226. Reaction of Isocyanates and Isothiocyanates with Butyraldazine; Formation of 1-Substituted 2-Pyrazolines

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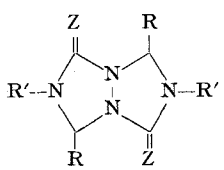
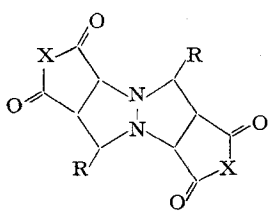
Summary. Phenyl isothiocyanate reacts with butyraldazine in presence of acidic catalysts to form a 2-pyrazoline (IV) whereas phenyl or benzyl isocyanates under similar conditions yield a mixture of the two isomeric 2-pyrazolines XIa and XII. On reaction with Ac_2O, IV gave the 1-acetyl derivative V. Reduction with $LiAlH_4$ led to the corresponding pyrazolidines. Reexamination of *Kost*'s three step preparation of a 1-phenylthiocarbamoyl 2-pyrazoline [19] such as X *via* formic acid cyclization [18] of butyraldazine revealed that his first step product was apparently a mixture of two stereoisomeric 1-formyl-2-pyrazolines VIIIa and VIIIb. A mechanism for the formation of these pyrazolines is proposed.

The term 'criss-cross' addition was first proposed by *Bailey* and co-workers [1] for the reactions of one mole of benzaldazine with two moles of cyanic or thiocyanic acid or phenyl isocyanate in the manner of a 1,3-2,4-bis-addition yielding perhydrotriazolono[1.2-*a*]triazolone derivatives (I). Similar reactions of cyanates or isocyanates or their thio-analogues with aldazines [2] or ketazines [3] have been reported to give compounds with structures similar to I (Z = O or S; R = alkyl, phenyl, etc.; R′ = H, phenyl) [4].

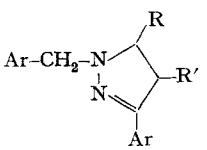
Benzaldazines also reacted with other dienophiles, such as maleic anhydride [5] [6] and N-substituted maleinimides [7] [8] forming perhydropyrazolo[1,2-*a*]pyrazoles (II, R = aryl; X = O or N-alkyl or N-aryl) as 1:2-adducts. Cycloaliphatic aldazines or ketazines, and N-alkylated maleinimides also gave 1:2-adducts, however, through an 'ene' or 'addition'-abstraction reaction [6] [8]. β-Lactones reacted with benzaldazines [9] at 1,3-positions to give 1:1-adducts which after CO_2 elimination yielded 1-benzyl-3-phenyl-2-pyrazolines (III, R, R′ = H, CH_3).



I



II



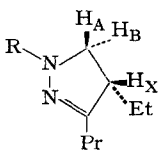
III

[1]) Part of this work was carried out at the University Chemical Laboratory, Lensfield Road, Cambridge, U. K., and the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Mass. 02139, U.S.A.

In contrast to the above 1,3-2,4- or 1,3-additions to azines the addition of isocyanates and isothiocyanates to butyraldazine in the presence of acidic catalysts takes a different course (see scheme, p. 1932) and yields 1:1-adducts (IV, VII, X, XI, XII) as described in this paper.

When phenyl isothiocyanate and butyraldazine were heated in xylene in the presence of picric acid, a crystalline product was obtained in 43% yield. Analysis and mass spectroscopy ($M^+ = 275.1432$) established the composition as a 1:1-adduct $C_{15}H_{21}N_3S$. Spectral data suggested the structure as *1-phenylthiocarbamoyl-3-propyl-4-ethyl-2-pyrazoline* (IV). There is one active hydrogen as shown by *Zerewitinoff* determination and only one proton which gives rise to a singlet at 1.12 τ in the NMR.-spectrum and is slowly exchangeable with D_2O.

The N–H proton of amides or thioamides are known [10] to exchange slowly with D_2O. An IR. band at 3.03 μ also indicated the presence of a –NH group. There are 5 aromatic protons in the region of 2.3–3.1 τ as multiplets, two methyl triplets centred at 9.00 and 9.06 τ, and a group of multiplets for 4 protons at 8.7–8.1 τ which altogether represents two CH_3–CH_2 groups each attached to a saturated carbon centre. A triplet for 2 protons at 7.73 τ ($J = 7.5$ Hz) indicated the presence of a methylene group (α) which is situated between another methylene group and a C=N. This established the Pr-C=N moiety of the structure. The remaining three protons appeared as an *ABX* system with H_A as a triplet at 5.80 τ, H_B as a quartet at 6.18 τ and H_X as a multiplet at 7.0 τ ($J_{AB} = J_{AX} = 12$ Hz, and $J_{BX} = 7.2$ Hz) (for NMR. spectra of 1,3- and 1,3,4-substituted 2-pyrazolines, see *e.g.* [11] [12] [13]). This allows the assignment of *geminal* protons H_A and H_B in agreement with collected data [14], and H_A and H_X as *cis* also corresponding with observed [12] values. Because of the lower τ-values of H_A and H_B, a sequence of Et-CH_X–CH_AH_B–N< is preferred.



