Department of Chemistry, University of Missouri

The Synthesis of 1,4,5-Trialkyl-2-pyrazolines from Monoalkylhydrazines and Aliphatic Aldehydes (1)

Norman Rabjohn, H. R. Havens, and J. L. Rutter (2)

It has been found that the thermal decomposition of heptanal methylhydrazone affords 5-hexyl-1-methyl-4-pentyl-2-pyrazoline (I), in addition to heptanenitrile and methylamine. The formation of I suggests the synthesis of 1,4,5-trialkyl-2-pyrazolines from monoalkylhydrazines and aliphatic aldehydes. A number of these compounds have been prepared in good yields by this method, or through the related hydrazones, and some of their physical and chemical properties have been studied.

In an investigation of the thermal decomposition of aliphatic methylhydrazones (3), it was found that heptanal methylhydrazone afforded at reflux temperature small quantities of an unknown compound (I), $C_{15}H_{30}N_2$, in addition to heptanenitrile and methylamine.

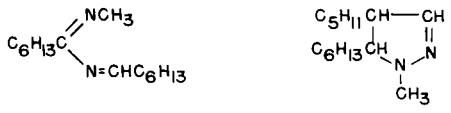
Compound I was shown to be a weak base with no NH stretching absorption in the infrared. A C=N absorption was present at 1590 cm^{-1}, compared to that of heptanal methylhydrazone at 1620 cm^{-1}. A similar bathochromic shift was observed in the ultraviolet absorption spectra of the two compounds, *i.e.*, λ max 245 mμ for I and λ max 233 mμ for the hydrazone. The molecular formula of I suggested that a molecule of the hydrazone might have combined with a molecule of heptaldehyde with the elimination of water.

When chloroform solutions of heptanal methylhydrazone and heptanal were mixed, a reaction took place with the separation of water and the formation of I in 75% yield.

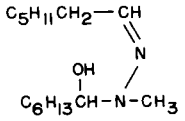
The data indicated that I might have structure A or B.

The former could arise by a Beckmann-type rearrangement of the hydrazone to an amidine which could tautomerize and then condense with heptaldehyde. Robev and co-workers (4) have shown that aldehyde arylhydrazones change to amidines in the presence of bases, and Kunckell and Bauer (5) have reported the formation of a diimino compound from the reaction of benzamidine with benzaldehyde. The 2-pyrazoline structure, B, could be visualized as resulting from the cyclization, with loss of water, of an intermediate (II), formed by addition of the amino nitrogen atom of the hydrazone to the carbonyl group of the aldehyde.

Compound I is very resistant to hydrolysis by acids and bases, but is reduced easily at room temperature in the presence of Raney nickel catalyst to give a diamine (III, Chart I) which contains primary and secondary amino groups. It forms a crystalline

