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BROMINATION OF 2-PYRAZOLINES AND 3,4,5-TRIMETHYLPYRAZOLE

NEW SYNTHESES OF THE 3H-PYRAZOLE SYSTEM[1]

G. L. CLOSS[2] and H. HEYN
Department of Chemistry, The University of Chicago, Chicago, Illinois 60637

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Abstract—Bromination of several 2-pyrazolines has been shown to give 3-bromo-1-pyrazolines which on base induced dehydrobromination gave mixtures of 3H-pyrazoles and 3-methylene-1-pyrazolines. Base catalyzed elimination of *p*-toluene-sulfinate from 1-*p*-toluenesulfonyl-2-pyrazolines was carried out in a variety of solvents at 70° without carbon skeleton rearrangements, leading to 3H-pyrazoles. Bromination of 3,4,5-trimethylpyrazole gave 3,4,5-trimethyl-4-bromo-4H-pyrazole which upon treatment with MeOH underwent bromide displacement under formation of 3,4,5-trimethyl-3-methoxy-3H-pyrazole.

IN CONNECTION with the recently discovered synthesis of alkylcyclopropenes from alkyl 3H-pyrazoles (pyrazolenines) by photolytic elimination of nitrogen,[3,4] it became desirable to find new and convenient methods for the preparation of these heterocycles. Base catalyzed cyclization of tosylhydrazones of α,β-unsaturated ketones had been shown to be a possible route to 3H-pyrazoles.[3] Bromination of the readily available 2-pyrazolines and dehydrobromination of the expected 3-bromo-1-pyrazolines appeared to be another promising approach.

Bromination of 3,5,5,-trimethyl-2-pyrazoline (I) has been reported by Elguero and Jacquier.[5] Repetition of this work and bromination with N-bromosuccinimide gave a product identical in all properties with those reported. However, the structure assigned to this compound by the French workers, 1-bromo-3,5,5-trimethyl-2-pyrazoline (XIV) is not compatible with the NMR spectrum. In carbon tetrachloride the spectrum shows signals originating from three uncoupled methyl groups. The high-field peak at 8·59 τ, with an intensity corresponding to six protons, must be attributed to a geminal dimethyl group at a saturated carbon. The chemical shift of the remaining methyl group (7·91 τ) indicates an adjacent double bond or an α-bromine atom. In addition, the spectrum reveals the presence of a methylene group with magnetically non-equivalent protons with chemical shifts at 7·74 and 8·35 τ and a coupling constant of 14·6 c/s. The latter feature of the spectrum proves unambiguously that the molecule does not have a plane of symmetry coinciding with the ring plane. This conclusion is further supported by the observation that the degeneracy of the chemical shifts of the two high-field methyl groups is accidental and can be lifted by employing other solvents. In toluene the signals are separated by 0·08 ppm and in

[1] Supported by grants from the National Science Foundation, GP-1076 and GP-4214, and from the A. P. Sloan Foundation.

[2] A. P. Sloan Foundation Research Fellow, 1962–1966.

[3] G. L. Closs and W. A. Böll, *Angew Chem.* **75**, 640 (1963); *Intern. Ed.* **2**, 399 (1963); *J. Amer. Chem. Soc.* **85**, 3904 (1963); G. L. Closs, L. E. Closs, W. A. Böll, *Ibid.* **85**, 3796 (1963).

[4] G. Ege, *Tetrahedron Letters* 1665 (1963).

[5] J. Elguero and R. Jacquier, *C.R. Acad. Sci., Paris* **256**, 720 (1963).

pyridine by 0·02 ppm. Consequently, XIV must be ruled out as possible structure for the bromination product since any deviation from planarity in this molecule would be of conformational origin and therefore of short duration relative to the frequency of separation of the methylene proton or the methyl proton signals.[6] In contrast, structure II, resulting from electrophilic attack by bromine at position 3, is in perfect agreement with the NMR parameters. Additional evidence against the N-bromo structure XIV is available in the lack of coupling between the methyl protons at position 3 and the methylene protons at C-4. All 2-pyrazolines of similar substitution patterns examined in this laboratory show a coupling of approximately 1 c/s between these hydrogens.

Dehydrobromination of II was easily effected with sodium methoxide in refluxing tetrahydrofuran. Under those conditions the reaction product was a mixture of the known 3,3,5-trimethyl-3H-pyrazole (III) and 3-methylene-5,5-dimethyl-1-pyrazoline (IV). The latter product was characterized by its NMR spectrum which shows the presence of a geminal dimethyl group (8·70 τ), a ring methylene group (7·91 τ) and a terminal methylene group (4·55 and 4·07 τ). A third product, 3-methoxymethyl-5,5-dimethyl-2-pyrazoline (V) was formed by base catalyzed addition of methanol to IV. For preparative purposes it was found advantageous to carry out the elimination with sodium ethoxide in ethanol–tetrahydrofuran under which condition IV was completely converted to the ethoxy derivative of V.[7]

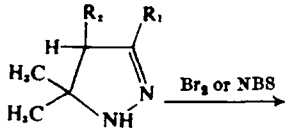
3,3,4,5-Tetramethyl-3H-pyrazole (VIII) and 3,3-dimethyl-5-phenyl-3H-pyrazole (XIII) were prepared in an analogous manner from the pyrazolines VI and XI, respectively. The corresponding bromides (VII and XII) were found to be very unstable and were dehydrobrominated without purification. However, the NMR spectra of the crude bromides clearly indicated that bromination had again occurred at position 3.

