Pyrazoles by Dealkylation of Pyrazolium Salts

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A rapid, convenient conversion of 1,2-dimethylpyrazolium salts (**1**) to 1-methylpyrazoles (**2**) is accomplished in piperidine or 3-methylpiperidine at temperatures ≥ 106°. This demethylation represents a particularly useful procedure for the synthesis of 3- and 5-substituted aminopyrazoles, which are not readily obtainable by other methods. The 50:50 mixture of piperidinopyrazole isomers **2b** can be obtained directly by treating 3-chloro-1,2-dimethyl-5-phenylpyrazolium iodide (**3b**) with piperidine in ethanol at 106°.

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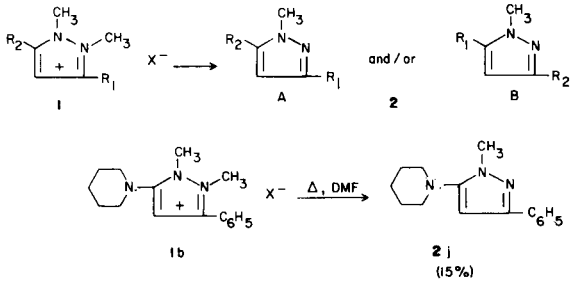
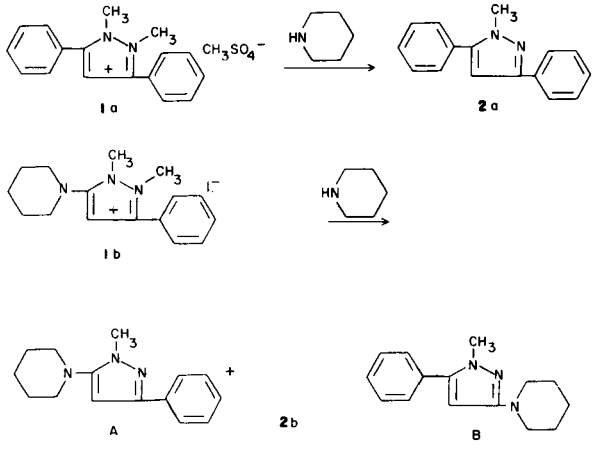
In the course of an investigation of pyrazolium salts as herbicical agents (1), we required a procedure for the demethylation of 1,2-dimethylpyrazolium salts (**1**) to a 1-methylpyrazoles (**2**). Pyrolytic dealkylation of pyrazolium salts (**1**) has received considerable attention (*e.g.*, 2a,b). Heating pyrazolium salts alone, however, requires reaction temperatures of 200° and greater and is often accompanied by extensive decomposition. Pyrolytic demethylation of *N*-methylpyridinium and *N*-methylquinolinium iodides has been achieved (3) by simply heating them under reflux in dimethylformamide. This procedure, when applied to 1,2-dimethyl-3-phenyl-5-piperidinopyrazolium iodide (**1b**) gave after extensive purification by dry column chromatography (4) only a 15% yield of 1-methyl-3-phenyl-5-piperidinopyrazole (**2j**). A demethylation process should involve the displacement of the methyl group of a quaternary salt by either counterion, as in the above pyrolyses, or by an external nucleophile. Posner and Ting (5) summarized demethylation processes of *N*-methyl quaternary ammonium salts with external nucleophiles. Effective reagents include lithium aluminum hydride (6a,b), lithium iodide (6c), and lithium triethylborohydride (6d), although ester groups present do not usually survive these conditions. Cuprous phenylmercaptide in anhydrous pyridine (5) may be used in the presence of ester groups, but product isolation from pyridine and the resulting thioanisole is somewhat tedious.



