32513-39-6; **28**, 32513-40-9; **30**, 32513-41-0; **31**, 32513-48-7; **42**, 32513-49-8; **43**, 32513-50-1; **44**, 32513-42-1; **32**, 32513-43-2; **33**, 32513-44-3; **34**, 32513-51-2; **45**, 723-87-5; **46**, 32513-53-4; **47**, 32513-45-4; **35**, 16511-38-9; **36**, 32513-47-6; **37**, 54-5; tropone, 539-80-0.

Lithiation of Substituted Pyrazoles. Synthesis of Isomerically Pure 1,3-, 1,3,5-, and 1,5-Substituted Pyrazoles

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Four syntheses of isomerically pure substituted pyrazoles are described (A–D). Using a lithiation procedure, 1,3,5- and 1,5-substituted pyrazoles can be obtained directly, *e.g.*, (A) 1,3-dimethyl-α-phenylpyrazole-5-methanol (**5**) and 3-methyl-α-phenyl-1-propylpyrazole-5-methanol (**11**), (B) 5-methyl-α-phenylpyrazole-1-ethanol (**8**), and (C) α-phenyl-1-propylpyrazole-5-methanol (**16**). (A) Treatment of a 2:1 mixture of 1,3-dimethylpyrazole (**2**) and 1,5-dimethylpyrazole (**7**) with *n*-butyllithium equivalent to less than the amount of **2** followed by the addition of benzaldehyde yields **5**. (B) Lithiation of pure **7** and reaction with benzaldehyde yields **8**. (C) Reaction of 1-propylpyrazole (**15**) with an equivalent of *n*-butyllithium followed by the addition of benzaldehyde yields **16**. Pure 1,3-disubstituted pyrazoles were synthesized in high yield in two steps. 5-Chloro-1-methyl-3-substituted pyrazoles lithiate on the 1-methyl group. Thus (D) 5-chloro-1,3-dimethylpyrazole (**3**) was allowed to react with *n*-butyllithium followed by benzaldehyde yielding 5-chloro-3-methyl-α-phenylpyrazole-1-ethanol (**17**). Catalytic hydrogenation of **17** yielded 3-methyl-α-phenylpyrazole-1-ethanol (**6**). Two generalizations have been drawn concerning the position of metalation: (1) a 1-methyl substituent on a pyrazole will undergo metalation with *n*-butyllithium to some extent; (2) a pyrazole with an unactivated 1 substituent and a 5-H undergoes metalation exclusively on the 5 position. Changes in the nmr spectra in $CDCl_3$ and DMSO-d_6 have been useful in differentiating isomeric 1,3- and 1,5-disubstituted pyrazoles. A pyrazolyl ketone, 1,3-dimethylpyrazol-5-yl phenyl ketone (**25**), was synthesized by addition of an excess of benzaldehyde to the corresponding pyrazolyl lithium reagent.

Most syntheses of 1-alkylpyrazoles result in mixtures of 1,3- and 1,5-disubstituted pyrazoles. From these mixtures, pure products are obtained with difficulty if at all.[1-6] One of us had earlier found the synthetic utility of 5-chloro-1,3-disubstituted 4-lithiopyrazoles (available by halogen–metal exchange).[7,8] Thus we decided to investigate the lithiation of some readily available unsymmetrical pyrazoles, pyrazole isomeric mixtures, and the conversion of the resulting lithio reagents to isomerically pure substituted pyrazoles. A recent publication on the "Lithiation of Five-membered Heteroaromatic Compounds" including the lateral metalation of 1,3,5,-trimethylpyrazole (**1**)[9] has led us to report some of our results with unsymmetrical pyrazoles.

Habraken and Moore[6] have prepared pure 1,3-dimethylpyrazole (**2**) in 20% yield by Raney nickel catalyzed hydrogenation of 5-chloro-1,3-dimethylpyrazole (**3**). These workers also reported the positions of the nmr signals for the methyl substituents. A number of reports on the lithiation of 1-methylpyrazoles have appeared.[5,10] These workers isolated products corresponding to lithiation at the 5 position. Our reinvestigation of the lithiation of 1-methylpyrazoles has shown that lithiation also occurs on the 1-(lateral) methyl group. The earlier workers had relied upon the melting points of the acids resulting from the carbonation of the lithio intermediates, since most of the expected acids were known. Stock, Donahue, and Amstutz have reported that the combination of sodium ethoxide, diethyl oxalate, and 1-methylpyrazole (**4**) reacts on the 1-methyl group.[11]

We chose to react the lithio intermediates with benzaldehyde because of the higher yields, greater stability, lower water solubility, experimental ease, and nonamphoteric nature of the expected products. These products would most likely be unknown; however, it was felt that the nmr studies of Habraken and Moore,[6] Finar and Mooney,[12] as well as those of Tensmeyer and Ainsworth[13] and others,[14a-e] would allow differentiation between 1,3-, 1,5-, and laterally substituted pyrazoles. Vapor phase chromatography was performed on samples of the crude hydrolyzed reaction mixtures as well as on the final products to avoid missing noncrystalline products.

The reaction of pure 1,3-dimethylpyrazole (**2**) with an equivalent of *n*-butyllithium followed by benzaldehyde resulted in a 90% yield of a 2:1 mixture of 1,3-dimethyl-α-phenylpyrazole-5-methanol (**5**) and 3-methyl-α-phenylpyrazole-1-ethanol (**6**).

Because of the yield reported by Habraken and Moore[6] in their preparation of **2**, we also reinvestigated the reaction of 4,4-dimethoxy-2-butanone with methyl-

(1) L. C. Behr, R. Fusco, and C. H. Jarboe in "Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings," Interscience, New York, N. Y., 1967, pp 6–8 and 13–16.
(2) T. L. Jacobs in "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1957, p 55.
(3) K. von Auwers and H. Hollmann, *Ber.*, **59**, 601, 1282 (1926).
(4) C. A. Rojahn, *ibid.*, **59**, 607 (1926).
(5) R. Hüttel and M. E. Schön, *Justus Liebigs Ann. Chem.*, **625**, 55 (1959).
(6) C. L. Habraken and J. A. Moore, *J. Org. Chem.*, **30**, 1892 (1965).
(7) H. A. DeWald and D. E. Butler, U. S. Patent 3,558,605 (Jan 1971).
(8) D. E. Butler and H. A. DeWald, *J. Org. Chem.*, **36**, 2542 (1971).
(9) R. G. Micetich, *Can. J. Chem.*, **48**, 2006 (1970).
(10) P. W. Alley and D. A. Shirley, *J. Amer. Chem. Soc.*, **80**, 6271 (1958).
(11) A. M. Stock, W. E. Donahue, and E. D. Amstutz, *J. Org. Chem.*, **23**, 1840 (1958).
(12) I. L. Finar and E. F. Mooney, *Spectrochim. Acta*, **20**, 1269 (1964).
(13) L. G. Tensmeyer and C. Ainsworth, *J. Org. Chem.*, **31**, 1878 (1966).
(14) (a) M. Cola and A. Perotti, *Gazz. Chim. Ital.*, **94**, 1268 (1964); (b) V. Papesch and R. M. Dodson, *J. Org. Chem.*, **30**, 199 (1965); (c) T. Yamanchi and J. A. Moore, *ibid.*, **31**, 42 (1966); (d) J. D. Albright and L. Goldman, *ibid.*, **31**, 273 (1966); (e) E. E. Zaev, V. K. Voronov, M. S. Shvartsberg, S. F. Vasilevsky, Yu. N. Molin, and I. L. Kotljarevsky, *Tetrahedron Lett.*, No. 5, 617 (1968).