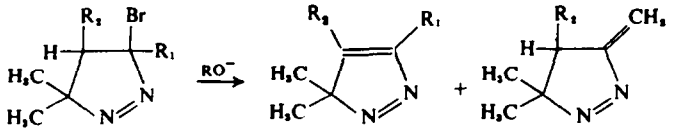
According to Ege,[4] the base catalyzed elimination of *p*-toluene-sulfinate from 1-*p*-toluenesulfonyl-3,5,5-trimethyl-2-pyrazoline (XV) is accompanied by carbon skeleton rearrangement to give 3,4,5-trimethylpyrazole (XVI). Since 3H-pyrazole–pyrazole rearrangements (III → XVI) are normally acid catalyzed[8] and because base catalysis of such a process is hard to visualize, we suspected that the glycol solvent in Ege's experiment might have functioned as a general acid catalyst and, in combination with unnecessary high temp (170°), might have been the cause of the rearrangement. Supporting this hypothesis is the observation that III is readily converted to XVI by treatment with hydrochloric acid at 25°. Accordingly, when the elimination on the tosylates (XV, XVII and XVIII) was carried out with sodium methoxide in refluxing tetrahydrofuran, rearrangement was avoided completely. When the pyrazoline carried a methyl substituent at C-3 (XV and XVII) the product consisted of approximately equimolar mixtures of the 3H-pyrazoles (III and VIII) and 3-methylene-1-pyrazolines (IV and IX). The tosylate of 3-phenyl-5,5-dimethyl-2-pyrazoline (XV) gave the 3H-pyrazole derivative XIII as the only product.

[6] In agreement with these considerations NMR spectra of the N-tosyl-2-pyrazolines XV and XVIII show resonances of magnetically equivalent protons at position 4.

[7] The structures of the alkyloxymethyl-2-pyrazolines are fully supported by their NMR and IR spectra given in the Experimental.

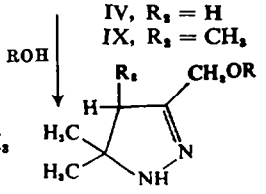
[8] R. Hüttel, J. Riedl, H. Martin and K. Franke, *Chem. Ber.* **93**, 1433 (1960); J. van Alphen, *Rec. Trav. Chim.* **62**, 491 (1943).





I, $R_1 = CH_3$, $R_2 = H$ II, $R_1 = CH_3$, $R_2 = H$ III, $R_1 = CH_3$, $R_2 = H$

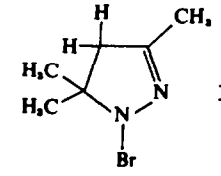
IV, $R_2 = H$
IX, $R_2 = CH_3$



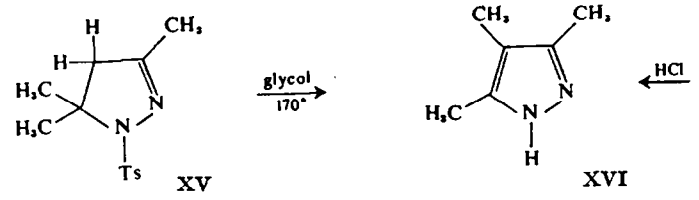
VI, $R_1 = R_2 = CH_3$ VII, $R_1 = R_2 = CH_3$ VIII, $R_1 = R_2 = CH_3$

XI, $R_1 = C_6H_5$, $R_2 = H$ XII, $R_1 = C_6H_5$, $R_2 = H$ XIII, $R_1 = C_6H_5$, $R_2 = H$

V, $R_2 = H$
X, $R_2 = CH_3$



XIV



XV XVI

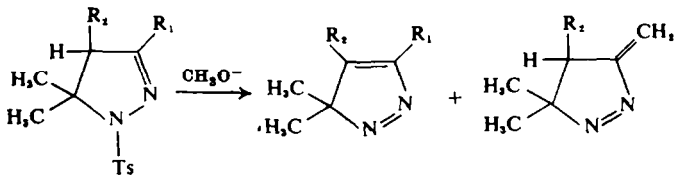
The reaction takes a different course, however, when C-3 of the N-tosylpyrazoline is unsubstituted. On treatment with base XIX underwent ring opening to give the nitrile XX. Similar eliminations under ring opening have observed previously.[9]