We have found that piperidine, serving as an external nucleophile and as solvent at reflux temperature, 106° is an effective and convenient demethylating agent for 1,2-dimethylpyrazolium compounds (1). Yields in many cases were almost quantitative (Table II) and product isolation was simply accomplished by cooling the reaction solution, filtering off the piperidine salt and evaporation of the solvent to give the 1-methylpyrazole (**2**). In this manner, 1,2-dimethyl-3,5-diphenylpyrazolium methyl sulfate (**1a**) gave after heating under reflux with piperidine for 16 hours a 97% isolated yield of 1-methyl-3,5-diphenylpyrazole (**2a**). Two pyrazole isomers are possible if the 3-and 5-positions of the pyrazolium ring bear different substituents. Surprisingly, in those examples examined, a constant 50:50 isomer ratio was maintained, which was invariant with the nature of the R_1 and R_2 substituents. The functional groups carboethoxy (**1d,e**) and methoxy (**1c**) survived piperidine *N*-dealkylation conditions, whereas ethanolamine (7), sometimes employed in the *N*-dealkylation of quaternary salts, is reported to cause the *O*-demethylation of methoxy groups (5). Most of the compounds reported in Table II were isolated and analyzed as the isomer mixture. The nmr spectra showed two discrete chemical shifts (deuteriochloroform) for *N*-methyl groups in the range of δ 3.56-3.85 and for the 4-CH proton of the pyrazole at δ 5.60-6.54. The isomers were resolved at 225° by gas liquid chromatography.



Chromatographic separation of pyrazole isomers **2g**, which were obtained from the reaction of 3-methylpiperidine and 1,2-dimethyl-3-phenyl-5-(3-methylpiperidino)-pyrazolium chloride (**1g**), was achieved on a dry-packed silica gel column using benzene as the eluent. The first

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fraction eluted, obtained in 25% yield, contained the 3-methyl-1-(1-methyl-3-phenyl-5-pyrazolyl)piperidine isomer (**2h**) with nmr (deuteriochloroform): δ 7.40 (m, 5, phenyl), 5.96 (s, 1, -CH=) and 3.6 (s, 3, NCH_3). The following intermediate fractions contained unresolved pyrazole isomer mixtures of **2g** in differing proportions, but fraction 5, obtained in 14% yield, contained the 3-methyl-1-(1-methyl-5-phenyl-3-pyrazolyl)piperidine isomer (**2i**) with nmr (deuteriochloroform): δ 7.12 (s, 5, phenyl), 5.62 (s, 1, -CH=) and 3.6 (s, 3, NCH_3).

Our assignment of structures **2i** and **2h** is based upon the proton magnetic resonance studies of Tensmeyer and Ainsworth (8) on phenylpyrazoles. They concluded that protons on a phenyl group attached to a pyrazole ring appear as a multiplet unless a substituent is α to the phenyl. Under the latter condition the phenyl proton resonance is a singlet. In addition van Vyve and Viehe (9) describe an unequivocal synthesis of 5-dimethylamino-1-methyl-3-phenylpyrazole from dichloromethylenedimethylammonium chloride and acetophenone methylhydrazone. The nmr of this product shows the phenyl protons as multiplets: δ 7.1 and 7.9. Multiplet resonances occur when *ortho*-phenyl protons reside in or near the plane of the pyrazole ring, but substitution of methyl α to the phenyl group reduces the coplanarity of the phenyl and pyrazole rings. The ultraviolet spectrum of **2i** shows a hypsochromic shift relative to that of **2h** as expected from steric inhibition of resonance and in agreement with previous observations in analogous cases (10).

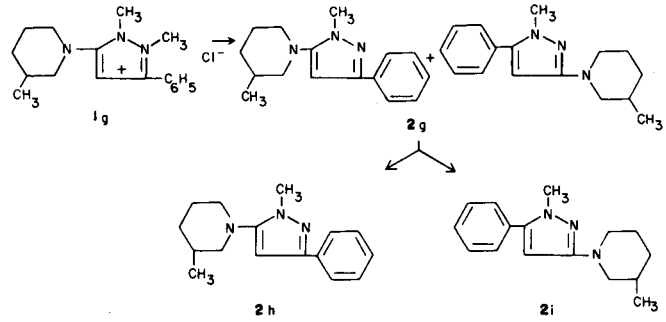
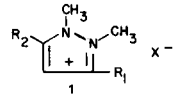
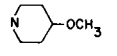
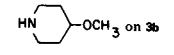
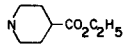
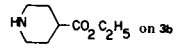
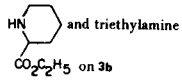
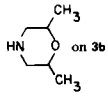
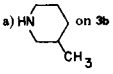