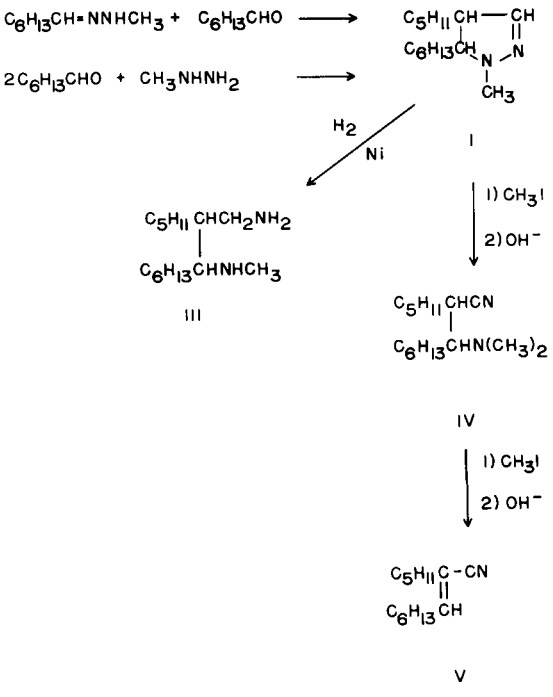


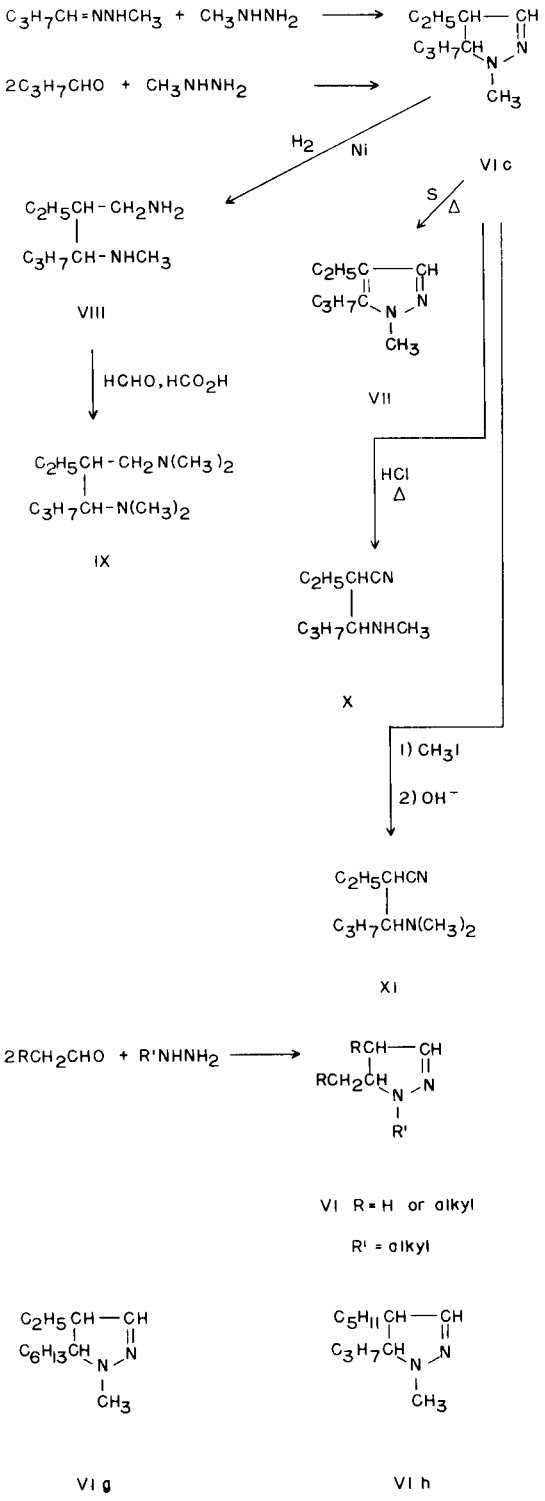
A B



II

CHART I





methiodide which on treatment with aqueous alkali gave a colorless oil, $C_{16}H_{32}N_2$ (IV), which was identified as a nitrile by its infrared spectrum. The aminonitrile was caused to react with methyl iodide and the resulting methiodide was degraded with alkali to an unsaturated nitrile, $C_{14}H_{25}N$ (V).

The conversion of pyrazolines to β-dialkylaminonitriles (the aminonitrile rearrangement) has been investigated by Ioffe and Zelenin (6). Also Kost and co-workers (7) have reported that pyrazolines undergo reductive cleavage at elevated temperatures and pressures. The pyrazoline structure, A, was confirmed by synthesis of I, in low yield, from heptanal azine and methyl iodide according to the method of Kost, Grandberg and Golubeva (8). In addition, 4-ethyl-1-methyl-5-propyl-2-pyrazoline (VIc) was dehydrogenated smoothly to the corresponding pyrazole (VII), by means of sulfur (9). von Auwers and Heimke (10) have indicated that lead dioxide is the reagent of choice for conversion of pyrazolines to pyrazoles, but only a moderate yield (26%) of the pyrazole was obtained under these conditions. Aromatization of the pyrazoline did not succeed with bromine, chloranil, hydrogen peroxide, or potassium permanganate.

The ease of formation of I from the aldehyde and hydrazone suggested that a more convenient method for the synthesis of 1,4,5-trialkyl-2-pyrazolines was at hand. Most commonly, 1-alkyl-2-pyrazolines have been prepared by the reaction of alkylhydrazines and α,β-unsaturated carbonyl compounds (10,11), by alkylation of pyrazolines unsubstituted on nitrogen (12), from β-hydrazinocarbonyl compounds (13), and by the addition of β-lactones to azines (14). These routes are lengthened by the necessity of preparing intermediates; furthermore, the presence of two or more substituents in the 2- and 3-positions of an α,β-unsaturated carbonyl compound increases the stability of the alkylhydrazone and makes cyclization to the pyrazoline difficult or impossible (11c).