A 3H-pyrazole derivative with a functional group at C-3 was prepared from the readily available 3,4,5-trimethylpyrazole (XXI). Contrary to an earlier report,[10] bromination of XXI with bromine or N-bromosuccinimide proceeded smoothly to give 4-bromo-3,4,5-trimethyl-4H-pyrazole (XXII). The structure of the unstable bromination product is evident from its NMR spectrum which shows unsplit methyl proton resonances at 8·30 and 7·71 τ with relative intensities of 1 : 2. In agreement with theoretical considerations,[11] electrophillic attack on the pyrazole ring is commonly

[9] I. I. Grandberg, G. A. Golubeva, *Zh. Obsch. Khim.* **33**, 244 (1963); I. I. Grandberg, A. N. Kost, Y. A. Naumov, *Dokl. Akad. Nauk. SSSR* **149**, 833 (1963), and Refs cited therein.

[10] R. Hüttel, H. Wagner and P. Jochum, *Liebigs Ann.* **593**, 179 (1955).

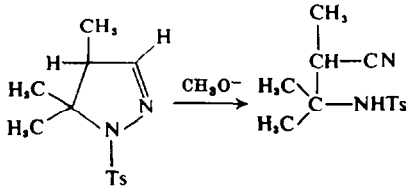
[11] R. D. Brown and M. L. Heffernan, *Austr. J. Chem.* **13**, 47 (1960).



XV, $R_1 = CH_3$, $R_2 = H$ III, $R_1 = CH_3$, $R_2 = H$ IV, $R_2 = H$

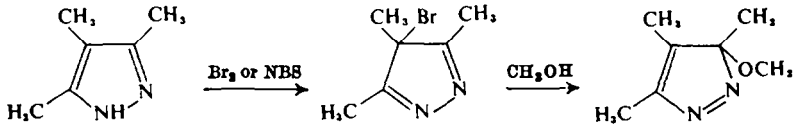
XVII, $R_1 = R_2 = CH_3$ VIII, $R_1 = R_2 = CH_3$ IX, $R_2 = CH_3$

XVIII, $R_1 = C_6H_5$, $R_2 = H$ XIII, $R_1 = C_6H_5$, $R_2 = H$



XIX XX

observed to proceed most readily at C-4.[10] On treatment with methanol XXII solvolyzes rapidly to give a methoxy compound which on the basis of spectral evidence was characterized as 3,4 5-trimethyl-3-methoxy-3H-pyrazole (XXIII). The NMR spectrum shows four signals of equal intensities at 8·73 8·24, 7·70 and 7·10 τ which must be assigned to the methyl groups at positions 3, 4, and 5, and to the methoxy group at C-3, respectively. The protons of the allylic methyl groups are mutually coupled by 1·3 c/s. The UV spectrum ($\lambda\lambda_{max}$ 278, 378 mμ; ϵ 2,230, 212) is consistent with the 3H-pyrazole chromophore. For preparative purposes it was found convenient to brominate XXI in methanol solution with N-bromosuccinimide. Under those conditions the bromide XXII is immediately converted to XXIII which can be isolated in 53% yield.



XXI XXII XXIII

The conversion of the 3H-pyrazole derivatives to cyclopropenes will be the subject of a separate paper.

EXPERIMENTAL

B.ps are uncorrected. IR spectra were recorded with a Beckman IR-7 spectrophotometer; NMR spectra were recorded with a Varian DP-60 or A-60 spectrometer. Chemical shifts are reported relative to internal tetramethylsilane on the τ-scale, using CCl_4 as solvent unless otherwise mentioned. Throughout this section the letters following the band position gives the type (s = singlet,

d = doublet, m = incompletely resolved multiplet) and the number gives the relative integrated area. Electronic spectra were recorded on a Cary Model 14 spectrophotometer. Vapor phase chromatograms were obtained with a Wilkens Instrument and Research, Incorporated, Aerograph 90-P.

3,5,5-*Trimethyl-2-pyrazoline* (I)

This was prepared by a procedure given by Curtius and Wirsing.[13] *NMR.* 8·80 (s, 6); 8·13 (t, 3; 1 cps); 7·70 (q, 2; 1 cps); 5·05 (s, 1). *IR.* 3280, 1624, 1462, 1430, 935, 907, 826, 735 cm^{-1}.

3,4,5,5-*Tetramethyl-2-pyrazoline* (IV)

2-Chloro-2,3-dimethylpentan-5-one[13] (24 g, 0·162 mole) and hydrazine (10 g, 0·31 mole) in MeOH (100 ml) were added dropwise to a refluxing solution of KOH (9·4 g, 0·17 mole) in MeOH (100 ml). Reflux was maintained for 30 min. The reaction mixture was diluted with water, extracted with CH_2Cl_2, dried over Na_2SO_4, and distilled over a three-foot spiral column. The product was collected at 65–67° (10 mm) (15·2 g, 74%). (Found: C, 66·90; H, 11·37; N, 22·10. $C_7H_{14}N_2$ requires: C, 66·62; H, 11·18; N, 22·10%.) NMR. 9·04 (d, 3; 7 c/s); 9·02 (s, 3); 8·83 (s, 3); 8·19 (d, 3; 1·1 c/s); 7·67 (m, 1); 5·13 (m, 1). IR. 3280, 1710, 1625, 1460, 930, 915, 785, 728 cm^{-1}.