IV R = Φ–NH–CS–
VII R = Φ–CH_2–NH–CO–
V R = CH_3CO–
XII R = Φ–NH–CO–

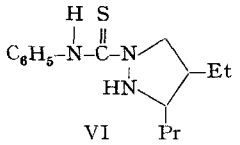
The mass spectrum (see [15], Fig. 4) confirmed structure IV.

In a reaction similar to the facile cleavage of N,N'-diaryl thioureas with acetic anhydride [16] IV was acetolyzed to an oil whose spectral data were very similar to those of the parent compound, suggesting again a 2-pyrazoline structure V. The mass spectrum includes a moderately intense molecular ion at *m/e* 182 which looses a ketene residue in a primary fragmentation step to form an ion at *m/e* 140 (*m** 107.8). Similar to IV (compare [15]) further sequential loss of an ethyl radical followed by a propylene molecule gives ions at *m/e* 111 (also the base peak) and 69 with approximately the same relative intensities as that in IV.

The NMR. spectrum of V shows no signal below 6.0 τ but includes a sharp singlet for 3 protons at 7.95 τ for the CH_3- of the N-acetyl group as well as the characteristic *ABX* system which appears at 6.21 τ (triplet, H_A), 6.59 τ (quartet, H_B) and 7.10 τ

(multiplet, H_X) ($J_{AB} = J_{AX} = 12$ Hz, and $J_{BX} = 8$ Hz), which also underlines the close relationship between IV and V.

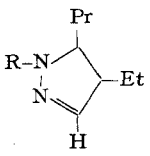
Reduction[2]) of IV with $LiAlH_4$ in ether gave a crystalline product, which analysed as the dihydro-derivative VI; this structure was confirmed by its mass spectrum [15]



VI

and by its NMR. spectrum. In addition to the protons present in the parent compound including the amide hydrogen and the *ABX* system, the amine proton is revealed at 5.27 τ as a broad envelope. This proton can readily be exchanged with D_2O. A multiplet centred at 6.83 τ for one proton accounts for the C-3 hydrogen.

Kost and coworkers have reacted [18] formic acid with butyraldazine to form a 1-formyl-2-pyrazoline with the proposed structure VIII[3]). On treatment with acids, VIII was hydrolysed to the base IX which in turn reacted with phenyl isothiocyanate [19] to give a crystalline solid, m. p. 54.5–55°, to which the corresponding structure X[3]) was assigned.



VIII R = CHO
IX R = H
X R = Φ–NH–CS–

Repeating these experiments we obtained a 44% yield of the N-formyl pyrazoline which, however, was shown by TLC. to consist of two main components. An attempt to separate these by preparative TLC. was unsuccessful. The NMR. spectrum (see Fig. 1) of the product mixture shows clearly two *AMX* systems, one for each of the two components. Apart from the slight difference in chemical shifts and in fine structure, these two *AMX* systems are very similar which suggests a close resemblance between the two structures. Mass spectra [15] taken at time intervals for this product mixture were found to be identical and the fragmentations are in good agreement with the structure VIII as proposed by *Kost* [19]. On the basis of the above data, it is tempting to suggest that this product mixture consisted of two stereoisomers of VIII, differing in their relative configurations at C-4 and C-5.

By computing the NMR. signals of both *AMX* sets we found a ratio of 1.83 of major (VIII b) to minor (VIII a) components which is in excellent agreement with the GC. results which showed the ratio as 1.79. Our observation is in contrast to that recorded in the literature [18] *i.e.* that 3-H-2-pyrazolines of type VIII obtained by acid cyclization of aldazines are pure products (see however [20]).

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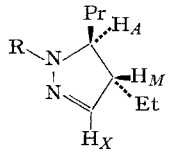
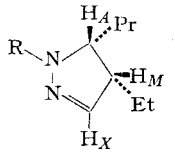
[2]) After completion of our work we learned of a similar reduction of 1-acyl 2-pyrazolines to 1-alkyl pyrazolidines [17].

[3]) Without specifying details of the geometry of substituents at C-4 and C-5.