Table I

1,2-Dimethylpyrazolium Salts



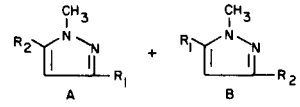
1

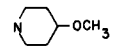
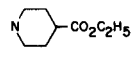
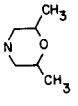
Compound No.	R_1	R_2	X	Reagents	Yield (%)	M.p. °C	Crystallization Solvent		Analysis (%) (a) Calcd.	Found
1a	C_6H_5	C_6H_5	CH_3SO_4	dimethyl sulfate on **2a**	51	146-148	acetone	C	59.98	59.87
								H	5.59	5.60
								N	7.77	7.66
								S	8.39	8.93
1b	C_6H_5		I	a) piperidine on **3a** b) potassium iodide	58	179-180	—	C	50.14	49.74
								H	5.80	5.65
								N	10.96	10.91
1c	C_6H_5		I	 on 3b	44	177-177.5	ethanol	C	49.40	49.26
								H	5.85	5.85
								N	10.17	10.20
1d	C_6H_5		I	 on 3b	87	52-55	ethanol	C	50.12	49.95
								H	5.76	5.90
								N	9.23	9.16
1e	C_6H_5		I	 and triethylamine	35	oil	—	-hygroscopic- (b)		
1f	C_6H_5		I	 on 3b	92	100-111	ethyl acetate	C	48.34	48.68
								H	5.91	5.98
								N	9.95	10.02
								(¼ H_2O)		
1g	C_6H_5		Cl	 on 3b	13	77-78	acetone-hexane	C	65.96	65.60
								H	7.98	8.01
								N	13.58	13.46
				b) crystallization				(¼ H_2O)		
1h	C_6H_5		CH_3SO_4	as **1g**	67	syrup	—	C	56.68	56.39
								H	7.14	7.15
								N	11.02	11.20
1k	C_6H_5	C_6H_5	ClO_4	perchloric acid on **1a**	99	183-184	water washed	C	58.75	58.68
								H	4.92	4.99
								N	8.05	8.11

(a) Most of these pyrazolium salts were hygroscopic; analytical samples were dried *in vacuo* at 56°. (b) Analysis unsatisfactory; converted to **2e**, Table II.

Table II

Pyrazoles (2) by the Demethylation of 1,2-Dimethylpyrazolium Salts (1)

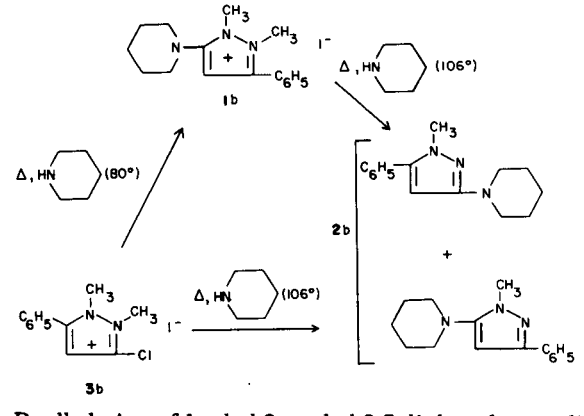


Compound No.	R_1	R_2	Procedure	Yield (%)	M.p. °C	Isomer Distribution (c) A	B	Nmr (Deuteriochloroform) δ 4-CH	δ N-CH_3		Analysis (%) Calcd.	Found
2a	C_6H_5	C_6H_5	piperidine on **1a**	98	59-60 (a)			6.54	3.85			
			piperidine on **1j**	97 (b)	59.60							
2b		C_6H_5	piperidine on **3b**	100	oil	50	50 (c,d)	5.80, 6.10	3.74, 3.80	C	72.25	72.40
			piperidine on **1b**	95	oil	50	50 (c)			H	8.09	8.05
										N	16.85	16.37
										(½ H_2O)		
2c		C_6H_5	piperidine on **1c**	78	oil	50	50 (d)			C	70.82	70.65
										H	7.80	7.89
										N	15.49	15.00
2d		C_6H_5	piperidine on **1d**	49	oil	50	50 (c)	5.60, 6.00	3.56, 3.59	C	68.98	69.08
										H	7.40	7.41
										N	13.41	13.35
2e		C_6H_5	piperidine on **1e**	82	oil	50	50 (c)	5.66, 6.22	3.61, 3.72	C	68.98	68.75
										H	7.40	7.31
										N	13.41	13.20
2f		C_6H_5	piperidine on **1f**	94	oil	50	50 (c)	5.70, 6.10	3.66, 3.70	C	70.82	70.61
										H	7.80	8.04
										N	15.49	15.68
2g		C_6H_5	piperidine on **1g**	99	oil	50	50 (c,d)	5.84, 5.90	3.56, 3.60	C	75.25	75.03
										H	8.29	8.54
										N	16.46	16.27