4,5,5-*Trimethyl-2-pyrazoline*

α,β-Dimethylcroton aldehyde (12·58 g, 0·128 mole) was reacted with hydrazine (4·35 g, 0·14 mole) in MeOH (20 ml) at 25°. The reaction mixture was diluted with water (50 ml) and extracted with CH_2Cl_2, washed with sat. NaClaq, and dried over Na_2SO_4. To complete the cyclization of the hydrazone, the solvent was evaporated and the residue was heated at 185° for 40 min. The product was distilled and the fraction b.p. 72–75°/25 mm was collected (6·2 g, 43%). (Found: C, 64·39; H, 11·02; N, 25·15. $C_6H_{12}N_2$ requires: C, 64·24; H, 10·78; N, 24·98%.) NMR. 9·01 (d, 3; 7·2 c/s); 8·98 (s, 3); 8·80 (s, 3); 7·48 (1 m); 3·63(d, 1; 1·2 c/s); 5·2 (broad, 1). IR. 3290, 3060, 1580, 1460, 995, 895, 770, 712 cm^{-1}.

3-*Phenyl-5,5-dimethyl-2-pyrazoline* (IX)

2-Methyl-4-phenylbut-2-ene-4-one[14] (13·6 g, 0·1 mole) in MeOH (20 ml) was added to hydrazine (3·5 g, 0·11 mole) in MeOH (20 ml) at 0°. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The solvent was evaporated and the residue was distilled. The pyrazoline was collected at 104–106°/0·4 mm (12·7 g, 85%). The compound decomposes at room temp. NMR. 8·82 (s, 6); 7·30 (s, 2); 4·75 (m, 1); 2·67 (m, 5). IR. 3280, 1675, 1660, 1597, 1498, 1463, 1445, 1060, 1013, 956, 920, 910, 846, 827, 760, 693 cm^{-1}.

3,5,5-*Trimethyl-3-bromo-1-pyrazoline* (II)

(a) Bromine (72 g, 0·45 mole) in CCl_4 (100 ml) was added over a period of 2 hr to a mixture of I (49 g, 0·437 moles) in CCl_4 (200 ml) and NaOHaq (20 g, 0·5 mole, in 100 ml water) at 0°. After stirring 12 hr the organic layer was separated, dried over Na_2SO_4 and the solvent evaporated. Distillation of the residue at 32°/0·025 mm gave the bromide (62 g, 72%).

(b) Compound I (20 g, 0·18 mole) in CCl_4 (100 ml) was added over a period of 30 min to a stirred suspension of N-bromosuccinimide (29·5 g, 0·18 mole) and anhydrous K_2CO_3 (12·5 g, 0·09 mole) in CCl_4 (100 ml). The mixture was stirred for 14 hr at 40°, filtered, and the solvent evaporated. The residue was distilled (slight dec) at 32°/0·025 mm. Redistilled material showed a m.p. of 15–17°. NMR. 8·59 (s, 6); 7·91 (s, 3); AB system with lines at 8·52, 8·26, 7·85, 7·61. In toluene the high-field line is split into a doublet of 0·08 ppm, in pyridine the splitting is 0·02 ppm. IR. 1546, 1465, 1440, 1376, 1365, 1135, 1045, 918 cm^{-1}. UV. λ_{max} (pentane) 332 mμ (66·6).

Debromination of 3,5,5-*trimethyl-3-bromo-1-pyrazoline* (II)

The bromide (8·79 g, 0·046 mole) was dissolved in MeOH (15 ml) and added to a solution of KI (0·05 mole) in water (20 ml). To the stirred mixture was added 2N H_2SO_4 (60 ml). After 3 hr the

[13] Th. Curtius and F. Wirsing, *J. prakt. Chem.* [2] **50**, 546 (1894).
[13] J. Cologne, and K. Mostavi, *Bull. Soc. Chim. France* [5] **6**, 344 (1939).
[14] L. I. Smith and R. E. Kelly, *J. Amer. Chem. Soc.* **74**, 3305 (1952).

mixture was diluted with water, the I_2 was removed with $NaHSO_3$ and NaOH added. The mixture was extracted with CH_2Cl_2, the organic layer separated, dried over KOH and the solvent evaporated. On distillation of the residue (I; 1·95 g; 38%) was collected at 46–48°/12 mm.