hydrazine reported by Burness.[15] We have found that by changing the reaction time and work-up conditions a 93% yield of a 2:1 mixture of **2** and 1,5-dimethylpyrazole (**7**) can be obtained. More importantly, the reaction of this mixture with *n*-butyllithium and benzaldehyde equivalent to slightly less than the amount of **2** present results in the conversion of that isomer into **5** with little contamination by other products (93–99% of the total crude alcohol by vpc). The trace products are **6** and 5-methyl-α-phenylpyrazole-1-ethanol (**8**). We believe that this result can be best explained by the intermediacy of laterally metalated **7** metalating **2** in the 5 position.

Since **7** apparently does not undergo nuclear metalation[16] and 1-alkyl groups larger than methyl are not readily metalated (see synthesis D), we concluded that a 1-(higher alkyl)-3(5)-substituted pyrazole mixture would show preferential nuclear metalation at the 5 position of the 1,3 isomer. To test this hypothesis, a mixture of 3-methyl-1-propylpyrazole (**9**) and 5-methyl-1-propylpyrazole (**10**) (63–37% by vpc) was prepared by alkylation of 3-methylpyrazole.[15] Metalation of this mixture with *n*-butyllithium equivalent to both isomers followed by an equivalent of benzaldehyde resulted in a 95% yield of 3-methyl-α-phenyl-1-propylpyrazole-5-methanol (**11**). This series of reactions constitutes a versatile synthesis of isomerically pure 1,3,5-trisubstituted pyrazoles from the readily prepared but difficulty separable 1,3(5)-disubstituted pyrazole mixtures (A).

Metalation of the 2:1 mixture of **2** and **7** with *n*-butyllithium equivalent to the total amount of pyrazole present followed by reaction with benzaldehyde gave a 40:35:25 mixture of **5**, **6**, and **8** in 90% combined yield. The presence of **8** (easily identified in the nmr) led us to synthesize pure **7** by decarboxylation of 1,5-dimethylpyrazole-3-carboxylic acid.[3] Pure **7** when treated with *n*-butyllithium followed by benzaldehyde gave an 80% yield of 5-methyl-α-phenylpyrazole-1-ethanol (**8**). Addition of cyclohexanone to the lithio reagent gave 1-[(5-methylpyrazol-1-yl)methyl]cyclohexanol (**12**). Thus this sequence affords pure 1,5-disubstituted pyrazoles (B); it is limited by the relative difficulty of obtaining pure 1-methyl-5-substituted pyrazoles.

The metalation of 1-methylpyrazole[17] (**4**) was investigated in the same manner resulting in a 88% yield of a 66:34 mixture of 1-methyl-α-phenylpyrazole-5-methanol (**13**) and α-phenylpyrazole-1-ethanol (**14**). The variance of our results from some of those reported earlier on the metalation of 1-methylpyrazoles can be explained by the inverse of our reasons for choosing the reaction with benzaldehyde for derivatization of the metalated intermediates. The relative insolubility and crystallinity of the α-phenyl-substituted pyrazole-1-ethanols was fortuitous.

As in the case of **9** and **10**, we concluded that a 1-(higher alkyl)-pyrazole would show preferential metalation on the 5 position. To test this hypothesis, 1-propylpyrazole (**15**) was prepared by alkylation of pyrazole. Reaction and derivatization of **15** in the same manner resulted in an 81% yield of α-phenyl-1-propylpyrazole-5-methanol (**16**). Hence, this sequence also affords pure 1,5-disubstituted pyrazoles (C).

We also investigated the reaction of 5-chloro-1-methyl-3-substituted pyrazoles and found exclusive lateral metalation. Thus the reaction of **3** with an equivalent of *n*-butyllithium followed by reaction of the lithio intermediate with benzaldehyde gives a high yield of 5-chloro-3-methyl-α-phenylpyrazole-1-ethanol (**17**). The nmr spectrum of **17** clearly shows the presence of the 3-methyl group and a complex abc pattern for the 1-CH_2CH–, demonstrating the position of lithiation. Removal of the 5-chloro substituent in this product or in other derivatives by Pd-catalyzed hydrogenation gives in high yield isomerically pure 1,3-disubstituted pyrazoles (D). This sequence allows the synthesis of a wide variety of 1,3-disubstituted pyrazoles unavailable by other methods (see Experimental Section for examples **6**, **18**, **19**, **23**, **24**). This sequence is limited by the fact that 1-alkyl groups other than methyl react only under forcing conditions to give complex mixtures. Our results are summarized in Scheme I.

Two generalizations can be drawn from this work: (1) a 1-methyl substituent on a pyrazole will undergo metalation with *n*-butyllithium to some extent; (2) a pyrazole with an unactivated 1-substituent and a 5-H undergoes metalation with *n*-butyllithium exclusively on the 5 position.

We believe that the results of lithiation on 1-alkylpyrazoles can best be explained by the following as stated by Kost and Grandberg.[18] The 1-nitrogen atom of the *n*-substituted pyrazoles contributes its electron pair to the formation of an aromatic sextet, and thus assumes some cationic character which is balanced by the slight anionic character assumed by the remaining ring atoms. The second nitrogen atom in the ring (like that in pyridine and in contrast to pyrrole) contributes two electrons in the formation of σ bonds and one electron toward the aromatic sextet and retains an electron pair which gives it basic properties. Thus the inductive effect of the "cationic character" of the 1-nitrogen activates the 1-methyl to lithiation as well as the 5-hydrogen and the inductive effect is not transmitted to the 3-hydrogen. It is also possible that the free pair of electrons on the second nitrogen atom has an anionic inductive effect on the 3-hydrogen which reinforces the preference for lithiation at the five position. Finar and coworkers[19,20] have published molecular orbital calculations of 1-alkylpyrazoles using both the LCAO–MO and CNDO/2 methods. Their data correctly predict electrophilic substitution by bromine at the 4 position. As we interpret their results, the differences between the 3 and 5 positions of 1-methylpyrazole are too small to account for the difference in reactivity toward *n*-butyllithium. It is possible that the latter reaction is nucleophilic and these molecular orbital calculations are only accurate for electrophilic substitution.

