13**. The reduction of 3-hydroxy-4-methyl-1-phenylpyrazole was surprising. 1-Phenylpyrrole is reported to be reduced with Raney nickel to 1-phenylpyrrolidine and then to 1-cyclohexylpyrrolidine.[6] Evidently the phenyl group in our compound is activated by the hydroxypyrazole.

An alkylation of **1** was carried out by using allyl bromide in acetone with potassium carbonate as base. The conditions were chosen to favor O alkylation.[7] The liquid product was identified as 3-alloxy-1-phenylpyrazole (**14**). The appearance in the nmr spectrum of the peaks due to the allyl protons was similar to that of the peaks of allyl ether, allyl vinyl ether, and allyl alcohol.[8] Neither the nmr nor the infrared spectra gave any evidence of a hydroxyl proton. The infrared had bands typical of a terminal methylene group at 1420, 1290, 985, and 920 cm^{-1}.[9]

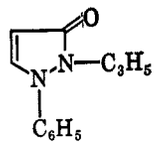
The allyl ether of 3-hydroxy-1-phenylpyrazole was heated at 250° both neat and in N,N-diethyl-*m*-toluidine. In both cases, rearranged and starting material were recovered. The solid product was identified as 4-allyl-3-hydroxy-1-phenylpyrazole (**15**). The infrared spectrum showed hydroxyl absorption from 3050 to 2500 cm^{-1} and bands due to terminal methylene at 1420, 1305, 950, and 904 cm^{-1}.[9]



14 **15**

The rearrangement of the neat liquid gave a 28% yield of **15** and a 29% yield of recovered starting material. Some product was lost in the purification. The reaction in solution resulted in a 49% yield of 4-allyl compound and 10% recovered **14**. No other products were identified. The possibility of forming **16** was suggested by the Claisen rearrangements reported in the pyrimidine,[10] pyridine,[11] and quinoline[12] series. The observed rearrangement may take place by dissociation, followed by electrophilic attack at the 4 position, rather than by a concerted mechanism.

(6) F. R. Signaigo and H. Adkins, *J. Am. Chem. Soc.*, **58**, 709 (1936).
(7) N. Kornblum, P. J. Berrigan, and W. J. leNoble, *ibid.*, **85**, 1141 (1963); N. Kornblum, R. Seltzer, and P. Haberfield, *ibid.*, **85**, 1148 (1963).
(8) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962.
(9) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 34.
(10) F. J. Dinan, H. J. Minnimeyer, and H. Tieckelmann, *J. Org. Chem.*, **28**, 1015 (1963).
(11) F. J. Dinan and H. Tieckelmann, *ibid.*, **29**, 892 (1964).
(12) A. E. Tschitschibabin and N. P. Jeletzsky, *Ber.*, **57B**, 1158 (1924).



16

An investigation of the details of this reaction is in progress.

3-Hydroxy-1-phenylpyrazole (**1**) was readily acetylated[1] to give 3-acetoxy-1-phenylpyrazole. Fries rearrangement of 3-acetoxy-1-phenylpyrazole gave a 48% yield of 4-acetyl-3-hydroxy-1-phenylpyrazole (**17**). The structure of the product followed from its infrared spectrum, which showed a carbonyl stretching band at 1630 cm^{-1} and associated OH (2-hydroxyphenyl ketones have carbonyl absorption between 1655 and 1635 cm^{-1} [13]), and from its nmr spectrum (Table I).

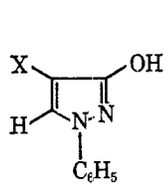
Alkylation of **17** with iodomethane and potassium carbonate in acetone gave a white crystalline material, 4-acetyl-3-methoxy-1-phenylpyrazole (**18**). The infrared spectrum of the product had a carbonyl at 1665 cm^{-1}, with no hydroxyl absorbance. The carbonyl frequency of phenyl ketones is usually from 1700 to 1680 cm^{-1}. A Friedel–Crafts acylation with acetic anhydride on 3-methoxy-1-phenylpyrazole (**4**) gave three products, **1**, **17**, and **18** in 60, 15, and 1% yields, respectively.

