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HETARYLNITRENES—III

THERMAL REARRANGEMENTS ON THE $C_4H_3N_3$ ENERGY SURFACE—THE ROLE OF 1-SUBSTITUTED PYRAZOLES

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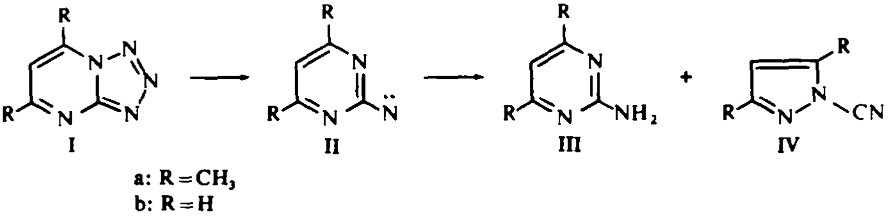
Abstract—Gas phase pyrolysis of tetrazolo[1,5-*a*]pyrimidines leads *via* ring contraction to 1-cyanopyrazoles, then at higher energy to N_2-loss and formation of unsaturated nitriles. 3-Cyano-3,5-dimethyl-3H-pyrazole (also obtained from pyrolysis of the 1-cyano derivative) is implicated as an intermediate in the case of 5,7-dimethyltetrazolo[1,5-*a*]pyrimidine. Pyrolysis of 1,3,5-trimethylpyrazole similarly results in Me migration/N_2-loss to give C_6H_{10} dienes. In this case a competing H_2-loss/ring expansion leads to 4,6-dimethylpyrimidine.

WE HAVE recently[1] discussed gas phase thermolysis of tetrazolo [1,5-*a*]pyrimidines (I)/2-azidopyrimidines[2] to aminopyrimidines (III) and 1-cyanopyrazoles (IV), presumably *via* transformations of nitrenes (II) on the $C_4H_3N_3$ energy surface.



Certain aspects of this reaction resemble the pyrolysis of azides,[3] notably the extensive formation of amines by H-capture, and the occasionally observed loss of the CN-group from IV to give pyrazoles. In the case of phenyl azides formation of azobenzenes and anilines were observed on mild pyrolysis, whereas ring contraction, CN-migration and CN-loss were characteristic of violent pyrolysis.[4] We ascribed the latter reactions to the formation of a vibronically excited ("hot") singlet nitrene. Progressive increases in the temperature of pyrolysis of 5,7-dimethyltetrazolo[1,5-*a*]pyrimidine (Ia) gave similarly interesting results. At 500° it gave, in addition to the normal products (IIIa, IVa), a low yield (3%) of a second nitrile, to which was assigned the structure 3-cyano-3,5-dimethyl-3H-pyrazole (V). The IR spectrum was devoid of NH-bands, and ν_{CN} 2253 cm^{-1} indicated that the CN-group was unconjugated. The UV spectrum in cyclohexane showed λ_{max} 232 nm (IVa had ν_{CN} 2264 cm^{-1}, λ_{max} 230 nm). The mass spectrum showed $M^+ = 121$, and the NMR spectrum showed signals at τ 3·85 (*s*, H_4), 7·56 (*s*, 3-CH_3) and 7·72 (*s*, 5-CH_3) in the correct integrated ratio of 1 : 3 : 3; no NH signal was detected.

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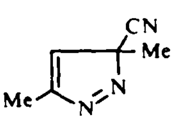
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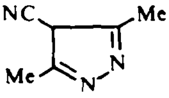
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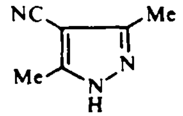
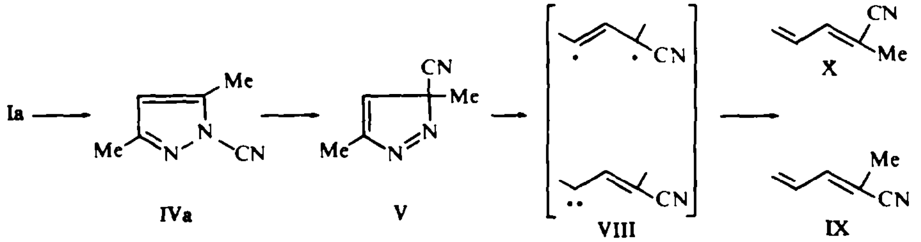