Dehydrobromination of 3,5,5-*Trimethyl*-3-*bromo*-1-*pyrazoline*

A solution of EtONa in EtOH and tetrahydrofuran was prepared from Na (10 g; 0·43 g atom) and EtOH (150 ml) and tetrahydrofuran (100 ml). The solution was heated to reflux and the bromide (62 g, 0·32 mole) was added with vigorous stirring. After 20 min the reaction mixture was poured onto ice and the organic material extracted with CH_2Cl_2. After drying over Na_2SO_4, the solvent was evaporated and the residue distilled on a three foot spiral column. Pure III (19 g, 53%) was collected at 51°/16 mm. The material proved identical in all spectral properties with a sample prepared by a different method.[3]

The higher boiling fraction (17·2 g, 34%) was collected at 40°/0·3 mm and proved to be 3-ethoxymethyl-5,5-dimethyl-2-pyrazoline. (Found: C, 61·60; H, 10·21; N, 17·75. $C_8H_{16}N_2O$ requires: C, 61·50; H, 10·32; N, 17·93%.) NMR 8·84 (t, 3; 7 c/s); 8·79 (s, 6); 7·56 (t, 2; 0·9 c/s); 6·55 (q, 2; 7 c/s); 5·95 (t, 2; 0·9 c/s); 4·8 (s, 1). IR. 3250, 1618, 1485, 1465, 1445, 1382, 1365, 1330, 1105, 825, cm^{-1}.

When a mixture of the bromide (17·12 g, 0·087 mole), MeONa (4·9 g, 0·09 mole) in tetrahydrofuran (100 ml) was heated to reflux for 2 hr, identical work-up yielded a mixture which was analyzed NMR to contain III (3·79 g, 38·4%), IV (1·59 g, 16·1%) and V (1·66 g, 13%).

Bromination and dehydrobromination of 3,4,5,5-*tetramethyl*-2-*pyrazoline* (VI)

Bromine (8·0 g, 0·05 mole) in CH_2Cl_2 (4 ml) was slowly added to a solution of the pyrazoline (6·3 g, 0·05 mole) in pyridine (25 ml) at 0°. The mixture was diluted with water, extracted with CH_2Cl_2 and the organic layer was dried over $CaCl_2$. After evaporation of the solvent the dark oil was distilled at 0·025 mm. The product was collected below 36°. Attempts to further purify this bromide failed as slow decomposition occurred even at 25°. The NMR spectrum of the crude material shows peaks at: 8·86 (d, 6; 0·8 c/s); 8·61 (s, 3); 7·87 (s, 3) and some low intensity resonances which could not be assigned beyond doubt to either compound or impurities.

The impure bromide (6·0 g) was treated with MeONa (6·0 g) in tetrahydrofuran (50 ml). After 1 hr reflux dry MeOH (20 ml) was added and the reflux temp was maintained for an additional 20 min. The reaction mixture was then poured on ice and extracted with CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4, and the solvent evaporated. Fractional distillation of the residue gave VIII (2·41 g, 39%, 42°/2·5 mm). (Found: C, 67·89; H, 9·81; N, 22·45. $C_7H_{12}N_2$ requires: C, 67·70; H, 9·74; N, 22·45%.) NMR. 8·79 (s, 6); 8·22 (q, 3; 1·2 c/s); 7·76 (q, 3; 1·2 c/s). IR. 1660, 1450, 1385, 1357, 1321, 1149, 1113, 987, 848, 720 cm^{-1}. UV. $\lambda\lambda_{max}$ (EtOH) 339 mμ (265), 269 mμ (6,900).

The second fraction (0·43 g; 5·5%, 60°/0·025 mm) contained 3-methoxymethyl-4,5,5-trimethyl-2-pyrazoline. (Found: C, 61·94; H, 10·31; N, 16·10. $C_8H_{16}N_2O$ requires: C, 61·50; H, 10·32; N, 17·94%.) NMR. 8·99 (d, 3; 7·5 c/s); 8·97 (s, 3); 8·82 (s, 3); 7·47 (q, 1; 7·5 c/s with fine splitting of 0·8 c/s); 6·76 (s, 3); 6·01 (AB system 2; fine splitting 0·8 c/s); 5·6 (s, 1).

Bromination and dehydrobromination of 3-*phenyl*-5,5-*dimethyl*-2-*pyrazoline* (IX)

Bromine (43·2 g, 0·27 mole) in pyridine (80 ml) at 0°. To the reaction mixture was added Na_2CO_3aq and the mixture stirred for 20 min at 0°, and was then extracted with CH_2Cl_2. The organic layer was washed with $NaHCO_3$aq dried over Na_2SO_4 and the solvent evaporated. The crude bromide was very unstable and turned dark and tarry.

The crude product was heated for 2 hr to reflux in a slurry of MeONa (13·5 g, 0·25 mole) in tetrahydrofuran (250 ml). After the addition of ice water, the reaction mixture was extracted with CH_2Cl_2 and the organic layer separated and dried over Na_2SO_4. The solvent was evaporated and the residue distilled at 0·35 mm; 3,3-dimethyl-5-phenyl-3H-pyrazole (13·1 g, 28%) was collected at 89–99°. The product solidified and was recrystallized from n-hexane, m.p. 48–49°. (Found: C, 76·53; H, 7·07; N, 16·05. $C_{11}H_{12}N_2$ requires: C, 76·71; H, 7·02; N, 16·25%.) NMR. 8·58 (s, 6); 3·11 (s, 1); 2·40 (m, 5).