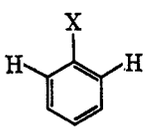
All the compounds studied except 1-cyclohexyl-3-hydroxy-4-methylpyrazole (**13**) showed vibrations near 1600 and 1500 cm^{-1} and C–H deformations near 760 and 690 cm^{-1} in their infrared spectra. The hydroxy compounds all have bands from 2500 to 3000 cm^{-1}, owing to association of the hydroxyls. Lynch reported that 1-phenylpyrazoles exhibited a strong band between 925 and 960 cm^{-1}, owing to the C–H vibrations of the pyrazole nucleus.[5b] Unsubstituted 1-phenylpyrazoles have absorption from 925 to 942 cm^{-1} and substituted 1-phenylpyrazoles absorb in the range 950–960 cm^{-1}.[5b] All of the compounds studied except **11** and **13** have a strong band in their infrared spectra between 930 and 950 cm^{-1}.

In Table II the peak position of the 5-proton is given as a function of the 4-substituent. These values are compared with the peak position of the *ortho* protons in monosubstituted benzenes. The same direction and in most cases the same magnitude of effect were observed for the pyrazoles and benzenes. We believe that these data can best be interpreted in terms of an aromatic nucleus.

TABLE II

EFFECT OF SUBSTITUTION ON THE PEAK POSITION OF THE *ortho* PROTONS IN BENZENE AND 5-PROTONS IN 3-HYDROXY-1-PHENYLPYRAZOLE



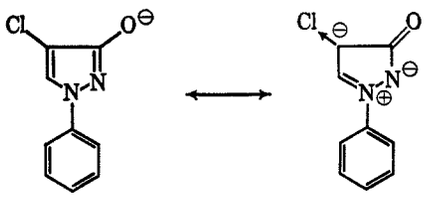


X	5-H	$\Delta\tau$[a]	2,6-H[b]	$\Delta\tau$[a]
NO_2	0.64	−0.97	1.76	−0.97
$COCH_3$	1.12	−0.63	2.10	−0.63
Cl	1.45	−0.30	2.73	0.00
Br	1.47	−0.28	2.73	0.00
H	1.75	...	2.73	...
$CH_2NC_5H_{10}$[c]	1.88	0.13	2.76	0.03
CH_3	2.01	0.25	2.86	0.10
NH_2	2.51	0.76	3.50	0.77

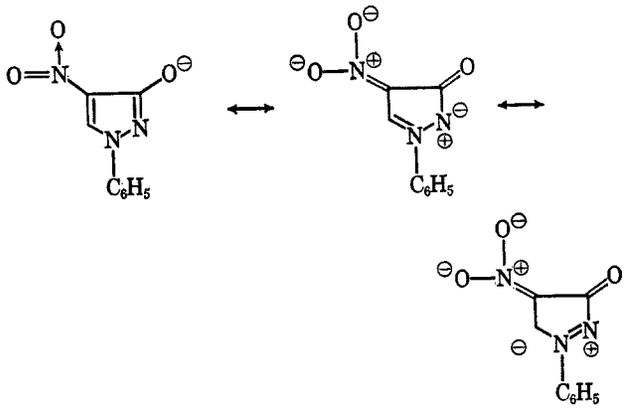
[a] $\Delta\tau$ refers to the chemical shift difference between *ortho* protons in the unsubstituted and substituted nuclei. [b] P. L. Corio and B. P. Dailey, *J. Am. Chem. Soc.*, **78**, 3043 (1956). [c] In the benzene system the substituent is CH_2NH_2.

(13) See ref 9, p 132.