The lithio reagents resulting from lateral or nuclear metalation undergo the typical reactions of alkyl-

(15) D. M. Burness, *J. Org. Chem.*, **21**, 97 (1956).

(16) This also explains the isolation of 1,3-dimethylpyrazole-5-carboxylic acid from presumably impure **7** (contaminated by **2**) by lithiation followed by carboxylation in the work of Hüttel and Schön.[5]

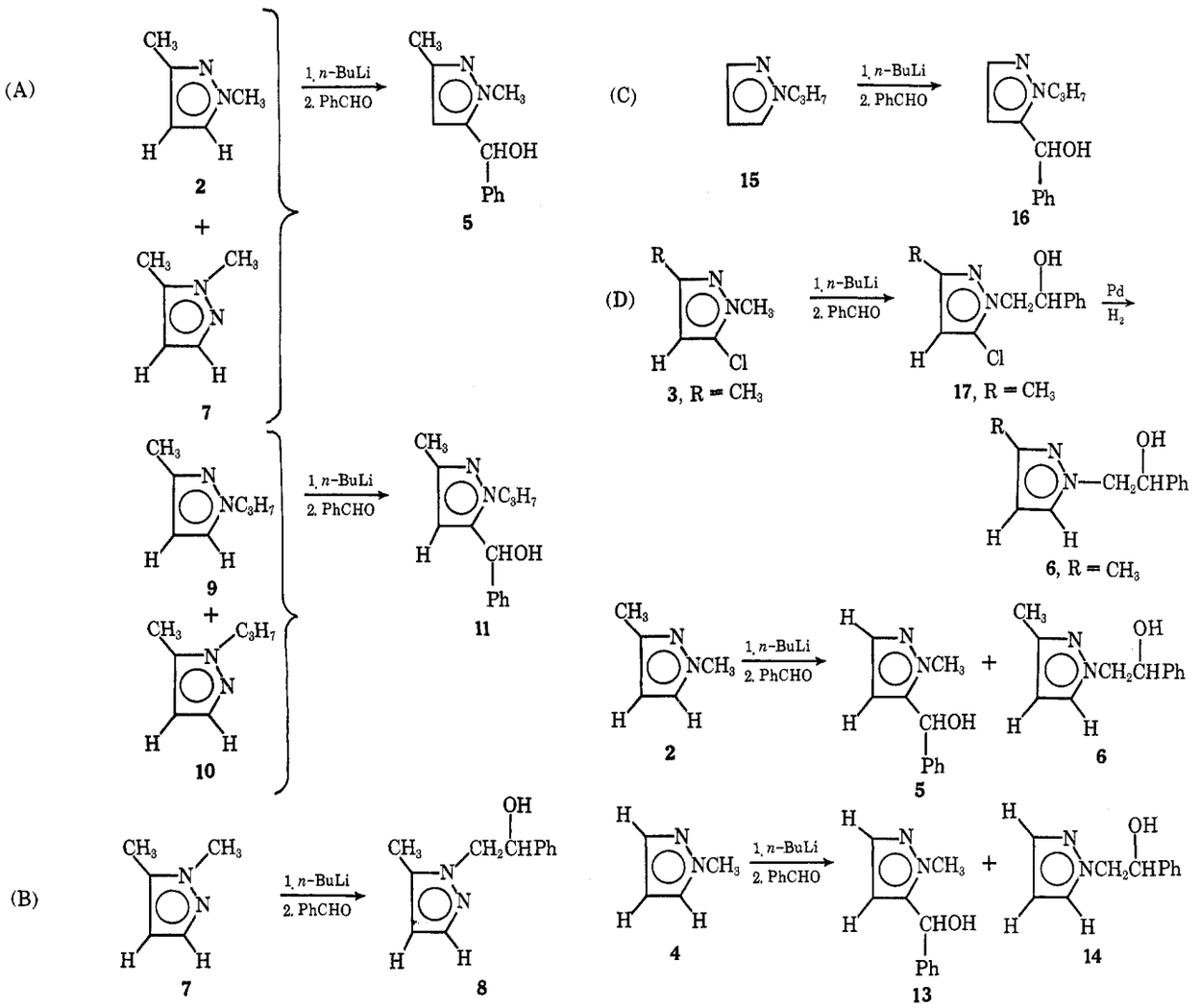
(17) I. L. Finar and G. H. Lord, *J. Chem. Soc.*, 3314 (1957).

(18) L. N. Kost and I. I. Grandberg, *Advan. Heterocycl. Chem.*, **6**, 389 (1966).

(19) I. L. Finar, *J. Chem. Soc. B*, 725 (1968).

(20) R. E. Burton and I. L. Finar, *ibid.*, 1692 (1970).

SCHEME I



and aryllithium compounds.[21] A number of examples have been included in the Experimental Section (**12**, **18**, **19**, **20**). Some of the products have been transformed into other substituted pyrazoles to demonstrate the versatility of these synthetic sequences (**22**, **23**, **24**, **25**).

The nmr spectra were used to establish the identity of the isomeric products from the metalation of all the pyrazoles investigated. Our results on the nmr spectra of **2** and **7** and mixtures are essentially identical with those of Habraken and Moore.[6] A potentially useful method of distinguishing the 1,3 and 1,5 isomers was found when the spectra in $CDCl_3$ were compared to those in DMSO-d_6. The doublet due to the C-5 pyrazole proton peak was shifted to a markedly lower field while the C-3 pyrazole proton peak is found at essentially the same position. Several examples of this spectral difference are recorded in the Experimental Section. The substituted α-phenylpyrazole-1-ethanols exhibit a complex abc pattern for the $-CH_2CH-$ protons, allowing easy identification.

An interesting experimental sidelight was the preparation of a pyrazolyl ketone, 1,3-dimethylpyrazol-5-yl phenyl ketone (**25**), by the slow addition of an excess of benzaldehyde to the corresponding lithio reagent.

(21) U. Schöllkopf in "Methoden Der Organischen Chemie," Vol 13/1, E. Müller, Ed., Georg Thieme Verlag, Stuttgart, 1970, p 170–224.