Hydrolysis of our N-formyl-pyrazoline mixture gave the corresponding bases which on reaction with phenyl isothiocyanate yielded two isomeric N-phenylthiocarbamoyl pyrazolines which are also isomeric with IV. The spectral data for the major component mp. 82–83° suggested the structure of *1-phenylthiocarbamoyl*-trans-*4-ethyl-5-propyl-2-pyrazoline* (Xa). For the minor component, m.p. 66–66.5°, we propose structure Xb with *cis*-configuration. This indicates that *Kost*'s compound [19] with m.p. 54.5–55° was a mixture of the two stereoisomers Xa and Xb.



VIIIa R = –CHO
IXa R = H
Xa R = *Φ*–NH–CS–
XIa R = *Φ*–NH–CO–



VIIIb R = –CHO
IXb R = H
Xb R = *Φ*–NH–CS–

The mass spectra [15] of Xa and Xb are identical.

The NMR. spectra of Xa and Xb are very similar. The main differences between these spectra are the chemical shifts and their fine structures for the three ring protons of each isomer. These signals correspond well to the two sets of *AMX* systems between 3.0 and 7.5 τ as shown in Fig. 1. Chemical shifts and the coupling constants are summarized in the Table:

Comparison of the Chemical Shifts and Coupling Constants of the AMX *Systems for Compounds Xa and Xb* (cf. [13])

H_α or $H_{\alpha'}$ represents the methylene protons of the alkyl side chains

Compound	Protons	Chemical Shifts	Coupling Constants
Xa	H_A (quintet)	5.51 τ	J_{AM} = 3.8; J_{AH_α} = 7.5; $J_{AH_{\alpha'}}$ = 3.8 Hz
	H_M (multiplet)	7.30 τ	J_{AM} = 3.8; J_{MX} = 1.8; J_{AH_α} = 6.5 Hz
	H_X (doublet)	3.21 τ	J_{MX} = 1.8 Hz
Xb	H_A (octet)	5.13 τ	J_{AM} = 10.5; J_{AH_α} = 7.0; $J_{AH_{\alpha'}}$ = 2.0 Hz
	H_M (multiplet)	6.87 τ	J_{AM} = 10.5; J_{MX} = 1.2; J_{AH_α} = 7.5 Hz
	H_X (doublet)	3.21 τ	J_{MX} = 1.2 Hz

The coupling constant J_{AM} is much smaller for Xa (3.8 Hz) than for Xb (10.5 Hz). This suggests that the stereochemistry [12] at C-4 and C-5 of Xa is *trans* and that of Xb is *cis*.

When phenyl isocyanate and butyraldazine were heated under conditions similar to those for the thio-analogue, two isomeric 1:1-adducts XIa (crystalline) and XII (oil) were obtained. The NMR. spectrum of XIa (Fig. 2) closely resembled that of Xa. The *AMX* system is revealed at 3.49 τ (H_X, doublet, J_{MX} = 1.7 Hz), 6.05 τ (H_A, quintet, J_{AM} = 4.0; J_{AH_α} = 8.2; $H_{AH_{\alpha'}}$ = 4.0 Hz) and 7.35 τ (H_M multiplet) which also suggested the stereochemistry of H_A and H_M to be *trans*. This, as well as the mass spectrum [15], confirmed the structure of XIa as *1-phenylcarbamoyl*-trans-*4-ethyl-5-propyl-2-pyrazoline*. The same substance was isolated as the major product when IX was reacted with phenyl isocyanate in refluxing benzene.

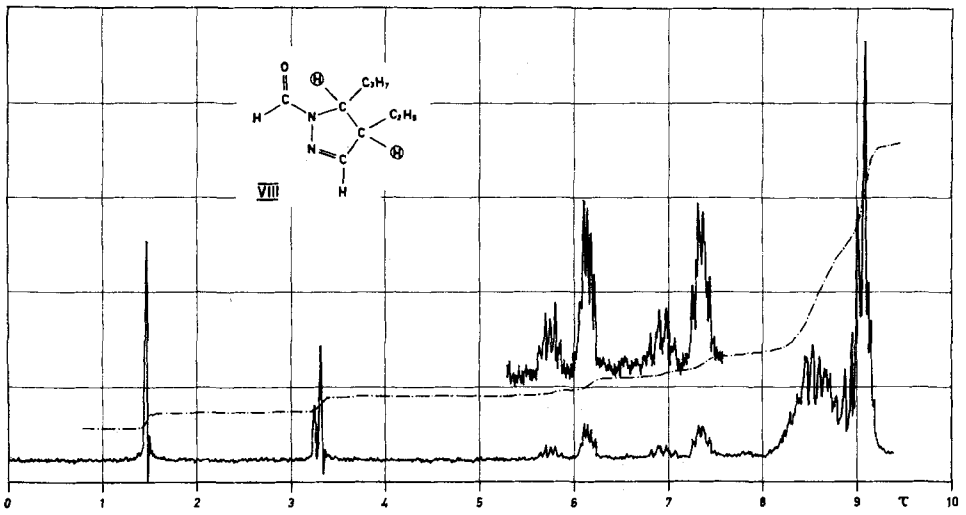
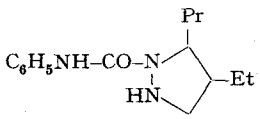