We have found that the reaction of an aliphatic aldehyde, possessing at least one α-hydrogen, with an aliphatic hydrazine affords 1,4,5-trialkyl-2-pyrazolines (VI) directly in yields of 54-86% (Table I). Structures were confirmed by independent syntheses, reference to known compounds, and by analytical and spectral data.

The possibility that this pyrazoline formation proceeds through an intermediate hydrazone was indicated by the previously mentioned condensation of heptanal with heptanal methylhydrazone. It was found to be true, and several of the compounds in Table I were prepared also in the latter manner.

The condensation of heptanal with butanal methylhydrazone was carried out in the hope that it might afford 4-ethyl-1-methyl-5-hexyl-2-pyrazoline (VIg), and thus permit greater variation of the alkyl groups in the 4- and 5-positions. The products of the reaction consisted of I and VIc, and probably VIg and VIh (as indicated by g.l.c.). Elemental analysis also agreed well with that required for the isomeric structures VIg and VIh. Apparently, the exchange between an aldehyde methylhydrazone and another aldehyde is quite rapid.

Other variations of the procedure were sought in the reactions between alkylhydrazones and formaldehyde or ketones. Condensations of this type with butanal methylhydrazone failed to give the

TABLE I

1,4,5-Trialkyl-2-pyrazolines (VI)

Compound	R	R'	B.P. (mm.)	n_D^{25}	Yield, %	Formula
I	C_5H_{11}	CH_3	102(0.3)	1.4596	65	$C_{15}H_{30}N_2$ (a)
VIa	H	CH_3	120(748)	1.4465	84	$C_5H_{10}N_2$ (b)
VIb	CH_3	CH_3	65(22)	1.4510	80	$C_7H_{14}N_2$ (c)
VIc	C_2H_5	CH_3	70(2)	1.4549	86	$C_9H_{18}N_2$ (d)
VId	$(CH_3)_2CH$	CH_3	84(11)	1.4562	58	$C_{11}H_{22}N_2$ (e)
VIe	C_2H_5	$CH_2C_6H_5$	120(1)	1.5176	54	$C_{15}H_{22}N_2$ (f)
VIf	C_2H_5	C_8H_{17}	132(7)	1.4592	58	$C_{16}H_{32}N_2$ (g)

(a) *Anal.* Calcd. for $C_{15}H_{30}N_2$: C, 75.56; H, 12.68; N, 11.75. Found: C, 75.76; H, 12.68; N, 11.75. (b) Ref. 10. (c) Ref. 11c. (d) *Anal.* Calcd. for $C_9H_{18}N_2$: C, 70.07; H, 11.76; N, 18.16. Found: C, 70.13; H, 11.96; N, 17.86. (e) Ref. 8. (f) A. N. Kost and G. A. Golubeva, *Zh. Obshch. Khim.*, 30, 494 (1960); *Chem. Abstr.*, 54, 24671 (1960). (g) *Anal.* Calcd. for $C_{16}H_{32}N_2$: C, 76.12; H, 12.78; N, 11.10. Found: C, 76.09; H, 12.52; N, 11.31.

TABLE II

Spectral Data

	Infrared, cm^{-1}			Ultraviolet		P.M.R., τ	
Compound	$N-CH_3$	C=N	CH=N	C=N λ max (EtOH) mμ	log ϵ	CH=N	$N-CH_3$
I	2815	1590	3090	245	3.56	3.33, 3.63	7.33, 7.36
VIa	2775	1580	3050	242	3.47	3.47	7.35
VIb	2775	1580	3035	243	3.52	3.44, 3.66	7.33, 7.36
VIc	2780	1580	3040	243	3.54	3.27, 3.57	7.31, 7.35
VId	2810	1580	3090	249	3.56	3.41, 3.64	7.30, 7.40
VIe	----	1590	3125	246	3.56	3.23, 3.52	----
VIf	----	1580	3080	247	3.55	3.32, 3.63	----
VII	2800	1570	3125	226	3.86	2.98	6.37

desired compounds; instead, only low yields of VIc were obtained.