Experimental Section[22]

Reagents and Starting Materials.—The following were purchased (source) and used as received: benzaldehyde (Matheson Coleman and Bell); methylhydrazine and hydrazine (Olin); styrene oxide (Dow); *n*-butyllithium and phenyllithium (Lithium Corp. of America or Foote Mineral Co.); pyrazole (K & K). 5-Chloro-1,3-dimethylpyrazole (**3**), bp 156–157° (lit. bp 157°), was prepared as desribed by von Auwers and Niemeyer.[23] 5-Chloro-1-methyl-3-phenylpyrazole, mp 61–62° (lit. mp 62°), was prepared by the method of Michaelis and Dorn.[24] 3-Methylpyrazole, bp 109–110° (8 mm) (lit. bp 200–202°), was prepared

(22) Melting points (uncorrected) were taken in open capillary tubes in a Thomas–Hoover melting point apparatus. Ir spectra were determined on a Beckman IR-9 instrument and were consistent with the structures; nmr spectra with a Varian A-60 spectrometer at ambient temperature (Me_4Si); and vapor phase chromatograms on a Hewlett–Packard (F & M) Model 8 10 instrument with a hydrogen flame detector. The column was 4 ft × 0.25 in. glass and was packed with 3% OV-17 on 100/120 mesh Gas-Chrom Q. The column was programmed for 150–300° at 10°/min and the flash heater and detector were at 300°. Vpc analyses are reported if less than 100%. We are indebted to Mr. C. E. Childs and associates for microanalyses and chromatographic data, Mr. W. Pearlman for the catalytic hydrogenations and to Dr. J. M. Vandenbelt and associates for the spectral data. We also appreciate the multipound samples of acetoacetaldehyde 1-dimethyl acetal furnished by Henley & Co., New York, N. Y. The reactions were carried out in three-necked, round bottom flasks fitted with silicone sealed stirrer, thermometer, reflux condenser, and a pressure-equalized dropping funnel under a N_2 atmosphere. Yields are based on *n*-butyllithium charged unless otherwise indicated.

(23) K. von Auwers and F. Niemeyer, *J. Prakt. Chem.*, [2] **110**, 153 (1925).

(24) A. Michaelis and H. Dorn, *Justus Liebigs Ann. Chem.*, **352**, 163 (1907).

as described by Burness.[15] 1,5-Dimethylpyrazole-3-carboxylic acid, mp 173–176° (recrystallized from acetonitrile) (lit. mp 176°), was prepared as described by von Auwers and Hollmann.[3] This acid, mp 165–170°, contained 10% of the other isomer, shown by the presence of **2** after pyrolysis. 1-Methylpyrazole (**4**), bp 124–126° (lit. bp 124–125°),[17] was prepared by alkylation of pyrazole.

1,3-Dimethylpyrazole (2).[25]—A solution of 5-chloro-1,3-dimethylpyrazole (**3**) (120 g, 0.9 mol) in methanol (500 ml) was treated with 20% Pd/C (1 g) and hydrogen at 50 psi. Hydrochloric acid (100 ml, 1.17 mol) was added and the reaction mixture was concentrated at reduced pressure. The residue was treated with 50% NaOH (160 g, 2.0 mol) and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent and product were distilled through a Vigreux column to yield **2**: 80 g (92.5%); vpc shows a trace (less than 2%) of the starting material; bp 135–137° (lit. bp 136–139°);[3] nmr ($CDCl_3$) δ (TMS) 7.20 (1 H, doublet, 5-H), 5.93 (1 H, doublet, 4-H), 3.75 (3 H, singlet, 1-CH_3), 2.22 (3 H, singlet, 3-CH_3); nmr (DMSO-d_6) δ (TMS) 7.51 (1 H, doublet, 5-H), 6.00 (1 H, doublet, 4-H), 3.73 (3 H, singlet, 1-CH_3), 2.12 (3 H, singlet, 3-CH_3).

Anal. Calcd for $C_5H_8N_2$: C, 62.47; H, 8.39; N, 29.14. Found: C, 62.20; H, 8.62; N, 29.09. Picrate mp 135–136° (lit. mp 136°).[3]

1,3-Dimethylpyrazole (2) and 1,5-Dimethylpyrazole (7).[26]—Methylhydrazine (184 g, 4.0 mol) was added to stirred and cooled 4,4-dimethoxy-2-butanone (20–25°) (528 g, 4.0 mol). The mixture was stirred for 16 hr at room temperature. The mixture of *cis*- and *trans*-methylhydrazone was poured into hydrochloric acid (780 ml, 6 *N*) with stirring. All of the methanol was removed by distillation and the solution was treated with charcoal, filtered through a filter aid, and cooled. The mixture was made basic (50% NaOH) and extracted with ether. The extracts were dried ($MgSO_4$) and distilled through a Vigreux column to yield **2** and **7**, 351 g (91.5%), bp 130–155°. A vpc showed the mixture to contain 63.5% **2** and 36.5% **7**: nmr ($CDCl_3$) δ (TMS) 7.32 (1 H, doublet, 3-H), 7.20 (1 H, doublet, 5-H), 5.95 (2 H, doublet, 2 4-H), 3.77 (3 H, singlet, 1-CH_3 of the 1,3 isomer), 3.72 (3 H, singlet, 1-CH_3 of the 1,5 isomer), 2.23 (6 H, singlet, 2 3-CH_3); nmr (DMSO-d_6) δ (TMS) 7.51 (1 H, doublet, 5-H), 7.29 (1 H, doublet, 3-H), 6.00 (2 H, doublet, 2 4-H), 3.73 (3 H, singlet, 1-CH_3 of the 1,3 isomer), 3.69 (3 H, singlet, 1-CH_3 of the 1,5 isomer), 2.22 (3 H, singlet, 3-CH_3 of the 1,5 isomer), 2.12 (3 H, singlet, 3-CH_3 of the 1,3 isomer).

1,3-Dimethyl-α-phenylpyrazole-5-methanol (5).—A solution of **2** and **7** (99 g, 1.03 mol of a 64:36 mixture) in ether (1 l.) was stirred and treated dropwise with a *n*-butyllithium (0.5 mol) solution in heptane (350 ml). The mixture was stirred and refluxed for 30 min, a solution of benzaldehyde (63.6 g, 0.6 mol) in ether (250 ml) was added in a steady stream, and refluxing was continued for 15 min. Water (200 ml) was added, the layers were separated, and the aqueous layer was extracted with ether. The organic layer was dried ($MgSO_4$) and distilled to yield **5**: 92.5 g (91.5%); bp 133–135° (0.3 mm); nmr ($CDCl_3$) δ (TMS) 7.33 (5 H, singlet aromatic CH), 5.80 (2 H, singlet, –CH–, 4-H), 5.6–5.1 (1 H, broad singlet, OH), 3.60 (3 H, singlet, NCH_3), 2.04 (3 H, singlet, 3-CH_3); nmr (DMSO-d_6) δ (TMS) 7.34 (5 H, broad singlet, aromatic CH), 6.06 (1 H, broad doublet, OH), 5.8 (1 H, broad doublet, –CH–), 3.63 (3 H, singlet, NCH_3), 2.05 (3 H, singlet, 3-CH_3).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.86. Found: C, 71.35; H, 7.06; N, 13.63.