(a) Lit. (19) m.p. 68°. (b) Isolated by pouring the reaction mixture into 2*N* hydrochloric acid and collecting the solid by filtration. (c) Isomer distribution measured by intensity of the 4-CH and N-CH_3 chemical shift peaks in the nmr spectrum (± 5%). (d) Isomer distribution determined using gas liquid chromatography on 5% OV-225 on 100/120 Gas Chrom O at 225°, by measuring the peak areas (± 5%).

Demethylation of 1,2-dimethylpyrazolium salts (**1**) by the piperidine procedure was sensitive to the reaction temperature. At the boiling point of 106° demethylation was rapid, but at 80° no demethylation occurred. This temperature differential was the basis for the preparation of 5-piperidinopyrazolium compounds (**1b,c,d,e,g,h**) by the reaction of the appropriate piperidine (or 2,6-dimethylmorpholine for **1f**) with 3-chloro-1,2-dimethyl-5-phenylpyrazolium methyl sulfate or iodide (**3a,b**) in ethanol at 80°. Conducting this reaction at 106° in piperidine gave pyrazole (**2b**) directly. The high reactivity towards nucleophiles of the chlorine group of 3-chloropyrazolium salts has been noted previously (11) for 3-chloro-1,5-dimethyl-2-phenylpyrazolium salts. This is in contrast with the known inertness of halopyrazoles towards replacement reactions (12).

This ammonolysis-demethylation procedure represents an attractive high yield route to relatively inaccessible 3-(and 5-) substituted amino 5- (and 3-) phenylpyrazoles (**2b-g**) (9 and 13). Both possible pyrazole isomers are formed in high yield when the starting material is unsymmetrically substituted ($R_1 \neq R_2$) and chromatographic separation can be achieved if required by silica gel dry column chromatography. Isomer characterization is accomplished using the proton nmr assignment rules proposed by Tensmeyer and Ainsworth (8).



Dealkylation of 1-ethyl-2-methyl-3,5-diphenylpyrazolium ethyl sulfate (**6**) with piperidine gave a mixture consisting of 87% 1-ethyl-3,5-diphenylpyrazole (**5**) and 13%

1-methyl-3,5-diphenylpyrazole (**2**). This result is in agreement with other reports on pyrolytic dealkylations (13) in which *N*-demethylation is more facile than *N*-deethylation.

No attempt was made to evaluate the role of the counterion in the piperidine *N*-demethylation process, but it appeared to be equally applicable to pyrazolium compounds with chloride, bromide, iodide, methyl sulfate, ethyl sulfate or perchlorate as counterions.

EXPERIMENTAL

All melting points are uncorrected. Microanalyses were performed at either the Analytical Section, Lederle Laboratories, American Cyanamid Company, Pearl River, NY, or by Galbraith Laboratories, Knoxville, TN. Infrared spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer Model 317 and nmr spectra were recorded on a Varian A-60 or Perkin-Elmer R32 spectrometer. Chemical shifts are reported as relative to TMS, using the following abbreviations: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Gas chromatography was accomplished on a Hewlett-Packard Model 7610-A instrument. Column chromatography was run on Woelm Brockmann activity III silica gel for dry column chromatography supplied by ICN Pharmaceuticals.

The following compounds were prepared using procedures reported in the literature: 5-chloro-1-methyl-3-phenylpyrazole (**4**), m.p. 62-62.5°, (lit. (14), m.p. 62°); 3,5-diphenylpyrazole, m.p. 199-200° (lit. (15), m.p. 199-200°); 4-methoxypiperidine, b.p. 62-63°/23 mm (lit. (16), b.p. 66°/10 mm); ethyl pipecolate hydrochloride, m.p. 202-203° (lit (17), m.p. 202-203°).