VII

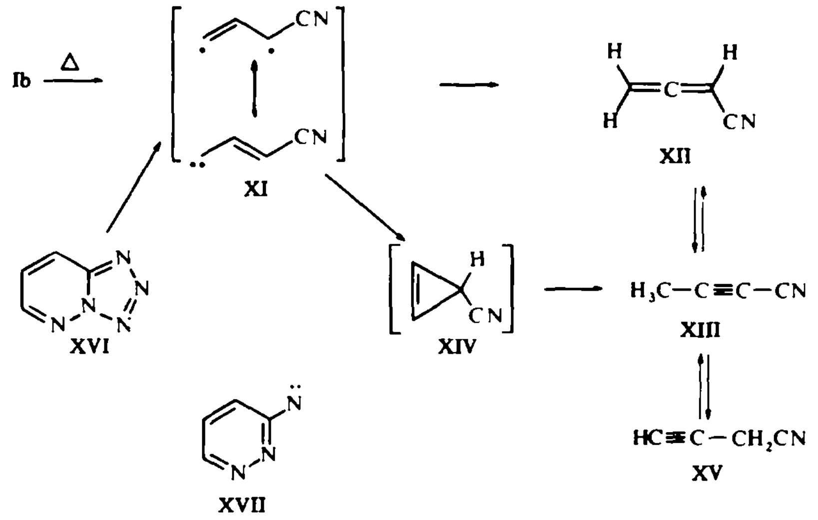
Of the possible cyanodimethylpyrazoles IVa, V, VI and VII, these data eliminate all but V. The only other unconjugated nitrile (VI), quite apart from the magnetic equivalence of the Me groups, would be expected to tautomerise to VII and exchange with D_2O/base, which did not occur. The possibility of a pyrazole/imidazole rearrangement[5] was eliminated as the dimethyl-1-cyanoimidazoles[1] are distinct from V. The same nitrile was obtained from pyrolysis of the 1-cyanopyrazole IVa, and the transformation appears to be another example of the CN-group shift previously noted[4] in the cyanocyclopentadienes and cyanopyrroles. The yield was, however, extremely low, no doubt due to the unfavourable electronic factors (unconjugated CN) and the thermal instability of V.

Pyrolysis of the tetrazolo[1,5-*a*]pyrimidine Ia under somewhat more vigorous conditions (700°/0·1 mm) gave a 15% yield of a 2 : 1 mixture of *cis*- and *trans*-2-methyl-2,4-pentadienonitriles (IX and X). Essentially the same results were obtained by similar pyrolysis of either of the cyanopyrazoles IVa or V. These results suggest rearrangement of the first formed product of ring contraction (IVa) to the 3H-pyrazole V, followed by thermal N_2-loss and isomerisation of the resultant intermediate VIII. Photochemical N_2-loss from 3H-pyrazoles[7] and pyrazolines[8] with formation of cyclopropenes, cyclopropanes and dienes are well established processes; under the experimental conditions we employed cyclopropenes would not survive.

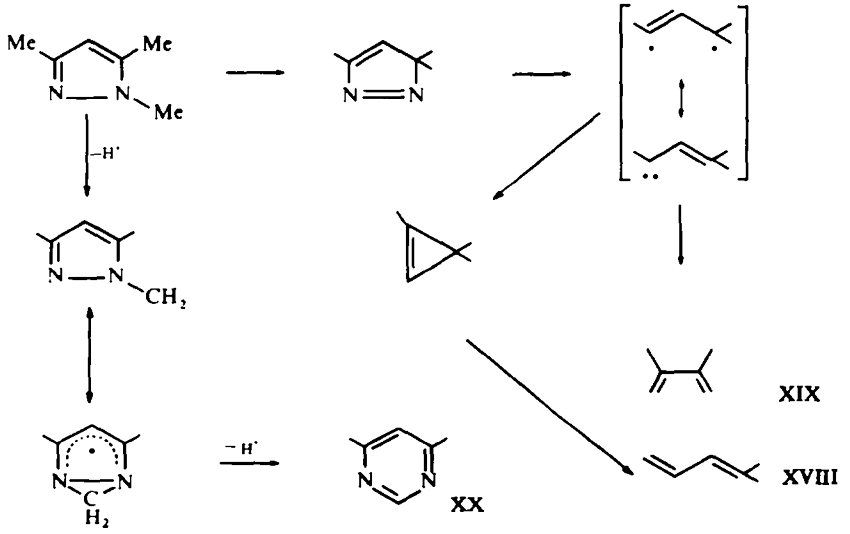


The nitriles X and IX were separated by GLC, the *cis*-isomer eluting first. The *trans*-isomer was prepared independently by the action of chlorosulphonyl isocyanate[5] on the corresponding acid; the chemical shift of the Me group was slightly higher than in the *cis*-isomer due to partial shielding by the 4,5-double bond. When tetrazolo[1,5-*a*]pyrimide itself (Ib), *or* 1-cyanpoyrazole (IVb) was pyrolysed at 800°/0·01 mm a 1 : 3 mixture of cyanoallen (XII) and tetrolonitrile (XIII) was obtained; the isomeric propargyl cyanide (XV) was not detected.