In Table III the effects of substituent on the acidity of some 3-hydroxy-1-phenylpyrazoles are tabulated. The 4-methyl group decreased the acidity of the molecule by a small but significant factor, *cf.* pK_a for phenol, 10.0; and for *o*-cresol, 10.2. The three +R,−I groups, chloro, bromo, and amino, each increased the acidity of the hydroxypyrazole. The pK_a of *o*-chlorophenol is 9.1 and that of *o*-aminophenol is 9.7. The stabilization of the anion by the inductive effect of these groups may be represented as shown. The 4-



nitro group has a large effect. The pK_a of benzoic acid is 4.2; therefore, the ΔpK_a for benzoic acid and phenol is approximately 6. Although the millivolt scale given in Table III is not strictly comparable to a pK_a scale, we can see that the difference in acidity between **1** and **9** is roughly that between phenol and benzoic acid, about 6 pK units. The pK_a of *o*-nitrophenol is 7.2, about 3 pK units more acidic than phenol. This is considered a large effect requiring the direct conjugation of the nitro group and the oxygen. Similarly, the effect is large for 3-hydroxypyrazoles and may be represented by these structures.

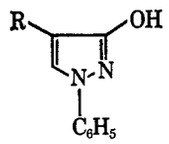


Experimental Section

All melting and boiling points are uncorrected. Nmr spectra were measured with a 60-Mc Varian high-resolution spectrometer, Model V-4302. Peak positions are expressed in parts per million relative to an internal tetramethylsilane standard (taken as τ 10). The audio side band method of calibration was used. The spectra are reported in Table I. The ultraviolet absorption spectra were obtained with a Cary 11 spectrophotometer. The spectra are given in Table IV. Infrared spectra were taken with Baird Models AK-1 or NR-1, or a Perkin-Elmer Infracord, Model 137, double-beam recording spectrophotometers, with sodium chloride optics. Samples were examined as potassium bromide pressings, unless otherwise noted.

TABLE III

HALF-NEUTRALIZATION POINTS (HNP) FROM NONAQUEOUS TITRATION OF 3-HYDROXY-1-PHENYLPYRAZOLES[a]

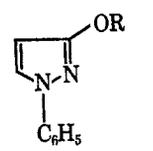


Compd	R	HNP, mv
7	NO_2	+90
8	NH_2	−100
9	Br	−130
10	Cl	−130
1[b]	H	−250
5	CH_3	−280
Benzoic acid		0
Phenol		−300

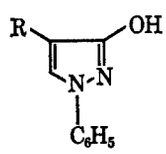
[a] The titrations were conducted in pyridine. The base was tetrabutylammonium hydroxide. [b] The pK_a of 1 was determined by aqueous titration to be 7.9 ± 0.1.

TABLE IV

ULTRAVIOLET ABSORPTION SPECTRA OF SOME 1-PHENYLPYRAZOLES[a]



Compd	R	λ, mμ	Log ε
1	H	272	4.28
4	CH_3	272	4.24
14	C_3H_5	272	4.28



5	CH_3	278	4.37
7	NO_2	326, 270, 238	3.98, 3.88, 4.15
8	NH_2	400, 297	2.38, 4.08
9	Br	280	4.30
10	Cl	279	4.30
11[b]	$C_6H_5N{=}N$	364, 258	4.34, 4.10
15	C_3H_5	279	4.30
17	$COCH_3$	300, 243	4.20, 4.11
18	$COCH_3$, 3-OCH_3	296, 230	4.22, 4.15

[a] The spectra were measured in 95% ethanol, unless otherwise noted. [b] Methanol.

3-Acetoxy-1-phenylpyrazole (6).[1]—A solution of 3-hydroxy-1-phenylpyrazole (10 g, 0.062 mole) in 50 ml of acetic anhydride containing 2 ml of pyridine was heated for 0.5 hr on a steam bath, and then poured onto 200 g of ice. The precipitate which formed was collected and recrystallized from 50% aqueous ethanol; mp 66–67°, yield 8.8 g, 70%. The infrared spectrum displayed an ester carbonyl stretching frequency at 1760 cm^{-1}.

Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.3; H, 5.0; N, 13.9. Found: C, 65.1; H, 5.0; N, 14.1.

3-Hydroxy-4-nitro-1-phenylpyrazole (7).[1]—The procedure used was a modification of that described by Harries and Loth.[1] A solution of 240 ml of 2:1 water–nitric acid was added slowly to 3-hydroxy-1-phenylpyrazole (20 g, 0.125 mole). The mixture was stirred for an additional 2 hr at room temperature. The solid material was collected and washed with water. It was dissolved in ethanol and recrystallized three times from ethanol. The product was a yellow crystalline material, mp 194–196°, 9.5 g, 38%.

4-Amino-3-hydroxy-1-phenylpyrazole (8).—A deoxygenated solution of 3-hydroxy-4-nitro-1-phenylpyrazole (65.0 g, 0.32 mole) in 350 ml of 2 *N* aqueous sodium hydroxide was treated with 90% sodium dithionate (185 g, 0.96 mole) in three portions over 2 hr. Sufficient base was added to keep the reaction mixture basic. The reaction was exothermic. The reaction mixture was neutralized with hydrochloric acid, and the resulting precipitate was collected and washed with water. After drying, the yellowish brown solid weighed 46 g, mp 197–200° dec, yield 83%. A sample was recrystallized from ethanol–ethyl acetate; mp 205–207° dec. The infrared spectrum has bands at 3380, 3300, and from 3000 to 2400 cm^{-1}.

4-Bromo-3-hydroxy-1-phenylpyrazole (9).—To a stirred suspension of 3-hydroxy-1-phenylpyrazole (1.6 g, 0.01 mole) in 50 ml of carbon tetrachloride, bromine (1.6 g, 0.01 mole) in 25 ml of carbon tetrachloride was added slowly. An immediate reaction occurred as evidenced by the decoloration of the bromine solution and the evolution of an acidic vapor. The suspended material disappeared and a new precipitate formed slowly. It was collected and recrystallized from 50% aqueous ethanol; mp 194–196°, yield 2.1 g, 88%.

Anal. Calcd for $C_9H_7BrN_2O$: C, 45.2; H, 2.9; Br, 33.4; N, 11.7. Found: C, 45.2; H, 3.0; Br, 33.8; N, 11.5.

The bromination was also effected in good yield by using chloroform solutions of 3-hydroxy-1-phenylpyrazole and bromine.

4-Chloro-3-hydroxy-1-phenylpyrazole (10).—A solution of 3-hydroxy-1-phenylpyrazole (4.0 g, 0.025 mole) in 50 ml of chloroform was treated with sulfuryl chloride (3.4 g, 0.025 mole) in 25 ml of chloroform while the solution was warmed on a steam bath. Immediate evolution of hydrogen chloride and sulfur dioxide was noted. After standing for 15 min at room temperature, the solution was evaporated to dryness. The white residue was recrystallized three times from 50% aqueous ethanol, giving 4.2 g of white product, mp 179–181°, yield 86%.

Anal. Calcd for $C_9H_7ClN_2O$: C, 55.5; H, 3.6; N, 14.4. Found: C, 55.5; H, 3.4; N, 14.4.

3-Hydroxy-4-phenylazo-1-phenylpyrazole (11).—A diazotized solution of aniline (4.7 g, 0.05 mole) in dilute hydrochloric acid at 0–5° was added, with stirring, for 15 min to 3-hydroxy-1-phenylpyrazole (8.0 g, 0.05 mole) dissolved in 600 ml of 2.5% sodium carbonate solution. After an additional hour, the solution was acidified with dilute hydrochloric acid to give a yellow precipitate. It was collected, washed with water, air dried, and recrystallized twice from ethanol to give 6.0 g of yellow solid, mp 163–164°, yield 46%.