Inspection of formula VI reveals the presence of chiral centers in the 4- and 5-positions which should lead to two pairs of RS modifications. Only a few examples of stereoisomerism in this ring system have been reported (15). Examination of the pyrazolines by g.l.c. on a 10 foot column of 15% Carbowax 20 M on Chromosorb revealed the presence of two closely spaced peaks.

In addition, the p.m.r. spectra showed two *N*-methyl peaks, separated by 2-5 c.p.s., and a widely spaced doublet (J = 14-18 c.p.s.) for the hydrogen of the 3-position. Slow distillation of 1,4-dimethyl-5-ethyl-2-pyrazoline through a spinning band column produced a final fraction which consisted of the higher-boiling racemic modification in approximately 95% purity (by g.l.c.). Surprisingly, the upfield peak of the "doublet" of the 3-hydrogen was almost negligible. Separation of the pyrazoline by preparative g.l.c. yielded the pure higher-boiling form. The lower-boiling product was obtained in about 50% purity. The p.m.r. spectrum of the pure higher-boiling modification showed only a single *N*-methyl resonance and a single peak due to the hydrogen in the 3-position. P.m.r. data for a number of pyrazolines have been recorded (16).

Ioffe and Zelenin have reported infrared data for many *N*-alkylpyrazolines (11c); the spectra of the pyrazolines prepared in this laboratory are in agreement with the assignments of these authors. Infrared, ultraviolet, and p.m.r. spectral data for the pyrazolines obtained in the present work are tabulated in Table II.

In Chart I are summarized the syntheses and additional reactions of the 2-pyrazolines described in the experimental section of this report.

EXPERIMENTAL

Melting points were taken by capillary and are corrected; boiling points are uncorrected. Microanalyses were performed by Drs. Weiler and Strauss, Oxford, England and on an F and M Model 185 C-H-N Analyzer. Infrared spectra were recorded on a Perkin-Elmer 237-B spectrophotometer and ultraviolet spectra were determined with a Beckmann DB-2 instrument. P.m.r. spectra were recorded at 60 mc. on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Gas chromatography was performed at various temperatures with a helium flow rate of 50 ml./min. on an Aerograph A90-P3 chromatograph.

Materials.

The methylhydrazine used in this study was either that supplied through the generosity of Olin's Research Laboratory, or purchased from Aldrich Chemical Co. The various aldehydes were commercial products which were distilled before use. Benzylhydrazine and *n*-octylhydrazine were prepared by the method of Westphal (17).

Thermal Decomposition of Heptanal Methylhydrazone.

Heptanal methylhydrazone, b.p. 60-61°/0.2 mm., n_D^{25} 1.4555, prepared by the procedure of Wiley and Irick (18) was heated at reflux under nitrogen for 21 hours. From 100 g. (0.7 mole) of the hydrazone there were isolated 14.6 g. (0.47 mole) of methylamine, 52.2 g. (0.47 mole) of heptanenitrile, 18.1 g. (0.13 mole) of unchanged hydrazone and 14.4 g. of residue. The latter was distilled from a Hickman still at 0.015 mm. and about 5 g. of material, I, was collected at an oil-bath temperature of 100-110°, n_D^{23} 1.4608.

Anal. Calcd. for $C_{15}H_{30}N_2$: C, 75.56; H, 12.68; N, 11.75. Found: C, 75.76; H, 12.68; N, 11.72.

Condensation of Heptanal Methylhydrazone with Heptanal.

A solution of 28.4 g. (0.2 mole) of heptanal methylhydrazone in 50 ml. of chloroform was stirred while a solution of 22.8 g. (0.2 mole) of heptanal in 50 ml. of chloroform was added slowly. The temperature of the reaction mixture rose to 50° and water began to separate. The mixture was allowed to stand at room temperature for several hours and the chloroform layer was separated and dried over calcium chloride. The solvent was removed and the residue was fractionated to give 25.9 g. (54%) of a colorless liquid, b.p. 118-120°/0.3 mm., micro b.p. 295-297°, n_D^{25} 1.4603. The compound was identical to I obtained in the previous experiment. Its hydrochloride, prepared in anhydrous ether, melted at 115-116°.