3-Methyl-1-propylpyrazole (9) and 5-Methyl-1-propylpyrazole (10).—A mixture of 3-methylpyrazole[15] (104 g, 1.27 mol), propyl bromide (187 g, 1.5 mol), and anhydrous potassium carbonate (527 g, 3.8 mol) in 2-butanone (700 ml) was refluxed with vigorous stirring for 72 hr. Tlc showed the absence of starting material. The mixture was filtered and treated with hydrochloric acid (150 ml, 1.75 mol) and concentrated *in vacuo*. The residue was dissolved in a minimum amount of water and washed with ether. The water layer was made strongly basic with 50% NaOH (160 g, 2.0 mol) and extracted with ether (four 1-l. portions). The combined extracts were dried ($MgSO_4$) and distilled through a Vigreux column to yield **9** and **10**: 125 g (78%); bp 51–58° (6 mm), 63–37% by vpc and nmr; nmr ($CDCl_3$) δ (TMS) 7.40 (1 H, doublet, 3-H), 7.25 (1 H, doublet, 5-H), 5.99 (2 H, doublet, 2 4-H), 3.99 (4 H, triplet, 2 NCH_2–), 2.26 (6 H, singlet, 2 3-CH_3), 2.25–1.55 (4 H, multiplet, 2 –CH_2–), 0.9 (6 H, triplet, 2 –CH_3); nmr (DMSO-d_6) δ (TMS) 7.52 (1 H, doublet, 5-H), 7.28 (1 H, doublet, 3-H), 5.97 (2 H, doublet, 2 4-H), 3.94 (4 H, triplet, 2 NCH_2–), 2.23 (3 H, singlet, 3-CH_3 of the 1,5 isomer), 2.12 (3 H, singlet of the 1,3 isomer), 2.11–1.4 (4 H, multiplet, 2 –CH_2–), 0.79 (6 H, triplet, 2 –CH_3).

Anal. Calcd for $C_7H_{12}N_2$: C, 67.69; H, 9.74; N, 22.57. Found: C, 67.95; H, 9.81; N, 23.85.[27]

3-Methyl-α-phenyl-1-propylpyrazole-5-methanol (11).—A solution of **9** and **10** (12.4 g, 0.1 mol) in ether (300 ml) was stirred and treated with a solution of *n*-butyllithium in heptane (0.1 mol). The mixture was stirred for 30 min and benzaldehyde (11.6 g, 0.11 mol) was added rapidly. The reaction was stirred for 2 min after the exothermic phase had subsided and water (100 ml) was added. The organic layer was dried ($MgSO_4$) and distilled to yield **11**: 14 g (95% based on the amount of **9** present); bp 115–117° (0.09 mm) (99.7% by vpc); nmr ($CDCl_3$) δ (TMS) 7.32 (5 H, singlet, aromatic CH), 5.88 (1 H, singlet, –CH–), 5.83 (1 H, singlet, 4-H), 4.9–4.3 (1 H, broad singlet, OH), 3.86 (2 H, triplet, NCH_2–), 2.10 (3 H, singlet, 3-CH_3), 2.09–1.15 (2 H, multiplet, –CH_2–), 0.77 (3 H, triplet, –CH_3).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.00; H, 7.88; N, 12.16. Found: C, 73.04; H, 8.02; N, 12.36.

1,5-Dimethylpyrazole (7).—1,5-Dimethylpyrazole-3-carboxylic acid[3] (28 g, 0.2 mol) was pyrolyzed at 240–255° to yield **7**: 17.5 g (91%); bp 157–158° (lit. bp 158°);[6] nmr ($CDCl_3$) δ (TMS) 7.33 (1 H, doublet, 3-H), 5.96 (1 H, multiplet,[28] 4-H), 3.74 (3 H, singlet, NCH_3), 2.23 (3 H, singlet, 5-CH_3); nmr (DMSO-d_6) δ (TMS) 7.26 (1 H, doublet, 3-H), 5.98 (1 H, multiplet, 4-H), 3.68 (3 H, singlet, NCH_3), 2.21 (3 H, singlet, 5-CH_3); **7** picrate mp 170–173° (lit. 172°)[3] (softens 160°).

5-Methyl-α-phenylpyrazole-1-ethanol (8).—A solution of **7** (10 g, 0.104 mol) in ether (350 ml) was treated with a solution of *n*-butyllithium (0.1 mol) in heptane (65 ml) with stirring and cooling (20–25°). The mixture was stirred for 30 min and benzaldehyde (12 g, 0.11 mol) was added. The mixture was stirred for 5 min and water (100 ml) was added. The mixture was cooled (0°) and the product was filtered and dried to yield **8**: 16 g (80%); mp 130–132°; nmr ($CDCl_3$) δ (TMS) 7.42 (1 H, doublet, 3-H), 7.28 (5 H, singlet, aromatic CH), 5.97 (1 H, multiplet, 4-H), 5.30–5.0 (1 H, multiplet, –CH–), 4.90–4.65 (1 H, broad singlet, OH), 4.28–4.06 (2 H, multiplet, –CH_2–), 2.04 (3 H, singlet, 5-CH_3); nmr (DMSO-d_6) δ (TMS) 7.31 (1 H, doublet, 3-H), 7.25 (5 H, singlet, aromatic CH), 5.92 (1 H, condensed multiplet, 4-H), 5.70–5.50 (1 H, broad singlet, OH), 5.15–4.75 (1 H, multiplet, –CH–), 4.25–4.00 (2 H, multiplet, NCH_2–), 2.02 (3 H, singlet, 5-CH_3).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.86. Found: C, 71.23; H, 7.04; N, 13.91.

1-Propylpyrazole (15).[29,30]—A mixture of sodium ethoxide (from 29 g, 1.2 g-atoms sodium metal), pyrazole (68 g, 1 mol), and ethanol (500 ml) was stirred and refluxed while propyl iodide (220 g, 1.29 mol) was added dropwise. The mixture was refluxed for 18 hr and cooled, hydrochloric acid (100 ml, 1.17 mol) was added, and the mixture was concentrated at reduced pressure. The residue was dissolved in a minimum of water, made strongly basic (NaOH), and extracted with ether (four 1-l. portions). The extracts were dried ($MgSO_4$) and distilled to yield **15**: 80 g (72%); bp 152–155° (760 mm) (lit. bp 166–167°);[30] nmr ($CDCl_3$) δ (TMS) 7.50 (1 H, doublet, 3-H), 7.37 (1 H, doublet, 5-H), 6.40–6.13 (1 H, multiplet, 4-H), 4.04 (2 H, triplet, NCH_2–), 2.15–1.58 (2 H, multiplet, –CH_2–), 0.97 (3 H, triplet, –CH_3); nmr (DMSO-d_6) δ (TMS) 7.66 (1 H, doublet, 5-H), 7.42 (1 H, doublet, 3-H), 6.33–6.16 (1 H, multiplet, 4-H), 4.04 (2 H, triplet, NCH_2–), 2.13–1.43 (2 H, multiplet, –CH_2–), 0.80 (3 H, triplet, –CH_3).

Anal. Calcd for $C_6H_{10}N_2$: C, 65.42; H, 9.15; N, 25.43. Found: C, 65.03; H, 9.13; N, 26.33.[27]

(25) This is merely a variation on the method of Habraken and Moore[6] resulting in a better yield. Most of the lower molecular weight alkylpyrazoles seem to codistill with many solvents, *i.e.*, benzene, heptane, methanol, and each other. Ether is the solvent of choice to minimize this problem; however, even this was always separated by distillation through a Vigreux column.