In a preceding paper[1] we reported the pyrolysis of tetrazolo [1,5-*b*]pyridazine XVI, which would also be expected, by formal analogy with other tetrazoloazines, to yield 1-cyanopyrazole. In fact this product was not detected, although the decomposition was conducted at a temperature (300°) substantially lower than that necessary for the thermal decomposition of 1-cyanopyrazole. The products were the same as those recorded (XII, XIII) in pyrolysis of 1-cyanopyrazole, and in addition both 3-cyanocyclopropene XIV and propargyl cyanide XV were detected. It is evident that in



this case fragmentation has occurred rather than ring contraction to IVb, and that this must be ascribed to an inherent instability in the nitrene XVII (presumably due to the destabilising influence of the N—N bond). Formation of the intermediate XI, either concerted with, or subsequent to, generation of the nitrene XVII, should lead to the production of cyanoallene[*] and cyanocyclopropene[†] as the primary products. The isolation of cyanoallene as the major component of the mixture is consistent with this, although the situation is somewhat obscured by the isomerisation of XV and XIII to XII and XIV on GLC at 100°; the tautomerisation of XII and XIII themselves is known to occur.[9]



Scheme I

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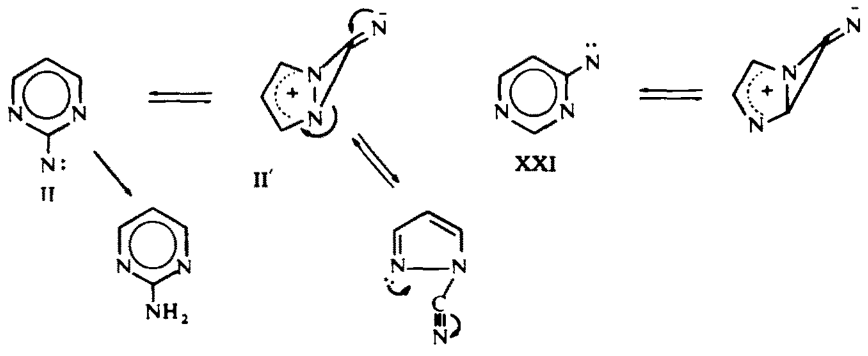
[*] By insertion in the C_2-H bond of XI or by rearrangement of cyanocyclopropene.

[†] By 1,3-bonding or insertion in the double bond in XI. Note that increasing vibrational energy in XI would militate against this process, as is the case with trimethylene in the gas phase.[10]

The N→C migration/N_2-elimination cycle in the 1-substituted pyrazoles was not confined to the cyano-group. We subjected 1,3,5-trimethylpyrazole to pyrolysis at 800°/0·05 mm, obtaining XVIII in 1–2% yield. At 900° this product (5%) was accompanied by 2,3-dimethylbutadiene (XIX-5%), benzene (0·5%), 4,6-dimethylpyrimidine (XX-8·5%) (Scheme I) and small amounts of a number of unidentified high-boiling components. The multiplicity of products, The low yields, and the drastic conditions required all point to the intervention of other radical pathways at this temperature. Formation of the dienes XVIII and XIX is analogous to the results obtained (*vide supra*) from pyrolysis of 1-cyanopyrazoles: the more intriguing aspect of Scheme I is the ring expansion/H_2-loss in the formation of XX—formally analogous to the previously recorded[11] ring expansion in methyl-cyanocyclopentadienes. In an earlier paper[1] we have compared the transition states for ring contraction in the isomeric nitrenes II and XXI and have proposed that the N—N bond in the transition state from II leads to a preference for nitrene-like behaviour (H-capture, fragmentation). It is interesting to note here the tendency for the N_1-carbon to insert between N_1 and N_2 to yield the pyrimidine XX, although discussion of the mechanistic details is not warranted at this stage. Reversal of the sequence 2-nitrenopyrimidine → 1-cyanoimidazole would be formally analogous to the formation of XX, with the exception that the species generated (II′) would be unstable *unless* H-*capture occurred* to give the 2-aminopyrimidine, as it does[1], i.e. 2-nitrenopyrimidine finds ring contraction a relatively unsatisfactory escape route from its energetic dilemma.



EXPERIMENTAL

The general conditions used in pyrolysis experiments and in product analysis have been described in earlier papers.[1] GLC columns referred to in the text are:

Column A: 20% Carbowax 20M on Embacel (12′ × 1/6″)

Column B: 5% Carbowax 20M on Aeropak (5′ × 1/6″)

The carrier gas used was helium (60 ml/min). Mass spectra were recorded on AEI MS902 and MS10C2 instruments as stated. NMR spectra were recorded at 60MHz unless stated otherwise.