Anal. Calcd. for $C_{15}H_{31}ClN_2$: C, 65.54; H, 11.37; Cl, 12.90; N, 10.19; neut. eq. 275. Found: C, 65.14; H, 11.44; Cl, 13.30; N, 10.19; neut. eq. 280.

Reduction of I.

A solution of 11.9 g. (0.05 mole) of I in 125 ml. of absolute alcohol was shaken with 1.5 g. of Raney nickel catalyst at room temperature at about 40 p.s.i. of hydrogen. The reaction was nearly complete after 1 hour, and within 2.5 hours approximately 0.1 mole of hydrogen had been absorbed. After removal of the catalyst and solvent, the residue was dissolved in dilute hydrochloric acid and the acid solution was extracted with ether. The aqueous layer was made alkaline, and extracted with ether. The extract was dried, concentrated and distilled to give 9 g. (75%) of a colorless liquid (III), b.p. 118-122°/0.1 mm., n_D^{25} 1.4560.

Anal. Calcd. for $C_{15}H_{34}N_2$: C, 74.31; H, 14.14; N, 11.56; neut. eq. 121. Found: C, 74.28; H, 14.12; N, 11.28; neut. eq. 123.

Degradation of I.

A solution of 11.9 g. (0.05 mole) of I and 14.2 g. (0.1 mole) of methyl iodide in 25 ml. of dry benzene was allowed to stand at room temperature for two days. The solid, 9.8 g. (52%), was removed by filtration, triturated with benzene and dried, m.p., 131-135°.

Anal. Calcd. for $C_{16}H_{33}IN_2$: C, 50.52; H, 8.74; N, 7.37; mol. wgt. 380. Found: C, 51.09; H, 8.55; N, 7.02; mol. wgt. 384.

A mixture of 7.6 g. (0.02 mole) of the methiodide and 25 ml. of 10% sodium hydroxide solution was stirred and heated on a steam bath for 10 minutes. It was cooled and the oil which separated was removed by ether extraction. The extract was washed with water, dried over magnesium sulfate and concentrated. The residue, 4.7 g. (93%), distilled at 115-117°/0.75 mm., n_D^{27} 1.4490, λ max 2230 cm^{-1}; no other functional group absorptions were evident.

Anal. Calcd. for $C_{16}H_{32}N_2$: C, 76.15; H, 12.78; N, 11.10. Found: C, 75.96; H, 12.72; N, 11.23.

The nitrile (IV) was converted to its methiodide, m.p., 125-127°, in the usual manner.

Anal. Calcd. for $C_{17}H_{35}IN_2$: C, 51.77; H, 8.95; I, 32.18; N, 7.10. Found: C, 51.85; H, 8.92; I, 32.30; N, 7.06.

A mixture of 1 g. of the methiodide and 50 ml. of 10% sodium hydroxide solution was heated on a steam bath for 30 minutes. An amine odor was detected and an oil separated. After cooling, the oil was taken into ether, the extract was dried over magnesium sulfate and the solution was concentrated. The residue boiled at 115-117°/2 mm., n_D^{24} 1.4500, λ max 2215 cm^{-1} and 1630 cm^{-1} which are in agreement with an α,β-unsaturated nitrile structure for V.

Anal. Calcd. for $C_{14}H_{25}N$: C, 81.09; H, 12.15; N, 6.76. Found: C, 80.92; H, 12.01; N, 7.23.

General Method for Preparing 1,4,5-Trialkyl-2-pyrazolines (VI).

To a stirred solution of 0.20 mole of an aliphatic aldehyde in 50 ml. of chloroform was added 0.10 mole of the alkylhydrazine, dissolved in 25 ml. of chloroform, at such a rate that the temperature was maintained between 45 and 50°. After a reflux period of 1-2 hours, the aqueous layer was withdrawn, and the product was separated from unreacted aldehyde and alkylhydrazine by extracting into 10% hydrochloric acid. The desired pyrazoline was obtained by adding an excess of sodium hydroxide pellets, extracting with ether, drying, and distilling (Table I).

1,5-Dimethylpyrazoline (VIa).