Anal. Calcd for $C_{15}H_{12}N_4O$: C, 68.2; H, 4.6; N, 21.2. Found: C, 68.5; H, 4.5; N, 20.9.

3-Hydroxy-1-phenyl-4-piperidinomethylpyrazole (12).—To a suspension of 3-hydroxy-1-phenylpyrazole (4.0 g, 0.025 mole) in 25 ml of water was added piperidine (2.3 g, 0.027 mole) and then, with thorough mixing, 5 ml of 30% aqueous formaldehyde. The pyrazole dissolved and a precipitate formed immediately. The precipitate was redissolved by adding to it 100 ml of ethanol and warming it for 1 hr on a steam bath. Upon chilling, a precipitate was formed, which was collected and recrystallized from ethanol; mp 208–209°, yield 4.3 g, 67%.

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.1; H, 7.4. Found: C, 69.8; H, 7.2.

Hydrogenolysis of 3-Hydroxy-1-phenyl-4-piperidinomethylpyrazole.—A solution of 3-hydroxy-1-phenyl-4-piperidinomethylpyrazole (1.2 g, 0.0047 mole) in 150 ml of ethanol was hydrogenated with 10% palladium on charcoal as catalyst. One equivalent of hydrogen was consumed. The catalyst was filtered off, and the brown solution was reduced in volume and cooled in an ice bath. The solid was collected, air dried, and recrystallized from ethanol–water; mp 210–212°, 0.60 g, 75%. The brown color of the solution was attributed to the liberated piperidine. The white solid had an infrared spectrum identical with that of 3-hydroxy-4-methyl-1-phenylpyrazole.

Reduction of 3-Hydroxy-4-methyl-1-phenylpyrazole.—A solution of 3-hydroxy-4-methyl-1-phenylpyrazole (8.7 g, 0.05 mole) and 130 ml of glacial acetic acid was hydrogenated in the presence of 1 g of rhodium-on-alumina catalyst. Approximately 3 equiv of hydrogen were used. The catalyst was filtered off, and the acetic acid was removed on a rotary film evaporator. The solid was recrystallized from ethanol and yielded 5.7 g of material, mp 160–171°. It was then chromatographed on basic alumina with acetone as an eluent. A white crystalline material was recovered from the chromatography and was recrystallized from ethanol; mp 185–186.5°, 3.0 g. The material was identified as 1-cyclohexyl-3-hydroxy-4-methylpyrazole from its spectral and analytical data.

Anal. Calcd for $C_{10}H_{16}N_2O$: C, 66.6; H, 8.9; N, 15.5. Found: C, 66.6; H, 8.8; N, 14.9.

3-Methoxy-1-phenylpyrazole (4).—A stirred mixture of 3-hydroxy-1-phenylpyrazole (50 g, 0.31 mole) in 500 ml of 0.6 *N* aqueous sodium hydroxide was treated dropwise at 5° with dimethyl sulfate (40 g, 0.31 mole). After the addition, the reaction mixture was warmed to reflux for 4 hr and allowed to cool overnight. The layers were separated and the aqueous portion was extracted with ether. The ether extracts were combined with the previous material and washed successively with water, dilute sulfuric acid, and water. The solution was dried over anhydrous calcium chloride. The ether was removed under reduced pressure, and the resulting orange liquid was vacuum distilled; bp 96–98° (0.35 mm), 24.4 g, yield 52% based on unrecovered starting material. The infrared spectrum (smear) of the liquid product revealed an absence of OH absorption.

The aqueous phase was acidified with dilute hydrochloric acid and the resulting solid was collected. It was recrystallized from ethanol; mp 153–155.5°, 4.5 g (3-hydroxy-1-phenylpyrazole, mp 154–155°).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 69.0; H, 5.8; N, 16.1. Found: C, 69.3; H, 5.8; N, 15.9.