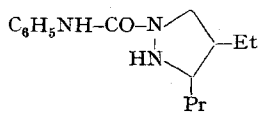
Fig. 1. *NMR. spectrum of product mixture VIIIa + VIIIb*

The NMR. and mass spectra of XII revealed its close relationship with IV; *e.g.*, the *ABX* system in the NMR. is almost indentical to that of IV, and the major fragment ions in the mass spectrum [15] are shown at *m/e* 242 (M – OH), 140 (M – C_6H_5NCO), 111 (base peak) and 69. The structure of XII was confirmed by treatment of IV with PbO in aqueous propanol [21], which gave an oil whose spectral and TLC. properties were identical to those of XII.

Reduction[2]) of XIa and XII with $LiAlH_4$ in ether at 0° gave the corresponding pyrazolidine derivatives, XIII and XIV, respectively, as oils.



XIII

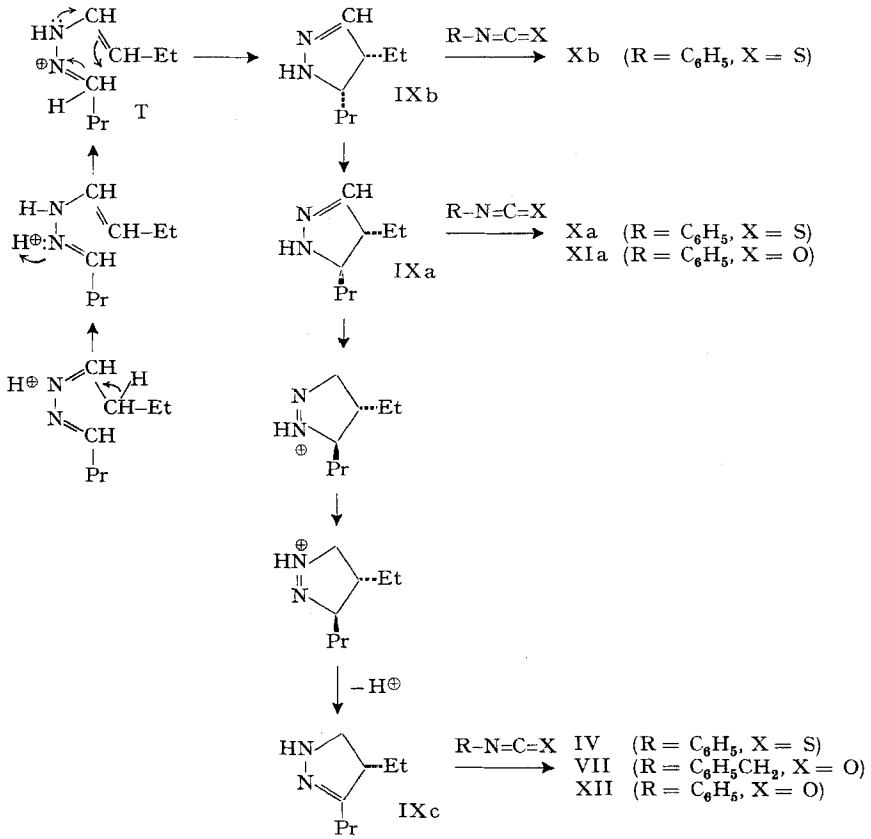


XIV

Benzyl isocyanate reacted with butyraldazine under similar conditions to give an oil the major component of which was the 1:1-adduct $C_{16}H_{23}N_3O$. The mass spectrum [15] and the NMR. spectrum of this product are again very similar to those of IV, except that the 5 aromatic protons of the phenyl ring appear as a singlet at 2.78 τ, and the methylene protons of the benzyl group as a doublet centred at 5.65 τ (J = 6.2 Hz). The amide hydrogen is revealed as a broad triplet centred at 6.02 τ. The *ABX* system is almost identical with that of IV. Therefore the structure VII is suggested for this product.