(26) Using conditions approximating those of Burness,[15] *i.e.*, 1 hr at 100°, only a 65% conversion (vpc) to the mixture of *cis*- and *trans*-methylhydrazone took place.

(27) This N analysis is anomalous.

(28) Others have reported this as a doublet.[6]

(29) R. G. Jones, *J. Amer. Chem. Soc.*, **71**, 3994 (1949).

(30) C. Alberti and G. Zerbi, *Farmaco, Ed. Sci.*, **16**, 527 (1961); *Chem. Abstr.*, **58**, 5660c (1963).

15 picrate had mp 96–98°.

Anal. Calcd for $C_{12}H_{13}N_5O_7$: C, 42.47; H, 3.87; N, 20.65. Found: C, 42.20; H, 3.83; N, 20.35.

α-Phenyl-1-propylpyrazole-5-methanol (16).—A solution of **15** (22 g, 0.2 mol) in ether (500 ml) was treated with a solution of *n*-butyllithium (0.2 mol) in heptane (140 ml) with stirring and cooling (20–25°). The mixture was stirred for 1 hr and benzaldehyde (21.2 g, 0.2 mol) was added rapidly. The mixture was stirred for 20 min and water (100 ml) was added. The organic layer was dried ($MgSO_4$) and distilled to yield **16**: 35 g (81%); bp 118–120° (0.15 mm); nmr ($CDCl_3$) δ (TMS) 7.29 (5 H, singlet, aromatic CH), 7.16 (1 H, doublet, 3-H), 5.93 (1 H, doublet, 4-H), 5.80 (1 H, singlet, –CH–), 5.16–4.66 (1 H, broad singlet, OH), 4.10–3.70 (2 H, multiplet, NCH_2–), 2.00–1.14 (2 H, multiplet, $-CH_2-$), 0.75 (3 H, triplet, $-CH_3$); nmr (DMSO-d_6) δ (TMS) 7.35 (5 H, singlet, aromatic CH), 7.31 (1 H, doublet partially superimposed on the aromatic singlet, 3-H), 6.23–5.74 (3 H, complex, 4-H, –CH–, OH), 4.16–3.84 (2 H, multiplet, NCH_2–), 2.00–1.24 (2 H, multiplet, $-CH_2-$), 0.74 (3 H, triplet, $-CH_3$).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.20; H, 7.46; N, 12.95. Found: C, 72.43; H, 7.51; N, 13.05.

5-Chloro-3-methyl-α-phenylpyrazole-1-ethanol (17).—A solution of *n*-butyllithium in heptane (0.5 mol) was added to a stirred, cooled (15–20°) solution of 5-chloro-1,3-dimethylpyrazole[23] (**3**) (60 g, 0.46 mol) in anhydrous ether (1 l.). The mixture was stirred at 15° for 30 min and a solution of benzaldehyde (53 g, 0.5 mol) in ether (100 ml) was added. The mixture was stirred at reflux for 5 min and cooled, and water (200 ml) was added. The organic layer was dried ($MgSO_4$) and concentrated, and the solid was triturated with petroleum ether (bp 30–60°) to yield **17**: 90 g (86%); mp 85–87°; nmr ($CDCl_3$) δ (TMS) 7.31 (5 H, singlet, aromatic CH), 5.98 (1 H, singlet, 4-H), 4.97–5.25 (1 H, quartet, –CH–), 4.07–4.45 (3 H, multiplet, $-CH_2-$ and OH), 2.20 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{12}H_{13}ClN_2O$: C, 60.89; H, 5.54; N, 11.83. Found: C, 60.69; H, 5.51; N, 11.83.

3-Methyl-α-phenylpyrazole-1-ethanol (6).—A solution of **17** (11.9 g, 0.05 mol) in methanol (120 ml) containing sodium acetate (4.3 g, 0.05 mol) was hydrogenated at 50 psi using 20% Pd/C (1 g) at 25°. The mixture was concentrated, dissolved in chloroform, and washed with dilute NaOH and water. The organic layer was dried ($MgSO_4$) and evaporated. The product was recrystallized (*n*-hexane) to yield **6**: 9.5 g (93%); mp 123–124°; nmr ($CDCl_3$) δ (TMS) 7.28 (5 H, singlet, aromatic CH), 7.17 (1 H, doublet, 5-H), 5.96 (1 H, doublet, 4-H), 5.2–4.9 (1 H, quartet, –CH–), 4.7–4.3 (1 H, broad singlet, OH), 4.3–4.04 (2 H, multiplet, $-CH_2-$); nmr (DMSO-d_6) δ (TMS) 7.45 (1 H, doublet, 5-H), 7.32 (5 H, singlet, aromatic CH), 5.96 (1 H, doublet, 4-H), 5.60 (1 H, doublet, OH), 5.15–4.88 (1 H, multiplet, –CH–), 4.12 (2 H, doublet, $1-CH_2-$), 2.14 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.86. Found: C, 71.30; H, 7.07; N, 13.78.

5-Chloro-α,α,3-triphenylpyrazole-1-ethanol (18).—A solution of 5-chloro-1-methyl-3-phenylpyrazole[24] (19.3 g, 0.10 mol) in ether (400 ml) was stirred, cooled (15–20°), and treated with *n*-butyllithium in heptane (0.10 mol). The mixture was stirred for 30 min and benzophenone (18.2 g, 0.10 mol) was added. After stirring for 5 min, water (100 ml) was added, and the organic layer was separated, dried ($MgSO_4$), and concentrated. The solid was recrystallized (methanol) to yield **18**: 34 g (90%); mp 107–109°; nmr ($CDCl_3$) δ (TMS) 7.9–7.2 (15 H, complex pattern, 15 aromatic CH), 6.7–6.55 (1 H, broad singlet, OH), 6.40 (1 H, singlet, 4-H), 4.85 (2 H, singlet, $-CH_2-$).

Anal. Calcd for $C_{23}H_{19}ClN_2O$: C, 73.71; H, 5.11; N, 7.47. Found: C, 73.49; H, 5.21; N, 7.37.

α,α,3-Triphenylpyrazole-1-ethanol (19).—**18** (12 g, 0.032 mol) was hydrogenated in the same manner as **17** to yield **19**, 9.5 g (87%) (after recrystallization from benzene–petroleum ether): mp 124–126°; nmr ($CDCl_3$) δ (TMS) 7.95–7.15 (16 H, complex, 15 aromatic CH and 5-H), 6.45–6.25 (2 H, doublet with broad singlet, 4-H and OH), 4.81 (2 H, singlet, $-CH_2-$).

Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.96; H, 6.00; N, 8.46.