1,2-Dimethyl-3,5-diphenylpyrazolium Methyl Sulfate (**1a**) and 1,2-Dimethyl-3,5-diphenylpyrazolium Sulfate 1:1 (**1j**).

Dimethyl sulfate (2.8 g., 0.022 mole) was added dropwise to a stirred solution of 1-methyl-3,5-diphenylpyrazole (**2a**, 5 g., 0.21 mole) in xylene (30 ml.) at 60°. After heating to 100° for 6 hours, the reaction mixture was cooled and the solid which precipitated was collected. The solid was slurried with molecular sieve-dried acetone (35 ml.) and filtered to give 3.90 g (51%) of 1,2-dimethyl-3,5-diphenylpyrazolium methyl sulfate (**1a**), m.p. 146-148°; nmr (deuteriodimethylsulfoxide): δ 3.34 (s, 3, CH_3SO_4), 4.08 (s, 6, $\dot{N}$-CH_3 × 2), 7.28 (s, 1, 4-CH of pyrazole), 7.67 (s, 10, C_6H_5 × 2).

The acetone filtrate was reduced in volume to give 1.2 g. (17%) of 1,2-dimethyl-3,5-diphenylpyrazolium sulfate 1:1 (**1j**), m.p. 188-189.5°; nmr (deuteriodimethylsulfoxide): δ 4.13 (s, $\dot{N}$-CH_3 × 2), 7.28 (s, 1, 4-CH of pyrazole), 7.68 (s, 10, C_6H_5 × 2). This phenyl singlet is in contrast with the multiplet phenyl signals for the starting material (**2a**).

Anal. Calcd. for $C_{17}H_{18}N_2O_4S$: C, 58.94; H, 5.23; N, 8.08; S, 9.26. Found: C, 59.12; H, 5.22; N, 7.92; S, 9.44.

1,2-Dimethyl-3,5-diphenylpyrazolium Perchlorate (**1k**).

Ice cold 10% perchloric acid was added to a stirred aqueous solution of 1,2-dimethyl-3,5-diphenylpyrazolium methyl sulfate (**1a**, 5 g., 0.0139 mole). A white precipitate was formed immediately and was filtered off, washed with ice-cold water, and dried *in vacuo* at 40° to give 31.8 g. (98%) of solid, m.p. 183-184° [lit. (17) gives m.p. 184-185°]; ir: ν (cm^{-1}) 1090 (ClO_4).

1,2-Dimethyl-3-phenyl-5-piperidinopyrazolium Iodide (**1b**).

Piperidine (2.56 g., 0.03 mole) was added to a stirred suspension of 3-chloro-1,2-dimethyl-5-phenylpyrazolium methyl sulfate (**3a**, 4.77 g., 0.015 mole) in absolute ethanol (30 ml.). The mixture became homogeneous on heating to 75°. After 4 hour's heating under reflux, the solution was filtered and evaporated to a brown oil, which was dissolved in water, washed with ether and then extracted with chloroform (3 × 100 ml.). The chloroform layer was evaporated to give an oil, which was redissolved in water and treated with a saturated potassium iodide solution. A copious precipitate was formed and collected on a filter pad. After ice water washing the solid was dried to give 3.37 g. (58%) with m.p. 179-180° and nmr (deuteriodimethylsulfoxide): δ 1.65 (m, 6, $(CH_2)_3$), 3.20 (m, 4, CH_2-N-CH_2), 3.93 (s, 6, $\dot{N}$-CH_3 × 2), 6.75 (s, 1, 4-CH of pyrazole), 7.77 (s, 5, C_6H_5).

1,2-Dimethyl-3-(3-methylpiperidino)-5-phenylpyrazolium Chloride (**1g**) and 1,2-Dimethyl-3-(3-methylpiperidino)-5-phenylpyrazolium Methyl Sulfate (**1h**).