Acetaldehyde (35.2 g., 0.80 mole) in 80 ml. of chloroform was cooled to -10°, and a solution of 18.4 g. (0.40 mole) of methylhydrazine in 20 ml. of chloroform was added dropwise. The temperature of the reaction mixture was maintained below -10° throughout the addition and for 2 hours after completion of the addition. The chloroform solution was dried and distilled. There was obtained 32.9 g. (84%) of VIa, a portion of which boiled at 120-121°/748 mm., n_D^{25} 1.4465, picrate, m.p. 113.4-115°; lit. (10), b.p. 124-125°/760 mm., n_D^{16} 1.4494, picrate, m.p. 112-113°.

4-Ethyl-1-methyl-5-propylpyrazoline (VIc) from Butanal Methylhydrazone.

A solution of 46.0 g. (1 mole) of methylhydrazine in 50 ml. of benzene was added dropwise, with cooling, to 72.0 g. (1 mole) of butanal in 100 ml. of benzene, at such a rate that the temperature was maintained below 5°. The water which formed was removed by azeotropic distillation. Distillation gave 76.1 g. (76%) of butanal methylhydrazone, b.p., 60-62°/15 mm., n_D^{25} 1.4527; lit. (18), b.p. 134°, n_D^{24} 1.4390. The hydrazone (16.2 g., 0.16 mole) was dissolved in 30 ml. of chloroform and a solution of 11.7 g. (0.16 mole) of butanal in 20 ml. of chloroform was added dropwise. After drying and distilling, there was obtained 20.5 g. (82%) of VIc, b.p. 59-62°/1 mm., n_D^{25} 1.4547.

Reaction of Butanal Methylhydrazone with Heptanal.

Heptanal (2.28 g., 0.02 mole), in 30 ml. of chloroform, was added dropwise to a well-stirred refluxing solution of 2.00 g. (0.02 mole) of butanal methylhydrazone dissolved in 30 ml. of chloroform. The mixture was refluxed for 3 hours following completion of the addition. Gas chromatography on a 6 foot column of 10% Carbowax 20 M on Chromosorb indicated the presence of three components in the reaction mixture, the first and third of which corresponded to pyrazolines I and VIc, respectively. The second peak, presumably due to compounds VIg and VIh, was approximately equal in area to each of the other two peaks.

The reaction was repeated, except on a 0.1 molar scale and with the addition of 0.1 g. of *p*-toluenesulfonic acid. The system was refluxed for 2 hours following completion of addition of the heptanal, then cooled and put through an acid-base extraction. Distillation through a spinning band column resulted in the isolation of 3 g. of 4-ethyl-1-methyl-5-propyl-2-pyrazoline (VIc), a portion of which boiled at 74°/9 mm., n_D^{25} 1.4543, 3.3 g. of 5-hexyl-1-methyl-4-pentyl-2-pyrazoline (I), a portion of which boiled at 122-124°/1 mm., n_D^{25} 1.4604, and intermediate material, a portion of which boiled at 100°/1 mm., n_D^{25} 1.4572, and showed four closely spaced peaks when examined by g.l.c. on a 10 foot column of 15% Carbowax 20 M on Chromosorb. The intermediate material was submitted for analysis.

Anal. Calcd. for $C_{12}H_{24}N_2$: C, 73.41; H, 12.32; N, 14.27. Found: C, 73.18; H, 12.40; N, 14.21.

4-Ethyl-1-methyl-5-propylpyrazole (VII).

4-Ethyl-1-methyl-5-propyl-2-pyrazoline (VIc) (14.4 g., 0.094 mole) and 3.2 g. (0.1 g.-atom) of sulfur were heated in an oil bath to 140°, at which time a slow evolution of hydrogen sulfide began. The bath temperature was gradually increased to 180°, with a more rapid evolution of hydrogen sulfide. The reaction mixture was heated for 2 hours after gas evolution had stopped, then was dissolved in 50 ml. of benzene, filtered to remove the excess sulfur, and shaken with two 20-ml. portions of lead acetate solution. The benzene solution

was dried and distilled to give 10 g. (73%) of VII, b.p. 100-102°/1 mm., n_D^{25} 1.4759.

Anal. Calcd. for $C_9H_{16}N_2$: C, 71.00; H, 10.59; N, 18.40. Found: C, 70.67; H, 10.42; N, 18.25.