1-[(5-Methylpyrazol-1-yl)methyl]cyclohexanol (12).—A solution of **7** (9.6 g, 0.1 mol) in ether (300 ml) was treated with a solution of *n*-butyllithium (0.1 mol) in heptane (65 ml). After refluxing for 15 min, the mixture was cooled to −78° and a solution of cyclohexanone (11 g, 0.11 mol) in ether (25 ml) was added dropwise. The mixture was allowed to warm to room temperature and water (50 ml) was added. The organic layer was dried ($MgSO_4$), concentrated, and distilled to yield **12**: 14 g (72%); bp 68–70° (0.15 mm); nmr ($CDCl_3$) δ (TMS) 7.40 (1 H, doublet, 3-H), 6.03 (1 H, multiplet, 4-H), 4.83–4.35 (1 H, broad singlet, OH), 3.93 (2 H, singlet, NCH_2–), 2.26 (3 H, singlet, $5-CH_3$), 2.0–0.95 (10 H, broad complex, five $-CH_2-$); nmr (DMSO-d_6) δ (TMS) 7.28 (1 H, doublet, 3-H), 5.98 (1 H, multiplet, 4-H), 4.47 (1 H, singlet, OH), 3.92 (2 H, singlet, NCH_2), 2.26 (3 H, singlet, $5-CH_3$), 2.0–0.83 (10 H, broad singlet, five $-CH_2-$).

Anal. Calcd for $C_{11}H_{18}N_2O$: C, 68.01; H, 9.34; N, 14.43. Found: C, 68.30; H, 9.56; N, 14.20.

1,3-Dimethyl-α-phenylpyrazole-5-ethanol (20).—A solution of **2** and **7** (192 g, 2 mol, 64–36%) in ether (2.5 l.) was stirred and cooled (−6 to 0°) and a solution of *n*-butyllithium (1 mol) in heptane (630 ml) was added dropwise over 2.5 hr. The pale yellow suspension was treated with a solution of styrene oxide (120 g, 1 mol) in ether (250 ml) (not exothermic). The mixture was refluxed for 2 hr after the addition of THF (1 l.). After cooling, water (250 ml) was added, and the organic layer was dried ($MgSO_4$) and distilled to yield **20**: 134 g (62%); bp 123–125° (0.1 mm); vpc shows 4% of a product assumed to be 1,3-dimethyl-β-phenylpyrazole-5-ethanol (**21**); nmr ($CDCl_3$) δ (TMS) 7.22 (5 H, singlet, aromatic CH), 5.77 (1 H, singlet, 4-H), 5.05–4.78 (2 H, multiplet superimposed upon a broad singlet, –CH– and OH), 3.26 (3 H, singlet, NCH_3), 3.1–2.75 (2 H, doublet, $-CH_2-$), 2.05 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.20; H, 7.46; N, 12.95. Found: C, 72.30; H, 7.56; N, 12.68.

5-Benzyl-1,3-dimethylpyrazole (22). Method A.—To a stirred solution of lithium aluminum hydride (20 g, 0.52 mol) in ether (600 ml) was added a solution of aluminum chloride (69 g, 0.52 mol) in ether–toluene (300–100 ml). The mixture was refluxed for 5 min and **5** (104 g, 0.52 mol) was added dropwise. The mixture was refluxed for 1 hr and with caution treated with water (20 ml), 25% NaOH (94 g), and water (52 ml). The slurry was filtered, concentrated, and distilled to yield **22**: 73 g (76%); bp 77–80° (0.1 mm); nmr ($CDCl_3$) δ (TMS) 7.50–6.90 (5 H, multiplet, aromatic CH), 5.80 (1 H, singlet, 4-H), 3.90 (2 H, singlet, $-CH_2-$), 3.60 (3 H, singlet, NCH_3), 2.21 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.37; H, 7.58; N, 15.04. Found: C, 77.07; H, 7.73; N, 15.02.

Method B.—A solution of **5** (66 g, 0.33 mol) in glacial acetic acid (500 ml) was hydrogenated at 50 psi using 20% Pd/C (10 g) as catalyst. The mixture was concentrated and distilled to yield **22**, 52 g (84%), bp 70–74° (90 μ); ir and nmr spectra identical with those from method A.

2-(5-Chloro-3-methylpyrazol-1-yl)acetophenone (23).[31]—A mixture of **17** (23.6 g, 0.1 mol), acetic anhydride (20.5 g, 0.2 mol), and dimethyl sulfoxide (300 ml) was heated on the steam bath for 18 hr and distilled at reduced pressure to yield **23**, 20 g (85%), bp 150–155° (0.25 mm), crystallized. Recrystallization from ether gave 15 g: mp 109–111°; nmr ($CDCl_3$) δ (TMS) 8.2–7.25 (5 H, complex pattern, aromatic CH), 6.11 (1 H, singlet, 4-H), 5.53 (2 H, singlet, NCH_2–), 2.25 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{12}H_{11}ClN_2O$: C, 61.41; H, 4.75; N, 11.93. Found: C, 61.38; H, 4.98; N, 12.08.

3-Methyl-1-phenethylpyrazole (24).—A mixture of **17** (71 g, 0.3 mol), sodium acetate (25 g, 0.3 mol), and 20% Pd/C (3 g) in glacial acetic acid (500 ml) was hydrogenated at 50 psi and 46°. The catalyst was filtered and the filtrate was concentrated *in vacuo* and dissolved in ether (1 l.). This solution was washed with dilute NaOH and water and dried ($MgSO_4$). Distillation yielded **24**: 51 g (91%); bp 118–120° (10 mm); nmr ($CDCl_3$) δ (TMS) 7.5–6.95 (5 H, multiplet, aromatic CH), 7.02 (1 H, doublet superimposed on the aromatic multiplet, 5-H), 5.92 (1 H, doublet, 4-H), 4.44–4.08 (2 H, multiplet, NCH_2–), 3.33–2.95 (2 H, multiplet, $-CH_2-$), 2.27 (3 H, singlet, $3-CH_3$); nmr (DMSO-d_6) δ (TMS) 7.42 (1 H, doublet, 5-H), 7.20 (5 H, singlet, aromatic CH), 5.94 (1 H, doublet, 4-H), 4.45–4.10 (2 H, multiplet, NCH_2–), 3.28–2.92 (2 H, multiplet, $-CH_2-$), 2.16 (3 H, singlet, $3-CH_3$).

Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.37; H, 7.58; N, 15.05. Found: C, 76.98; H, 7.79; N, 15.10.

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(31) J. D. Albright and L. Goldman, *J. Amer. Chem. Soc.*, **87**, 4214 (1965).