1-*Tosyl*-3,5,5-*trimethyl*-2-*pyrazoline* (XV)

A solution of I (11·2 g, 0·1 mole) and pyridine (10 ml) in ether (100 ml) was added with stirring to *p*-toluenesulfonyl chloride (19·1 g, 0·1 mole) in ether (150 ml). The temp was kept at 0°. The

solvent was evaporated, the residue dissolved in CH_2Cl_2, washed with water, and dried over Na_2SO_4. The solvent was removed and the dark brown residue was crystallized from EtOH. Recrystallization from benzene or EtOH afforded colorless crystals (11·3 g, 43%) m.p. 163°. (Found: C, 58·65; H, 6·70; N, 10·42. $C_{18}H_{18}N_2O_2S$ requires: C, 58·62; H, 6·81; N, 10·52%.) NMR. 8·50 (s, 6); 8·03 (t, 3; 1 c/s); 7·57 (s, 3); 7·37 (q, 2; 1 c/s); 2·43 (m, 4). IR. 1636, 1598, 1457, 1436, 1345, 1170, 1158, 825, 716, 675 cm^{-1}.

1-*Tosyl*-3,4,5,5-*tetramethyl*-2-*pyrazoline* (XVII)

Compound VI (14 g, 0·11 mole) was added at 25° to a solution of *p*-toluenesulfonyl chloride (21 g, 0·11 mole) in pyridine (30 ml). After 1 hr at room temp EtOH (80 ml) was added, and the mixture stored for 10 hr at −30°. The precipitate was filtered, washed with EtOH and dried. Dilution of the filtrate with EtOH and cooling to 0° afforded another crop to give a combined yield of 34%. The analytical sample was recrystallized from 95% EtOH, m.p. 122–123°. (Found: C, 59·90; H, 7·17; N, 10·17. $C_{14}H_{20}N_2O_3S$ requires: C, 59·97; H, 7·19; N, 9·99%.) NMR 9·00 (d, 3; 7 c/s); 8·74 (s, 3); 8·50 (s, 3); 8·12 (d, 3; 1 c/s); 7·58 (s, 3); 7·43 (q, 1; 7 c/s and fine splitting 1 c/s); 2·50 (m, 4). IR. 1636, 1598, 1496, 1455, 1340, 1170, 1145, 825, 711, 670 cm^{-1}.

1-*Tosyl*-4,5,5-*trimethyl*-2-*pyrazoline* (XIX)

A solution of 4,5,5-trimethyl-2-pyrazoline (3·1 g, 0·028 mole) in pyridine (3·5 ml) was added to a solution of *p*-toluenesulfonyl chloride (6·15 g, 0·032 mole) in tetrahydrofuran (20 ml) which was cooled to −70°. The reaction mixture was allowed to warm up slowly to room temp and was then stored for 12 hr at −30°. The solvent was evaporated *in vacuo* and the residue treated with EtOH. The crystals (3·0 g, 41%, m.p. 97°) were filtered off and recrystallized from n-heptane (m.p. 96·5–97·5°). (Found: C, 58·92; H, 6·86; N, 10·47. $C_{13}H_{18}N_2O_2S$ requires: C, 58·62; H, 6·81; N, 10·52%.) NMR. 8·99 (d, 3; 7 c/s); 8·72 (s, 3); 8·58 (s, 3) 7·6 (s, 3); 7·29 (q, 1; 7 c/s) with fine splitting of 1·3 c/s); 2·53 (m, 4).

1-*Tosyl*-3-*phenyl*-5,5-*dimethyl*-2-*pyrazoline* (XVIII)

p-Toluenesulfonyl chloride (19·8 g, 0·10 mole) in tetrahydrofuran (30 ml) was added at 0° to a solution of IX (18 g, 0·10 mole) and pyridine (10 ml) in tetrahydrofuran (30 ml). The reaction mixture was kept for 3 hr at room temp and was then diluted with EtOH. The tosylate crystallized and was filtered (15 g, 44%, m.p. 161–163°). The analytical sample was recrystallized from benzene–EtOH (m.p. 162–163°). (Found: C, 66·03; H, 6·40; N, 8·47. $C_{18}H_{20}N_2O_2S$ requires: C, 65·81; H, 6·14; N, 8·54%.) NMR. ($CDCl_3$ ext. TMS): 8·47 (s, 6); 7·65 (s, 3); 7·00 (s, 2): 2·5 (m, 4).