A possible pathway for the formation of these isomeric 1:1 adducts is proposed in the Scheme. The main distinction between butyraldazine and benzaldazine is that the former contains hydrogen atoms at the β-carbon (relative to N) which are more acidic than the one in the partial structure –N=CH–. Such hydrogen is absent in benzalazine, probably the main reason why these two azines react so differently even with the same

Scheme



type of reactants (compare also [7]). Protonation of butyraldazine promotes the expulsion of a β-hydrogen and leads to the formation of an enamine imine intermediate [22], T, which in a disrotatory cyclization [23] gives rise to the *cis*-pyrazoline IXb. The latter then rearranges to the more stable *trans* isomer IXa (see scheme). This sequence was substantiated by the following evidence.

Butyraldazine heated alone in xylene up to 200° yielded only a very small amount of IX as shown by GC. analysis. However, in the presence of 1% of an acid catalyst such as picric acid or BF_3–$C_2H_5NH_2$ nearly quantitative cyclization took place above 110° yielding the pyrazoline mixture IXa and IXb in ratios from 1.47 (110°) to 1.77 (170°). These values correspond well with the ratios of the two epimeric 1-formyl-2-pyrazolines VIIIa and VIIIb in the product obtained by *Kost*'s reaction (see above).

At higher temperature, further isomerization of IXa should give IXc [20] [23]. This argument is based on work of *Elguero & Jacquier* [24], who received pure 1-formyl 5-methyl-pyrazoline-2, an analogue of our structures IXa/IXb, on cyclization of acetaldazine with formic acid. On hydrolysis with acid this product gave a 2:1 mixture of 5-methyl-2-pyrazoline and of 3-methyl-2-pyrazoline, the latter being related to our isomer IXc. Similar observations have been made by the Russion workers [25].

When we reacted (a) phenyl isocyanate with butyraldazine in presence of a trace of acid at 200°, derivatives XIa and XII of the pyrazoline isomers IXa and IXc were found; when (b) phenyl isothiocyanate or benzyl isocyanate were reacted, derivatives

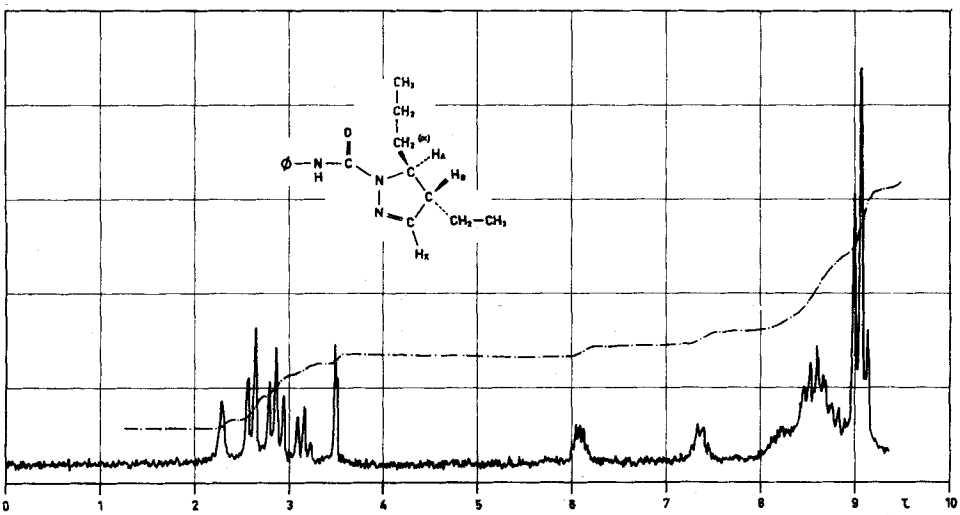


Fig. 2. *NMR. spectrum of XIa*

IV or VII of the most stable pyrazoline isomer IXc were isolated. This indicates that the rate of addition of the isocyanate in (a) was similar to the rate of isomerization IXa → IXc, while in (b) the addition rate is evidently smaller, in agreement with the observed (see *e.g.* [26]) smaller reactivity of phenyl isothiocyanate compared to phenyl isocyanate in addition reactions.

Experimental Part

All m.p.'s were recorded with a *Culatti* apparatus and are not corrected; UV. spectra were measured in ethanol on the *Perkin Elmer* 137 UV. spectrophotometer, IR. spectra on a *Perkin Elmer* 137 NaCl infracord. NMR. spectra were recorded with a *Varian* HA 100 spectrometer in CCl_4 with tetramethylsilane as internal standard; for mass spectra see [15]. GC. were run on a *Pye* series 104 chromatograph with 40 ml He/min with column QF-1 (trifluoropropyl methyl silicon oil) at 150°, and a heat conductivity detector at 220°.