To a mixture of 7.7 g. (0.05 mole) of VIc and 12.0 g. (0.05 mole) of lead (IV) oxide was added 50 ml. of acetic acid in portions. After about 10 ml. of acid had been added, the temperature had risen to nearly 100°; moderation with a cold water bath was necessary. The system was maintained at 85° for 3 hours in an oil bath. The acetic acid was then distilled off, the mixture was cooled, and 100 ml. of ether was added. The ether solution was washed with 10% sodium hydroxide solution (2 x 50-ml.), dried, and distilled to give 2.03 g. (27%) of pyrazole, b.p. 67-69°/2 mm., n_D^{25} 1.4700. Its infrared spectrum was identical to that of VII prepared by oxidation with sulfur.

2-Ethyl-3-(*N*-methylamino)hexylamine (VIII) and 1,3-Di(*N*,*N*-dimethylamino)-2-ethylhexane (IX).

The procedure described for the reduction of I was applied to 4-ethyl-1-methyl-5-propyl-2-pyrazoline (VIc). The diamine (VIII) was obtained in 90% yield, b.p. 80-81°/1 mm., n_D^{24} 1.4518.

Anal. Calcd. for $C_9H_{22}N_2$: C, 68.28; H, 14.01; N, 17.70. Found: C, 68.01; H, 13.86; N, 17.95.

Formic acid (13.4 g., 0.23 mole) was cooled to 5° and 9.2 g. (0.06 mole) of VIII was added dropwise over a period of 30 minutes. After this addition, 12.9 g. (0.16 mole) of 37% formaldehyde solution was added dropwise. The reaction mixture then was heated in an oil bath at 85-95° for 12 hours. By this time, carbon dioxide evolution had stopped. The mixture was cooled, and 100 ml. of 2*N* hydrochloric acid and 100 ml. of ether were added. The ether layer was removed and washed with an additional 50 ml. of hydrochloric acid. The aqueous extracts were combined, extracted with 50 ml. of ether, and then made basic with 10% sodium hydroxide solution. The oily layer which separated was extracted with ether and the extract was dried and distilled to give 10.3 g. (89%) of IX, b.p., 93-94°/4 mm., n_D^{25} 1.4439.

Anal. Calcd. for $C_{12}H_{28}N_2$: C, 71.93; H, 14.09; N, 13.98. Found: C, 71.57; H, 13.84; N, 14.32.

2-Ethyl-3-(*N*-methylamino)hexanenitrile (X).

A solution of 15.4 g. of VIc in 30 ml. of concentrated hydrochloric acid was heated in an oil bath at 180°. By the time 25 ml. of water had distilled, the mixture had turned from light pink to brown and the temperature had risen to 210°. At this point, a vigorous reaction occurred. The system was heated for 240° for 15 minutes, and then cooled. Addition of 50 ml. of 20% aqueous sodium hydroxide to the resultant brown solid produced an oil which was extracted into ether, washed with 50 ml. of water, and dried over magnesium sulfate. The solvent was removed and the residue was distilled to give 7.2 g. (46%) of X, b.p. 94-95°/10 mm., n_D^{25} 1.4430.

Anal. Calcd. for $C_9H_{18}N_2$: C, 70.07; H, 11.76; N, 18.16. Found: C, 70.29; H, 11.92; N, 18.09.

3-(*N*,*N*-Dimethylamino)-2-ethylhexanenitrile (XI).

4-Ethyl-1-methyl-5-propyl-2-pyrazoline (VIc) (5 g., 0.032 mole) was converted to its methiodide by reaction with 5 g. (0.035 mole) of methyl iodide in 25 ml. of benzene. The solid (5.5 g.) which had precipitated after one day was removed by filtration and added in portions to 20 ml. of 50% potassium hydroxide solution. The oily layer which had separated after 2 hours was extracted with ether (2 x 30-ml.), and the extract was dried and concentrated. The residue was distilled to give 3.8 g. (71%) of XI, b.p. 78-79°/6 mm., n_D^{25} 1.4415.

Anal. Calcd. for $C_{10}H_{20}N_2$: C, 71.37; H, 11.98; N, 16.65. Found: C, 71.13; H, 11.79; N, 17.18.

Acknowledgment.

This investigation was supported, in part, by PHS Research Grant No. CA-04662 from the National Cancer Institute, Public Health Service.