Eliminations of p-*toluenesulfinate from* 1-*tosyl*-3,5,5-*trimethyl*-2-*pyrazoline* (XV)

(a) A 3-necked flask was equipped with mechanical stirrer and distillation head leading to a cooled (−70°) receiver. A slurry of the tosylate (10·7 g, 0·04 mole) and MeONa (2·4 g, 0·045 mole) in dimethoxytetraethylene glycol (100 ml) was slowly heated at 0·05 mm until the solvent distilled constantly at 78°. The total heating period was 2 hr. The contents of the receiver were diluted with pentane and washed with water. The washings were made alkaline and reextracted with ether. The combined organic extracts were dried over Na_2SO_4 fate and the solvent evaporated. Distillation at 25 mm yielded a mixture (3·5 g, 79%) of III and IV. Analysis by NMR showed that the two compounds were present in a ratio of 55:45. Attempts to separate this mixture by either fractional distillation or by vapor phase chromatography failed to give complete separation of the isomers. Finally, a 3:1 mixture (3H-pyrazole:pyrazoline) was analyzed. (Found: C, 65·55; H, 9·37; N, 24·60. $C_6H_{10}N_2$ requires: C, 65·42; H, 9·15; N, 25·43%.) NMR. (only peaks originating from 3-methylene-5,5-dimethyl-1-pyrazoline are reported): 8·70 (s, 6); 7·91 (t, 2; 2·4 c/s); 4·55 (t, 1; 2·35 c/s); 4·07 (t, 1; 2·65 c/s).

(b) The tosylate (10·7 g, 0·04 mole) and MeONa (2·6 g, 0·048 mole) were heated to reflux in tetrahydrofuran (100 ml) for 3 hr. To this reaction mixture was added MeOH (35 ml) and MeONa (1·5 g, 0·03 mole) and heating was continued for 30 min. The mixture was then diluted with water (300 ml) and extracted with CH_2Cl_2. After drying over Na_2SO_4 the solvent was evaporated and the residue fractionally distilled. The first fraction (1·91 g, 43·5%, b.p. 34°/10 mm) was shown to be III by comparison of its NMR and IR spectra with an authentic sample.[8] The second fraction (1·28 g,

26%, b.p. 40°/0·03 mm) was V. A sample of this compound was further purified by vapor phase chromatography (SF 96 on firebrick, 120°). (Found: C, 59·01; H, 9·95; N, 19·40. $C_7H_{14}N_2O$ requires: C, 59·12; H, 9·92; N, 19·70%.) NMR. 8·73 (s, 6); 7·60 (t, 2; 0·9 c/s); 6·75 (s, 6); 6·02 (t: 2; 0·9 c/s); 5·17 (s, 1). IR. 3315, 1615, 1100, 900, 825, 720 cm^{-1}.

Elimination of p-*toluenesulfinate from* 1-*tosyl*-3,4,5,5-*tetramethyl*-2-*pyrazoline* (XVII)

A slurry of the tosylate (23 g, 0·082 mole) and MeONa (4·9 g, 0·090 mole) in tetrahydrofuran (300 ml) was heated to reflux for 2 hr. The reaction mixture was diluted with water and extracted with CH_2Cl_2. After drying of the organic layer, the solvent was evaporated and fractionally distilled on a spinning band column at 3 mm. Separation of the VIII and the 3-methylene-4,5,5-trimethyl-1-pyrazoline which were formed in equimolar mixture was achieved only with great losses of intermediate fractions containing both isomers. A pure sample of 3-methylene-4,5,5-trimethyl-1-pyrazoline was collected at 42°/3 mm while the 3H-pyrazole derivative was collected at 42°/2·5 mm. (Found: C, 67·64; H, 9·97; N, 22·36. $C_7H_{12}N_2$ requires: C, 67·70; H, 9·74; N, 22·45%.) NMR. 8·98 (d, 3; 7 c/s); 8·96 (s, 3); 8·65 (s, 3); 7·96 (m, 1); 4·81 (d, 1; 2·2 c/s); 4·07 (d, 1; 2·7 c/s). IR. 3110, 1656, 1480, 1452, 1356, 922, 900 cm^{-1}. UV. $\lambda\lambda_{max\ (EtOH)}$ 244 mμ (6,400), 352 mμ (254).

In another run MeOH (40 ml) was added to the reaction mixture after the initial reflux period of 2 hr, heating was continued for 20 min. The reaction mixture was worked up as described for the dehydrobromination of II, giving identical results.

Elimination of p-*toluenesulfinate from* 1-*tosyl*-3-*phenyl*-5,5-*dimethyl*-2-*pyrazoline* (XVIII)

Tosylate (9·5 g, 0·029 mole), MeONa (1·8 g, 0·033 mole) and tetrahydrofuran (100 ml) were heated to reflux for 2 hr. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4 and the solvent evaporated. The partly crystalline product was recrystallized from heptane (2·15 g, 50%, m.p. 48–49°).