(a)

3-Methylpiperidine (950 g., 9.5 moles) was added all at once to a well stirred suspension of 3-chloro-1,2-dimethyl-5-phenylpyrazolium methyl sulfate (**3a**, 1.43 kg., 4.5 moles) in 3B ethanol (6 ℓ.). Immediately the reaction mixture became homogeneous and the exothermic reaction was allowed to attain 65°. After standing at room temperature overnight, the solution was heated under reflux for 8 hours, cooled, the ethanol removed under reduced pressure and the residual syrup dissolved in aqueous saturated sodium bicarbonate solution. The aqueous layer was extracted first with toluene, which was discarded, then chloroform, and this layer after drying over sodium chloride gave on removal of the chloroform a brown syrup (1.15 kg.). Benzene was added and the solid which precipitated was removed by filtration and recrystallized from hexane to give a white powder (200 g., 13%) as a dihydrate, m.p. 70.5-72°; nmr (deuteriodimethylsulfoxide): δ 1 (d, 3, CH_3), 1.75 (m, 5, CH_2CH_2CH), 3.18 (m, 4, CH_2NCH_2), 3.26 (s, 4, $2H_2O$), 3.82 (s, 6, $\dot{N}$-CH_3 × 2), 6.52 (s, 1, CH of pyrazolium, 7.44 (s, 5, C_6H_5). The 3.26 signal was shifted on the addition of deuteriohydrogen chloride. The benzene filtrate from above was evaporated *in vacuo* to a syrup (1.15 kg., 67%) which was identified as the methyl sulfate salt (**1h**), with a 95% purity; nmr (deuteriodimethylsulfoxide): δ all signals identical with **1g** with the exception of a signal at 3.26 (s, 3, CH_3SO_4), which was not shifted upon the addition of deuterium chloride, ir: ν (cm^{-1}) 1220-1250 strong (CH_3SO_4).

(b)

An aqueous solution of **1h** was passed through a Dowex 1-X8 resin (anion as chloride) and gave **1g**, m.p. 72-72.5° on evaporation of the water eluate.

1-Methyl-3,5-diphenylpyrazoles (**2a**).

1,2-Dimethyl-3,5-diphenylpyrazolium methyl sulfate (**1a**, 10 g., 0.0278 mole) was suspended in piperidine (100 ml.) and heated under reflux during 16 hours, cooled, filtered and the filtrate evaporated to an oil. Crystallization from hexane gave 6.32 g. (97%) with m.p. 59-60° of **2a** (lit. (18) m.p. 68°) and nmr (deuteriochloroform): δ 3.35 (s, 3, N-CH_3), 6.54 (s, 1, CH on pyrazole). Other demethylations were carried out in a similar manner for compounds **2b,c,d,e,f.** In some cases the oils failed to crystallize, in which case analyses were obtained on the oils without further purification.

1-(1-Methyl-3-phenyl-5-pyrazolyl)piperidine and 1-(1-Methyl-5-phenyl-3-pyrazolyl)piperidine (**2b**).

A solution of 3-chloro-1,2-dimethyl-5-phenylpyrazolium iodide (**3b**, 5 g., 0.0149 mole) in piperidine (75 ml.) was heated under reflux for 16 hours. After cooling and filtering the solution was evaporated *in vacuo* to a brown oil. Gas liquid chromatography at 225° indicated two components and nmr (deuteriochloroform) confirmed a 1:1 isomer mixture: δ 1.64 (m, 6, $CH_2CH_2CH_2$), 2.95 and 3.20 (m, 4, CH_2NCH_2), 3.74, 3.80 (as d, 3, N-CH_3), 5.80 and 6.1 (s, 1, CH on pyrazole), 7.48 (s) and 7.5 (m, 5, C_6H_5). The oil was dried *in vacuo* at 40° for 12 hours to give **2b**, 3.72 g. (100%).

3-Methyl-1-(1-methyl-3-phenyl-5-pyrazolyl)piperidine (**2h**) and 3-Methyl-1-(1-methyl-5-phenyl-3-pyrazolyl)piperidine (**2i**).