1,3-Dimethylpyrazol-5-yl Phenyl Ketone (25).[32]—A mixture of **2** and **7** (20 g, 0.208 mol, 63–37%) in ether (300 ml) was treated with a solution of *n*-butyllithium (0.1 mol) in heptane (65 ml). The mixture was stirred and refluxed for 30 min and benzaldehyde (32 g, 0.3 mol) was added dropwise. The amount of benzaldehyde used for the oxidation was added over a 2-hr period. Water (100 ml) was added and the layers were separated. The organic layer was evaporated and the residue was mixed with 48% HBr (25 ml) and heated on the steam bath overnight to hydrolyze any benzyl benzoate. The mixture was poured into excess dilute NaOH and extracted with ether (three 250-ml portions). The extracts were dried ($MgSO_4$) and distilled to yield **25**: 17 g (85%); bp 86–88° (0.1 mm); ir 1652 cm^{-1} (C=O); nmr ($CDCl_3$) δ (TMS) 8.00–7.30 (5 H, multiplet, aromatic CH), 6.44 (1 H, singlet, 4-H), 4.12 (3 H, singlet, NCH_3), 2.28 (3 H, singlet, 3-CH_3).

Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.93; H, 6.04; N, 14.00. Found: C, 72.14; H, 6.04; N, 13.75.

Results of Lithiation of Pure 2 with an Equivalent of *n*-Butyllithium Followed by Benzaldehyde.—A solution of **2** (9.6 g, 0.1 mol) in ether (250 ml) was stirred and treated with a solution of *n*-butyllithium in heptane (65 ml, 0.1 mol). The mixture was refluxed for 30 min, a solution of benzaldehyde (11.7 g, 0.11 mol) was added, and refluxing was continued for 30 min. Water (100 ml) was added and a vpc showed a 66:34 mixture of **5** and **6**. The organic layer was dried ($MgSO_4$) and distilled to yield **5** and **6**, 17 g (84%), bp 120–124° (0.2 mm). Fractional crystallization from methanol yielded **6**, 3 g, mp 120–122°, ir and nmr identical with those of **6** prepared by hydrogenation of **17**. In one experiment, phenyllithium gave the same mixture of products.

Results of Lithiation of the Mixture of 2 and 7 with a Full Equivalent of *n*-Butyllithium Followed by Benzaldehyde.—A solution of **2** and **7** (96 g, 1 mol), 66:34 mixture in ether (1.5 l.), was stirred, cooled (−20 to −30°), and treated with a solution of *n*-butyllithium (1 mol) in heptane (630 ml). The mixture was stirred for 30 min and treated with a solution of benzaldehyde (106 g, 1 mol) in ether (250 ml). After stirring for 30 min, water (200 ml) was added and the organic layer was dried ($MgSO_4$). A vpc on this solution showed a three-alcohol mixture (40:35:25) of **5**, **6**, and **8**. The organic layer was concentrated and allowed to stand overnight. A crop of crystals was separated. This was a mixture of **5** and **8**, 50 g, mp 109–120° (34:66) by nmr. The second crop, 21 g, mp 103–105°, was a 66:34 mixture of **5** and **8**. Distillation of the mother liquors yielded **5** and **6**, 110 g, bp 120–145° (0.2 mm), partially crystalline. The total weight of 181 g corresponds to a 90% conversion of the starting pyrazoles.

Results of the Lithiation of 1-Methylpyrazole (4).[17]—A solution of **4** (16 g, 0.2 mol) in ether (300 ml) was treated with a solution of *n*-butyllithium in heptane (0.2 mol). The mixture was stirred for 90 min and benzaldehyde (21.2 g, 0.2 mol) was added at 10°. Water (100 ml) was added and the organic layer was separated and dried ($MgSO_4$). The product was crystallized from benzene–petroleum ether to yield 20 g (62.5%), mp 88.5–92°. A vpc indicated a 69:31 mixture. An nmr indicated a mixture of 1-methyl-α-phenylpyrazole-5-methanol (**13**) and α-phenylpyrazole-1-ethanol (**14**). Fractional crystallization from ether yielded **13**: 1.6 g; mp 106.5–110°; vpc 100%; nmr ($CDCl_3$) δ (TMS) 7.30 (5 H, singlet, aromatic CH), 7.18 (1 H, doublet, 3-H), 5.96 (1 H, doublet, 4-H), 5.88 [1 H, doublet (singlet after a D_2O wash), -CH-], 4.86 [1 H, doublet (removed by D_2O wash), OH], 3.59 (3 H, singlet, NCH_3); nmr (DMSO-d_6) 7.35 (5 H, singlet, aromatic CH), 7.28 (1 H, doublet, 3-H), 6.2–5.8 (3 H, a multiplet superimposed on a doublet at 5.92, 4-H, -CH-, OH), 3.72 (3 H, singlet, NCH_3). An nmr on the crude product (mp 88.5–92°) clearly showed the typical abc pattern for the α-phenylpyrazole-1-ethanol (**14**) as well as the multiplet at 6.20–6.00 for the 4-H in a 1-substituted pyrazole.

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.42; N, 14.88. Found: C, 70.15; H, 6.57; N, 15.07.

The mixture was sublimed and the sublimated compound was recrystallized twice from chloroform to yield **14**: 0.95 g; mp 123–127°; vpc 100%; nmr ($CDCl_3$) δ (TMS) 7.47 (1 H, doublet, 3-H), 7.29 (5 H, singlet, aromatic CH), 7.24 (1 H, doublet, 5-H), 6.19 (1 H, triplet, 4-H), 5.18–4.92 (1 H, multiplet, -CH-), 4.43–3.93 (3 H, multiplet superimposed on singlet at 4.27, OH, $-CH_2-$); nmr (DMSO-d_6) δ (TMS) 7.56 (1 H, doublet, 5-H), 7.41 (1 H, doublet, 3-H), 7.29 (5 H, singlet, aromatic CH), 6.17 (1 H, triplet, 4-H), 5.63 (1 H, doublet, OH), 5.14–4.80 (1 H, multiplet, -CH-), 4.23 (2 H, doublet, $-CH_2-$).

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.42; N, 14.88. Found: C, 70.00; H, 6.40; N, 14.77.

Registry No.—**2**, 694-48-4; **5**, 32492-99-2; **6**, 32493-00-8; **7**, 694-31-5; **8**, 32493-01-9; **9**, 32493-02-0; **10**, 32493-03-1; **11**, 32493-04-2; **12**, 32493-05-3; **13**, 32500-65-5; **14**, 32500-66-6; **15**, 32500-67-7; **15** picrate, 32544-40-4; **16**, 32500-68-8; **17**, 32500-69-9; **18**, 32500-70-2; **19**, 32500-71-3; **20**, 32500-72-4; **22**, 32500-73-5; **23**, 32500-74-6; **24**, 32500-75-7; **25**, 32500-76-8.

(32) This constitutes a synthesis of ketones from lithium reagents simply by adding an excess of aldehyde. This resembles a variation of the Oppenauer oxidation and Meerwein–Pondorff–Verley reduction using lithium as the metal. Marshall[33] reported using phenyl Grignard reagent and benzaldehyde to prepare benzophenone.

(33) J. Marshall, *J. Chem. Soc.*, **105**, 527 (1914).