REFERENCES

(1) Presented in part at the First Midwest Regional Meeting of the American Chemical Society, Kansas City, Missouri, November 4-5, 1965.

(2) NASA Fellow in Chemistry, 1965-1966.

(3) Norman Robjohn, C. L. King, and H. R. Havens, unpublished work.

(4) S. Robev and D. Tsitovich, *Compt. Rend. Acad. Bulgare Sci.*, 17, 737 (1964); *Chem. Abstr.*, 61, 14492 (1964), and earlier references.

(5a) F. Kunckell, *Ber.*, 34, 637 (1901); (b) F. Kunckell and R. Bauer, *ibid.*, 34, 3029 (1901).

(6) B. V. Ioffe and K. N. Zelenin, *Zh. Obshch. Khim.*, 33, 3231 (1963); *Chem. Abstr.*, 60, 5331 (1964).

(7a) A. N. Kost, G. A. Golubeva, and R. G. Stepanov, *Zh. Obshch. Khim.*, 32, 2240 (1962); *Chem. Abstr.*, 58, 7814 (1963); (b) A. N. Kost, G. A. Golubeva, and A. P. Terent'ev, *Dokl. Akad. Nauk SSSR*, 129, 1300 (1959); *Chem. Abstr.*, 54, 9893 (1960).

(8) A. N. Kost, I. I. Grandberg, and G. A. Golubeva, *Zh. Obshch. Khim.*, 26, 2604 (1956); *Chem. Abstr.*, 51, 5054 (1957).

(9) I. I. Grandberg and A. N. Kost, *Zh. Obshch. Khim.*, 28, 3071 (1958); *Chem. Abstr.*, 53, 10188 (1959).

(10) K. von Auwers and P. Heimke, *Ann.*, 458, 186 (1927).

(11a) T. L. Jacobs, in "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, p. 45, and references therein; (b) M. Julia, in "Traite de Chimie Organique," Vol. 20, V. Grignard, Ed., Masson and Co., Paris, 1953, p. 762, and references therein; (c) B. V. Ioffe and K. N. Zelenin, *Zh. Obshch. Khim.*, 33, 3589 (1963); *Chem. Abstr.*, 60, 8016 (1964).

(12a) I. I. Grandberg and A. N. Kost, *Zh. Obshch. Khim.*, 30, 208 (1960); *Chem. Abstr.*, 54, 22584 (1960); (b) A. N. Kost, G. A. Golubeva, and I. I. Grandberg, *Zh. Obshch. Khim.*, 26, 1976 (1956); *Chem. Abstr.*, 51, 5054 (1957).

(13a) R. L. Hinman, R. D. Ellefson, and R. D. Campbell, *J. Am. Chem. Soc.*, 82, 3988 (1960); (b) C. Mannich and G. Heilner, *Ber.*, 55, 365 (1922).

(14) L. Zirngibl and T. Wagner-Jauregg, *Chimia (Aarau)*, 18, 394 (1964); *Chem. Abstr.*, 62, 5267 (1965).

(15a) W. M. Jones, *J. Am. Chem. Soc.*, 81, 5153 (1959); (b) E. E. Baroni, K. A. Kovyrzina, and E. A. Andreeshchev, *Zh. Obshch. Khim.*, 30, 2002 (1960); *Chem. Abstr.*, 55, 6471 (1961); (c) A. J. Hassner and M. J. Michelson, *J. Org. Chem.*, 27, 298 (1962); (d) W. M. Jones and Wun-Ten Tai, *ibid.*, 27, 1324 (1962).

(16a) W. S. Brey, Jr. and W. M. Jones, *ibid.*, 26, 1912 (1961); (b) A. J. Hassner and M. J. Michelson, *ibid.*, 27, 3974 (1962); (c) V. S. Stopskii, V. B. Lebedev, B. V. Ioffe, and A. A. Petrov, *Dokl. Akad. Nauk SSSR*, 166, 399 (1966); *Chem. Abstr.*, 64, 15210 (1966).

(17) O. Westphal, *Chem. Ber.*, 74, 759 (1941).

(18) R. H. Wiley and G. Irick, *J. Org. Chem.*, 24, 1925 (1959).

Received August 26, 1966 Columbia, Missouri 65201