Butyraldazine was prepared according to the literature: recorded [18] yield 80%, bp. 80°/26 Torr, $n_D^{20} = 1.4520$; found yield 85–92%, b.p. 68–70°/13 Torr, $n_D^{20} = 1.4523$. GC. retention time 1.1 min; for comparison: butyraldehyde, 0.4 min.

Reaction of phenyl isothiocyanate with butyraldazine: IV. A mixture of phenyl isothiocyanate (60.84 g, 452 mmoles), butyraldazine (33.03 g, 236 mmoles), hydroquinone (0.2 g), phenyl β-naphthylamine (0.1 g) and picric acid (0.2 g) was heated in absolute xylene (315 ml) in an autoclave for 10 h at 200°. The mixture was evaporated *in vacuo* and the residue was treated with petrol ether to remove N,N'-diphenyl thiourea, m.p. 135–142° (10.6 g). Further amounts of this material were removed by distillation up to 200° (bath temp.) at 12 Torr. The residue was distilled to give a reddish oil, b.p. 125–178°/0,01 Torr (35.8 g) which on crystallization from ether yielded 28.8 g (104.5 mmoles, 43% theoretical yield) *1-phenylthiocarbamoyl-3-propyl-4-ethyl-2-pyrazoline* (IV) as needles, m.p. 55–60°. The analytical sample, m.p. 60.5–61.5° was obtained by recrystallization from petrol ether. UV: λ_{max} 281–282 nm ($\varepsilon = 29100$). IR. in KBr: 3.03 μ (–NH), 6.26 μ (–C=N–,

for 1,4,5-trialkyl-2-pyrazolines (see *e.g.* [27]) 6.3 μ), 6.16 and 6.68 μ (phenyl), 6.46 *ss* (–C=S, similar to N,N'-diphenyl thiourea).

$C_{15}H_{21}N_3S$	Calc.	C 65.37	H 7.69	N 15.28	S 11.64	active H 0.36%
	Found	,, 65.57	,, 7.81	,, 15.49	,, 11.62	,, ,, 0.37% (*Zerewitinoff*)

Reaction of IV with acetic anhydride: V. A mixture of IV (0.826 g, 3 mmoles) and acetic anhydride (10 ml) was heated under reflux for 1 h. It was evaporated in *vacuo*, diluted with ether, and extracted with 2N HCl (3 × 30 ml). The combined acidic solution was made alkaline and extracted with ether. The dried organic layer was distilled to give *1-acetyl-3-propyl-4-ethyl-2-pyrazoline* (*V*) as an oil, b.p. 83–87°/0.05 Torr, $n_D^{20} = 1.4868$ (0.56 g, quantitative yield). UV.: λ_{max} 240–241 nm (ε = 13200). IR., film: 2.9 μ m (>CO, –C=N– overtones), 6.05 μ (–C=N–; found for butyraldazine, 6.02 μ), 6.1–6.2 μ (N–$COCH_3$).

$C_{10}H_{18}N_2O$ Calc. C 65.90 H 9.92 N 15.37% Found C 65.67 H 10.09 N 14.95%

Reduction of IV with $LiAlH_4$. A solution of IV (10.09 g, 36.4 mmoles) in dry ether (300 ml) was treated with $LiAlH_4$ (4.14 g, 109.1 mmoles) in small portions at 0°. Stirring was continued for 5 h at this temp. After decomposition with a small quantity of water, the organic layer was separated and on evaporation yielded a solid, m.p. 69–75° (7.63 g). Recrystallization from petrol ether gave pure *1-phenylthiocarbamoyl-3-propyl-4-ethyl-2-pyrazolidine* (VI), m.p. 92–93° (7.63 g). UV.: λ_{max} 253–256 nm (ε = 19200). IR. in KBr: 3.1 and 3.2 μ (two –NH–), bands at 6.26, 6.4, 6.67 μ as in IV; band at 6.25 μ of IV disappeared.