Base-treatment of 1-*tosyl*-4,5,5-*trimethyl*-2-*pyrazoline*

Tosylate (0·60 g, 2·26 mmole) MeONa (0·125 g, 2·29 mmole) and tetrahydrofuran (15 ml) were heated to reflux for 2 hr. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4 and the solvent evaporated. Recrystallization from EtOH afforded 2-methyl-2-tosylamino-3-cyanobutane (0·48 g, 80%, m.p. 88°–90°). (Found: C, 58·75; H, 6·78; N, 10·59. $C_{12}H_{16}N_2O_2S$ requires: C, 58·62; H, 6·81; N, 10·52%.) NMR. 8·80, 8·75, 8·66 (9); 7·62 (s, 3); 6·82 (q, 1; 7 c/s); 4·32 (s, 1); 2·53 (m, 4). The signal at 4·32 disappeared on shaking the solution with D_2O.

Preparation of 3,4,5-*trimethyl-pyrazole* (XXI) *from* 3,5,5-*trimethyl*-2-*pyrazoline* (I)

Bromine (64 g, 0·4 mole) was added at 0° with stirring to a solution of I (44·8 g, 0·4 mole) in CH_2Cl_2 (250 ml) and 2N NaOH (250 ml). After 2 hr the layers were separated. The organic solvent was removed *in vacuo* and the dark oil added to a refluxing solution of KOH (56 g, 1 mole) in MeOH (500 ml). After 40 min reflux, conveniently done with mechanical stirring to prevent bumping, the mixture was diluted with water and extracted with $CHCl_3$. The $CHCl_3$-solution was added to 250 ml 3N HCl and the organic solvent chased off on a steam bath. After turning the acidic solution strongly alkaline with solid KOH an exhaustive steam distillation followed. The NaCl saturated distillate was extracted with $CHCl_3$, the organic layer dried over Na_2SO_4 and the residue after evaporation recrystallized from n-hexane. Compound XVI (14·8 g, 34%) was obtained, m.p. 135–139°. The material used for all reactions was sublimed at 130°.

Bromination of 3,4,5-*trimethyl-pyrazole* (XXI)

(a) A 1·5 molar solution of the pyrazole in $CDCl_3$ was prepared in an NMR-tube; resonances were found at −2·05 (1), 7·83 (6), 8·10 (3).

Succinimide served as an internal standard for the next reactions its resonance taken to be at 7·32.

This solution was added to an equimolar amount of N-bromosuccinimide suspended in about the same amount of solvent as the first sample. A reaction started immediately after shaking of the tube for a few moments; the solution remained clear and turned orange.

The spectrum taken immediately after mixing of the reactants shows the resonances belonging to NBS, succinimide, and two singlet resonances at 7·71 (2) and 8·38 (1).

The next spectrum, taken after 3 min, shows already further reactions leading to a complex spectrum with relatively sharp lines at 5·55 (2), 7·65 (2), 7·78 (3), 8·05 (3).

Any attempts to isolate definite products from larger scale runs proved to be difficult and were abandoned.

An identical run, quenched after 2 min with MeOH, showed among decomposition products the spectrum of 3,4,5-trimethyl-5-methoxy-1-pyrazole.

The bromination in pyridine conducted in the analogous fashion with NBS produced cleanly as first intermediate the same bromide which on standing decomposed under slight gas evolution and formation of a black precipitate.

(b) To a mixture of the pyrazole (0·22 g, 2 mmole) in 2 ml $CHCl_3$ and 5 ml 1N KOH stirred at 0° was added Br_2 (0·32 g, 2 mmole) in 0·48 g CCl_4. Samples were withdrawn after 1, 10, and 30 min and showed consistently the NMR spectrum of XXII in good purity. After ten min at room temp the colorless samples turned orange and decomposed under gas evolution. The NMR spectra then were very complex.

3,4,5-*Trimethyl*-3-*methoxy*-3H-*pyrazole* (XXIII)

N-Bromosuccinimide (5·34 g, 0·030 mole) was added with magnetic stirring to a solution of XXI (3·3 g, 0·030 mole) in MeOH (30 ml). 1N KOH in MeOH (33 ml) was added at 0° over a period of 10 min. The solvent of the reaction mixture was then evaporated on a rotary evaporator. The residue was distributed between water (20 ml) and pentane (20 ml). The aqueous phase was extracted 4 times with small portions of pentane (20 ml). The combined organic extracts were dried over Na_2SO_4, the solvent was evaporated and the remainder was distilled at 3 mm. Compound XXIII (2·2 g, 53%) was obtained as a pale yellow liquid (b.p. 56°/3 mm). (Found: C, 59·67; H, 8·66. $C_7H_{12}N_2O$ requires: C, 59·97; H, 8·63%.) NMR. 8·73 (s, 3); 8·24 (q, 3; 1·3 c/s); 7·70 (q, 3; 1·3 c/s); 7·10 (s, 3). IR. 2830, 1681, 1308, 1143, 1053, 950, 895 cm^{-1}. UV. $\lambda\lambda_{max\ (EtoH)}$ 278 mμ (2,230), 378 mμ (212).