A solution of 1,2-dimethyl-3-phenyl-5-(3-methylpiperidino)pyrazolium chloride (**1g**, 27.5 g., 0.08 mole) and 3-methylpiperidine (220 ml.) was heated under reflux for 5 hours. On cooling, a white crystalline solid was filtered off, crystallized from ethanol and identified as 3-methylpiperidine hydrochloride (5 g., 46%) with m.p. 175-175.5° (20). The filtrate from above was evaporated to an oil (20 g., 98%), which failed to crystallize. Gas liquid chromatography on 10% OV-17 on 100/120 Gas Chrom Q at 225° showed two peaks of equal intensity. Separation of the

two components was partially achieved by chromatography on a dry packed Brockmann III Woelm silica gel column using benzene as the eluent. The first fraction as an oil contained **2h**, 3-methyl-1-(1-methyl-3-phenyl-5-pyrazolyl)piperidine (5 g., 25%) with nmr (deuteriochloroform): δ 0.84 and 0.94 (d, 3, CH_3), 2 (m, 5, CH_2CH_2CH), 3.50 (m, 4, CH_2NCH_2), 3.6 (s, 3, NCH_3), 5.96 (s, 1, CH on pyrazole), 7.40 (m, 5, C_6H_5).

Anal. Calcd. for $C_{16}H_{21}N_3$: C, 75.25; H, 8.29; N, 16.46. Found: C, 75.49; H, 8.46; N, 16.41.

Further elution with benzene gave intermediate fractions containing isomer mixtures of differing composition. Fraction 5, however, contained a single isomer (**2i**) identified as 3-methyl-1-(1-methyl-5-phenyl-3-pyrazolyl) piperidine as a colorless oil; nmr (deuteriochloroform): δ .85 and .96 (d, 3, CH_3), 2 (m, 5, CH_2CH_2CH), 3.50 (m, 4, CH_2NCH_2), 3.6 (s, 3, NCH_3), 5.62 (s, 1, CH on pyrazole), 7.12 (s, 5, C_6H_5).

Anal. Calcd. for $C_{16}H_{21}N_3$: C, 75.25; H, 8.29; N, 16.46. Found: C, 75.22; H, 8.29; N, 16.74.

The ultraviolet absorption spectra of **2h** and **2i** were determined with a Cary Model 219 spectrophotometer using 10 mm quartz cells. Samples were prepared by Photrex heptane by dilution of a .00522g./100 ml. solution of **2h** and of 0.00541g./100 ml. solution of **2i**. Spectra were recorded at 29.9 and 30.3° respectively; uv: (isomer **2h**) λ max (heptane) 252.5 ± .2 (ε 16,950); uv: (isomer **2i**) λ max (heptane) 247.5 ± .2 (ε 15,510).

1-Methyl-3-phenyl-5-piperidinopyrazole (**2j**).

1,2-Dimethyl-3-phenyl-5-piperidinopyrazolium iodide (**1b**, 3.83 g., 0.01 mole) was dissolved in dimethylformamide (55 ml.) and the solution heated under reflux for 2 days. After cooling, the solution was poured into ice water to give a syrup. Dry column chromatography on a dry-packed silica gel column afforded a white solid obtained by development with hexane and cutting out the major component, 0.37 g. (15%), m.p. 68-70°; nmr (deuteriochloroform): δ 1.65 (m, 6, $CH_2CH_2CH_2$), 2.85 (d, 4, CH_2NCH_2), 3.78 (s, 3, N-CH_3), 6.14 (s, 1, CH of pyrazole), 7.60 (m, 5, phenyl).

Anal. Calcd. for $C_{15}H_{19}N_3$: C, 74.65; H, 7.94; N, 17.41. Found: C, 74.56; H, 8.13; N, 17.11.

Compound mixture **2b**, Table II, shows all the peaks associated with **2j**. Additionally **2b** shows: δ 7.45 (s, 1, phenyl), 5.8 (s, 1, CH) and 3.8 (s, 3, N-CH_3). The phenyl multiplet for **2j** is consistent with the β orientation of phenyl to methyl. Further, the upfield shift of the N-methyl isomer (**2j**) of 3.78 compared with 3.80 for (**2b**) is consistant with this assignment. Albright and Goldman (21) attribute the lower field shift to deshielding by the phenyl groups in close proximity to the *N*-methyl group.

3-Chloro-1,2-dimethyl-5-phenylpyrazolium Methyl Sulfate (**3a**) and 3-Chloro-1,2-dimethyl-5-phenylpyrazolium Iodide (**3b**).