3-Alloxy-1-phenylpyrazole (14).—A suspension of 3-hydroxy-1-phenylpyrazole (16 g, 0.10 mole), allyl bromide (13 g, 0.11 mole), and powdered anhydrous potassium carbonate (14 g, 0.10 mole) was allowed to reflux for 18 hr in 250 ml of dry acetone. The suspension was filtered and the acetone solution was evaporated to an oil. The residual oil was taken up in ether and washed with two 50-ml portions of 5% sodium hydroxide solution, water, and then dried. Upon evaporation of the ether, the residual oil was distilled under reduced pressure; bp 117–120° (0.15 mm), yield 13 g, 65%.

Anal. Calcd for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 72.2; H, 6.1; N, 14.0, 14.2.

Thermal Rearrangement of 3-Alloxy-1-phenylpyrazole.—3-Alloxy-1-phenylpyrazole (9.0 g, 0.047 mole) was heated in an oil bath to 265° for 1 hr under nitrogen. After cooling, the black liquid was dissolved in ether, which was extracted with 10% sodium hydroxide solution and washed with water; 1.6 g of ether-insoluble tar was present. The ether solution was dried over magnesium sulfate and removed under reduced pressure. A yellow oil was recovered (2.6 g) which was identified as starting ether by its infrared spectrum. The aqueous extracts were acidified with 6 *N* hydrochloric acid and extracted with ether. The ether solution was dried over magnesium sulfate and removed on the rotary film evaporator. A yellow solid, 4.9 g, was left which was recrystallized three times from ethanol–water, giving a white solid, mp 111–113°, 2.5 g, yield 39% based on unrecovered starting material. The yield of crude material was 77%.

Anal. Calcd for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.7; H, 5.9; N, 13.8.

The rearrangement was conducted again in N,N-diethyl-*m*-toluidine. A solution of 3-alloxy-1-phenylpyrazole (3.70 g, 0.018 mole) in 20 ml of N,N-diethyl-*m*-toluidine was heated under nitrogen at 250–255° for 7.5 hr. The reaction mixture was taken up in 4:1 ether–chloroform solution and extracted with 10% aqueous sodium carbonate, washed with water, and dried over magnesium sulfate. The ether–chloroform solution was removed under vacuum, leaving a deep red solution. The basic solution was acidified and extracted with ether. The ether was dried over magnesium sulfate, and removed on a rotary film evaporator. A yellow solid was recovered, 1.29 g. The remaining aqueous portion was extracted continuously with ether for 60 hr, but yielded no further material. The yellow solid was recrystallized from ethanol, mp 111–113°, 0.75 g. The infrared spectrum of the solid was identical with that of the product from the neat thermal rearrangement, 4-allyl-3-hydroxy-1-phenylpyrazole.

The red solution was distilled under vacuum, and N,N-diethyl-*m*-toluidine was collected; bp 72–79° (0.7 mm). The residue, 2.6 g, was dissolved in benzene and chromatographed on 60 g of neutral alumina, activity grade 1. A graded series of eluents was used in the following order: benzene, dichloromethane, 1:1 dichloromethane–ethyl acetate, ethyl acetate, 1:1 ethyl acetate–acetone, acetone, 10:1 acetone–methanol, and methanol. The first fraction yielded a small amount of the amine solvent, and 0.38 g of yellow oil, whose infrared spectrum was the same as that of the starting ether. A dark yellow-brown solid, 0.50 g, was recovered from later fractions. It was recrystallized from ethanol; mp 104–107°, yield 0.28 g. The infrared spectrum was the same as that for 4-allyl-3-hydroxy-1-phenylpyrazole. The total yield of this product was 1.79 g, 54% based on unrecovered starting material.