$C_{15}H_{23}N_3S$	Calc.	C 64.94	H 8.36	N 15.15	S 11.56%
	Found	,, 64.95	,, 8.55	,, 15.03	,, 11.41%

Reaction of IV with PbO. A mixture of IV (3.11 g), *n*-propanol (25 ml), water (7,5 ml) and PbO (2.2 g) was heated under reflux with stirring according to a published method [21] for 72 h. The reaction mixture was cooled and filtered. The filtrate was evaporated *in vacuo* and the residue separated on silica with cyclohexane-chloroform 1:1 and then with benzene petrol ether-ether 1:1:1 by dry column chromatography [28] to give starting material (1.81 g) and an oil, b.p. 175–180°/0.005 Torr (0.4 g) whose UV. and IR. spectra were practically identical with the spectra of the oily adduct XII though analysis showed a little impurity from the starting material:

$C_{15}H_{23}N_3O$	Calc.	C 69.47	H 8.16	N 16.21	S 0%
	Found	,, 70.11	,, 8.27	,, 15.60	,, 0.34%

Reaction of formic acid with butyraldazine [18]. Formic acid (9.20 g) was added dropwise to butyraldazine (14.02 g, 100 mmoles) which was cooled in an ice bath to avoid a sudden increase in temperature. After the addition, the mixture was allowed to warm to room temperature. After standing for two days, the mixture was rendered alkaline with ammonia under cooling. After addition of water (50 ml) it was extracted with ether (3 × 30 ml). The dried ethereal solution on distillation gave three similar colourless liquid fractions (7.40 g; 44%); the major one consisted of two isomeric 1-formyl-2-pyrazolines (VIIIa, VIIIb) b.p. 127–133°/13 Torr, $n_D^{20} = 1.4818$. IR.-film: 5.9–6.0 μ (–CHO), 6.24 μ (–C=N–). TLC. (silica gel, petrol ether-ether 9:1) revealed two major spots; GC. showed two isomers with assigned structures VIIIb and VIIIa, retention times 10.3 and 13.05 min respectively, peak area ratio 1.79 to 1. NMR. showed two sets of *AMX* systems and a singlet for 1H at 1.46 τ (–CHO) (see Fig. 1).

$C_9H_{16}N_2O$ Calc. C 64.26 H 9.59 N 16.66% Found C 64.55 H 9.74 N 16.69%

When formic acid was added at room temperature without cooling, the temperature of the mixture rose suddenly to about 95° and the mixture became turbid. The yield was somewhat reduced.

Reaction of 1-formyl-2-pyrazolines (VIIIa, VIIIb) with HCl. The above mixture of isomeric 1-formyl-2-pyrazolines (2.0 g, 11.4 mmoles) was dissolved in conc. HCl (4 g). The solution was evaporated *in vacuo*. The residue was treated with conc. ammonia (24 ml) and extracted with ether (3 × 30 ml). The dried ethereal solution, on distillation, gave two fractions, b.p. 43–47°/0.001 Torr, $n_D^{20} = 1.4657$, and b.p. 47–55°/0.001 Torr, $n_D^{20} = 1.4665$. According to TLC. both fractions contained the two isomeric 2-pyrazolines. These isomers (IXa) and (IXb) had GC. retention times 3.2 and 3.6 min respectively and a peak area ratio of 1.47 to 1.

Reaction of 1-H-pyrazolines (IXa, IXb) with phenyl isothiocyanate [19]: Xa and Xb. A mixture of the isomeric 2-pyrazolines (1.85 g, 13.2 mmoles), phenyl isothiocyanate (1.77 g, 13.1 mmoles)

and dry benzene (37 ml) was heated under reflux for 1 h. The solution was evaporated to dryness and the crystalline residue (0.715 g, m.p. 73.5–78°) was treated with charcoal and recrystallized from aqueous ethanol to give *1-phenylthiocarbamoyl-4-ethyl-5-propyl-2-pyrazoline* (Xa), m.p. 82–83°. UV.: λ_{max} 284–288 nm (ε = 23600). IR. in KBr: 3.03 μ *m* (–NH–), 3.27, 3.32 μ *w* (–CH=N, [27], 3.2–3.3 μ), 6.3 μ (–C=N–, [27], 6.3 μ), 6.6 μ *ss* (–C=S).

$C_{15}H_{21}N_3S$ Calc. C 65.37 H 7.69 N 15.28 S 11.62%
Found ,, 65.23 ,, 7.77 ,, 14.05 ,, 11.57%

The residue obtained from the mother liquor on evaporation solidified (m.p. 64–65°); it contained two major components as revealed by TLC. It was separated on silica gel by elution with benzene to give first Xa, Rf 0.68 (silica gel TLC., benzene-acetone 10:1), closely followed by its isomer Xb, Rf 0.62, fine needles from petrol ether, m.p. 66–66.5°. UV: λ_{max} 288 nm (ε=23300). IR. in KBr: Main bands very similar to those of Xa, considerable differences in the finger print region.