To a solution of 5-chloro-1-methyl-3-phenylpyrazole (**4**, 39.5 g., 0.2 mole) in dry xylene (350 ml.) was added dimethyl sulfate (30 g., 0.22 mole) and the mixture was stirred and heated at 105-115° for 17 hours. After cooling, xylene was decanted from the heavy oil that had separated and then dry acetone was added. Upon agitation a white crystalline solid separated which was collected by filtration to give 33.8 g. (55%) of material with m.p. 100-102°; ir: ν (cm^{-1}) 1220, 1240 (d) and 1010, 1020 (d) as CH_3SO_4.

Anal. Calcd. for $C_{12}H_{15}ClO_4S$: C, 45.22; H, 4.74; N, 8.79; Cl, 11.13. Found: C, 45.32; H, 4.24; N, 8.93; Cl, 11.24.

The iodide (**3b**) with m.p. 160° was obtained in 44% yield by the addition of saturated potassium iodide solution to an aqueous extract of the above filtrate; nmr (deuteriodimethylsulfoxide): δ 4.10 and 4.18 (d, 6, $\overset{+}{N}$-CH_3 × 2), 7.50 (s, 1, CH of pyrazole), 7.71 (s, 5, C_6H_5).

Anal. Calcd. for $C_{11}H_{12}ClIN_2$: C, 39.49; H, 3.62; N, 8.38; Cl, 10.64; I, 37.93. Found: C, 39.46; H, 3.61; N, 8.44; Cl, 10.47; I, 37.85.

1-Ethyl-3,5-diphenylpyrazole (**5**).

(a)

Diethyl sulfate (25.42 g., 0.165 mole) was added to a mixture of 3,5-diphenylpyrazole (15) (16.5 g., 0.074 mole), anhydrous sodium carbonate (15.9 g., 0.15 mole) and 1-propanol (150 ml.) and the mixture stirred at 70° for 4 days. On cooling the reaction mixture was poured into water and the aqueous solution extracted with methylene chloride. After removal of the solvent the residual oil was dissolved in benzene and purified by chromatography through a silica gel column, eluent benzene. The first fraction eluted from the column contained **5** obtained after crystallization from hexane with m.p. 59.5-60.5°.

Anal. Calcd. for $C_{17}H_{16}N_2$: C, 82.22; H, 6.50; N, 11.28. Found: C, 82.46; H, 6.72; N, 11.59.

(b)

A solution of 1-ethyl-2-methyl-3,5-diphenylpyrazolium ethyl sulfate (**6**, 0.35 g.) was dissolved and heated under reflux in piperidine (35 ml.) for 16 hours. Filtration and evaporation gave an oil which was an 85:13 mixture of *N*-ethyl and *N*-methylpyrazole products; nmr (deuteriochloroform): δ 1.45 (t, 3, 0.87 of CH_3), 3.88 (3, 0.13 of N-CH_3), 4.2 (q, 2, 0.87 of CH_2), 6.58 (d, 1, CH on pyrazole).

1-Ethyl-2-methyl-3,5-diphenylpyrazolium Ethyl Sulfate (**6**).

Diethyl sulfate (5.4 g. 0.035 mole) in dry xylene (5 ml.) was added at 60° to a stirred solution of 1-methyl-3,5-diphenylpyrazole (**2a**, 7.04 g., 0.030 mole) in dry xylene (60 ml.). The reaction mixture was heated at 110° for 23 hours and the two phase mixture was cooled. A solid separated out and was collected by filtration and washed with xylene. On stirring the solid with dry acetone a material (**6**, 3.3 g., 29%) with m.p. 109-111° was collected; nmr (deuteriodimethylsulfoxide): δ 1.06 (t, 3, CH_3 of $CH_2CH_2SO_4$), 1.45 (t, 3, CH_3 of N-CH_2CH_3), 3.76 (q, 2, OSO_2CH_2), 4.18 (s, 3, N-CH_3), 4.57 (q, 2, N-CH_2), 7.33 (s, 1, CH of pyrazolium), 7.72 (s, 10, C_6H_5 × 2); ir: ν (cm^{-1}) 1215, 1250 (d, strong, $C_2H_5SO_4$).

Anal. Calcd. for $C_{20}H_{24}N_4SO_4$: C, 61.84; H, 6.23; N, 7.21. Found: C, 61.45; H, 6.42; N, 7.23.

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