4-Acetyl-3-hydroxy-1-phenylpyrazole (17).—A stirred mixture of anhydrous aluminum chloride (48 g, 0.35 mole) in 50 ml of carbon disulfide, maintained at room temperature with a water bath, was treated with a slurry of 3-acetoxy-1-phenylpyrazole (6 g, 0.04 mole) in 200 ml of carbon disulfide. After the addition was completed, the reaction mixture was refluxed for 3 hr to evolve hydrogen chloride. The carbon disulfide was distilled, bp 47°. The residual paste was cooled in an ice bath and a solution of 40 ml of 6 *N* hydrochloric acid and 100 ml of ice water was added slowly to decompose the aluminum chloride salts. The mixture was stirred and then allowed to stand overnight. The solid was collected, washed with water, and air dried. It was recrystallized from ethanol; mp 175–177°, 2.9 g, yield 48%.

Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.3; H, 5.0; N, 13.9. Found: C, 65.2; H, 5.0; N, 13.6.

4-Acetyl-3-methoxy-1-phenylpyrazole (18).—A mixture of 4-acetyl-3-hydroxy-1-phenylpyrazole (1.0 g, 0.005 mole), anhydrous potassium carbonate (0.7 g, 0.005 mole), iodomethane (1.5 g, 0.011 mole), and 40 ml of dry acetone was refluxed for 24 hr. After cooling, 15 ml of water was added to the mixture; the solid was collected. The acetone in the filtrate was removed on the rotary evaporator. The resulting basic aqueous solution was extracted with ether. After drying over anhydrous magnesium sulfate, the ether was removed under vacuum. The residue was crystallized from ethanol–water solution; mp 133–134°, 0.35 g, yield 32%.

Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.6; H, 5.6; N, 13.0. Found: C, 66.2; H, 5.6; N, 12.8.

Friedel–Crafts Acetylation of 3-Methoxy-1-phenylpyrazole.—A solution of freshly distilled (from CaH_2) 3-methoxy-1-phenylpyrazole (22.0 g, 0.126 mole) and 75 ml of reagent grade carbon disulfide was mixed with aluminum chloride (40 g, 0.30 mole) while cooling. A small amount of charring occurred. The mixture was treated dropwise with fresh acetic anhydride (12.9 g, 0.126 mole). Following the addition, the reaction mixture was warmed for 2 hr, then cooled and added to 500 g of ice and 80 ml of hydrochloric acid.

The mixture was extracted with ether. An insoluble material was present at the interface. It was collected by filtration, and then dissolved in 10% sodium hydroxide. The basic solution was extracted with ether. The ether extracts were washed with water and then combined with the ether extracts of the original mixture and filtrate. The ether was dried over anhydrous magnesium sulfate and removed under reduced pressure, leaving a yellow oil (3.9 g, 0.022 mole). The infrared spectrum of the oil was identical with that of the starting 3-methoxy-1-phenylpyrazole. The basic solution was acidified with hydrochloric acid. The precipitate was collected and crystallized from ethanol. The first two crops, 2.75 g, mp 176–177°, were identical in melting point and infrared spectra with those of 4-acetyl-3-hydroxy-1-phenylpyrazole. The third crop appeared to be a mixture. It softened at 154° and melted at 174–177°, 0.40 g. The infrared spectrum had the bands formed in the spectra of 4-acetyl-3-hydroxy-1-phenylpyrazole and 4-acetyl-3-methoxy-1-phenylpyrazole. The mixture appeared to have equal amounts of each compound. The yield of 4-acetyl-3-hydroxy-1-phenylpyrazole (2.95 g, 0.015 mole) was 15%, and that of 4-acetyl-3-methoxy-1-phenylpyrazole (0.20 g, 0.001 mole) was 1%, based on unrecovered starting material. Finally, the original aqueous solution was reduced in volume and extracted continuously with ether for several days to give a solid whose infrared spectrum was identical with that of 3-hydroxy-1-phenylpyrazole (9.25 g, 0.058 mole), mp 147–151°, yield 60%.

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