Found C 65.9 H 7.9 N 15.1 S 11.55%

Reaction of phenyl isocyanate with butyraldazine: XIa and XII. A mixture of butyraldazine (38.85 g, 277 mmoles), phenyl isocyanate (32.40 g, 272 mmoles) hydroquinone (0.2 g), picric acid (0.25 g) and phenyl β-naphthylamine (0.1 g) was heated in an autoclave for 10 h at 200°. The mixture was distilled to give an oil, b.p. 80–245°/0.15 Torr (40.27 g). Crystallization from petrol ether gave XIa as fine colourless nedles, m.p. 76–77° (9.49 g). UV.: λ_{max} 258 nm (ε = 21300). IR. in KBr: 3.02, 6.05, 6.52 μ (R–NH–CO–), 6.15 μ (–C=N–).

$C_{15}H_{21}N_3O$ Calc. C 69.47 H 8.16 N 16.21% Found C 69.76 H 8.12 N 16.11%

The combined mother liquor was chromatographed on alumina (*Woelm*) to give, first, another crop of XIa (1.5 g, total yield 16%). Further elution with CH_2Cl_2 and $CHCl_3$ gave an oily adduct XII, b.p. 145–146°/0.001 Torr, n_D^{20} = 1.5608 (8.9 g, 13%). UV.: λ_{max} 256–257 nm (ε=21000). IR.; film: 2.9, 5.95, 6.55 μ (R–NH–CO–), 6.25 μ (–C=N).

$C_{15}H_{23}N_3O$ Calc. C 69.47 H 8.16 N 16.21% Found C 69.56 H 8.26 N 16.03%

Reaction of 1-H-2-pyrazolines (IX) with phenyl isocyanate. A mixture of 1-*H*-2-pyrazolines (1 g, 7.14 mmoles), phenyl isocyanate (0.96 g, 8.05 mmoles) and dry benzene (20 ml) was heated under reflux for 1 h. It was evaporated *in vacuo*, and the residue was crystallized from xylene to remove a by-product, m.p. 232–237° (0.05 g). Separation of the mother liquor by preparative TLC (*Merck* PSC Al_2O_3 plates), starting with petrol ether as mobile phase, then with increasing proportions of isopropyl ether, gave a product, m.p. 67–75° (0.64 g). Recrystallization from petrol ether gave crystals of XIa, m.p. and mixed m.p. 77.5–78°. The IR. spectrum was identical with that of an authentic sample.

Reduction of XIa to XIII. – (a) *With $LiAlH_4$.* To a solution of XI a (1.00 g, 3.86 mmoles) in dry ether (30 ml) $LiAlH_4$ (0.44 g, 11.58 mmoles) was added in small portions at 0°. After 2.5 h stirring at this temperature a small quantity of water and 2N NaOH was added and the organic layer was separated. By distillation it gave an oil, b.p. 181°/0.001 Torr (0.80 g). UV.: λ_{max} 242 nm (ε = 16150). IR., film: 2.95 and 3.0 μ (–NHCO–, –NH–); region 6–7 μ basically unchanged.

$C_{15}H_{23}N_3O$ Calc. C 68.92 H 8.87 N 16.08% Found C 68.88 H 9.02 N 16.03%

(b) *With sodium in liquid ammonia-ether* the same product was obtained.

Reduction of XII to XIV. A solution of XII (1.07 g, 4.14 mmoles) was similarly treated with $LiAlH_4$ (see above) to give an oil, b.p. 186–188°/0.001 Torr (0.92 g). UV.: λ_{max} 246–248 nm (ε = 18920). IR., film: 3.0 and 3.07 μ (–NH–CO–, –NH–); region of 6–7 μ practically unchanged.

$C_{15}H_{23}N_3O$ Calc. C 68.92 H 8.87 N 16.08% Found C 69.29 H 9.19 N 15.66%

Reaction of benzyl isocyanate with butyraldazine: VII. Benzyl isocyanate (27.7 g, 208 mmoles) was mixed with butyraldazine (29.16 g, 208 mmoles), hydroquinone (0.2 g), phenyl β-naphthylamine (0.1 g) and picric acid (0.2 g) in dry xylene (200 ml). A by-product m.p. 227–230° (1.92 g) was formed and separated. The filtrate was heated in a closed vessel for 10 h at 200°. After cooling, more of the by-product was removed (2.82 g). The filtrate was distilled. The principal fraction, b.p. 162–176°/0.02 Torr (33.0 g, 121.6 mmoles, 59%, TLC. revealed one major spot) gave by repeated fractional distillation VII as an oil, b.p. 160–166°/0.005 Torr, n_D^{20} = 1.5390. UV.: λ_{max} 244–247 nm (ε = 11630). IR., film: 3.0, 6.02 μ (R–NH–CO–).

$C_{16}H_{23}N_3O$ Calc. C 70.30 H 8.48 N 15.37% Found C 70.44 H 8.65 N 15.27%

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