1. *Pyrolysis of* 5,7-*Dimethyltetrazolo*[1,5-a]*pyrimidine* (Ia)

(a) *At* 500°/0·1 mm. (*volatilisation temperature* 140°). Compounds IVa and IIIa were obtained as described previously, together with a new compound, eluting shortly before IVa on Column B. This was assigned the structure 3-*cyano*-3,5-*dimethyl*-3H-*pyrazole* (V), and formed colourless prisms, m.p. 48–49° (yield 3%); *Mass spectrum*: M^+, 121 (100%), M—H (22%), M—CH_3 (3·5%), M—HCN (3·5%). Other physical data are given in the discussion.

(b) *At* 800°/0·1 mm (0·5 g; *volatilisation temperature* 100°). A dark red tar and 2-amino-4,6-dimethylpyrimidine (5%) were obtained together with a volatile liquid (0·047 g; 15%) which was shown by GLC to be an almost pure mixture of IX and X, in the ratio 2 : 1. The *cis*-isomer eluted first. The *trans*-isomer was prepared bya an independent synthesis (*vide infra*). Spectroscopic data are listed below.

cis: ν_{max}: 2218 s, 930 s (═C—H), 1860 s (2ν), 1420 s, 2900–3000 m, 3080 (═CH) cm^{-1}λ_{max}(C_6H_{12}): 245 (27000) nm; *NMR*: τ 3·40 (*m*, 2H), 4·60 (*m*, 2H), 8·00 (*s*, 3H); *Mass spectrum*: M^+=93·05888 (Calc. 93·05785) (100%), M—H (40%), M—CH_3 (12%), M—HCN (137%, m*).

trans: ν_{max} 2215 s cm^{-1}; IR, UV and mass spectra otherwise as for the *cis*-isomer; *NMR*: τ 3·40 (m, 2H), 4·60 (*m*, 2H), 8·06 (*s*, 3H).

2. *Pyrolysis of* 1-*Cyano*-3,5-*dimethylpyrazole* (IVa)

0·33 g was pyrolysed at 650°/0·05 mm over 20 min to yield a total pyrolysate of 0·30 g. This consisted of unchanged starting material containing 5% 3,5-dimethylpyrazole, 2–3% of the open chain nitriles IX and X, and a trace of Va, identified by its retention time on GLC and by its mass spectrum. Further experiments with increasing temperatures led progressively to increased yields of open chain nitriles and a lower recovery of the starting material.

3. *Pyrolysis of tetrazolo*[1,5-*a*]*pyrimidine* (Ib)

The tetrazole (0·60 g) was pyrolysed at 800°/0·1 mm, and an ether extract of the products was subjected to GLC (Column B); two nitriles (T_R = 3·0 and 7·6 min) were idenfied as tetrolonitrile (10%) and cyanoallene (3·3%). 2-Aminopyrimidine (2–3%) was eluted later. Tetrolonitrile (XIII) had the same properties as the compound described in 6 below: m.p. 17–18° (*cf* refs 12, 13): *IR*(*LF.*) 2160 w, 2270 s; IR(CCl_4) 2270 s, with comparatively weak bands at 2230, 1430, 1380, and 2900–3000 cm^{-1}; λ_{max} (C_6H_{12}) *ca* 220 nm; 100 *MHz NMR*: τ 8·02 (*cf* ref 7); *Mass spectrum*: M^+ 65 (100%), M—H (54%), M—HCN (63%). Cyanoallene (XII) was a liquid, ν_{max} (LF): 2235 m, 2230 s, 1970 v.s., 1410 s, 984 m, 920 m, 865 s, 840 s cm^{-1} (identical with the spectrum in ref 14) ν_{max} (CCL_4): 2235, 1975, 1412, 987 cm^{-1}; λ_{max} (MeOH): 215 (14200) nm.[14] The mass spectrum was identical with that of tetrolonitrile; *NMR*: τ 4·60 (*cf* ref 9).

4. *Pyrolysis of* 1,3,5-*trimethylpyrazole*

Pyrolysis at 800°/0·05 mm (0·65 g; volatilisation temperature 20°) gave (GLC, Column A, 50° isothermal) unchanged starting material and XVIII (1–2% M^+ = 82, M—CH^3 (100%), m/e 39, 41), identified by its IR and NMR spectra.[15] At 900°/0·1–0·2 mm both this product (5%) and XIX, (5%) were obtained, together with benzene (2·5%) and 4,6-dimethylpyrimidine (8·5%), the last was identified by comparison with a synthetic specimen.[16] Numerous other high-boiling components were formed in lower yield (⩽ 1%), but were not investigated in detail. The most abundant of these has a mass spectrum indicative of a trimethylpyrimidine (M^+ = 122, intense M-1 and M—HCN peaks).

5. trans-2-*Methyl*-2,4-*pentadienonitrile* (X)

Trans-2-Methyl-2,4-Pentadienoic acid [17] (2·78 g) in methylene chloride (25 ml) was treated at 0° with chlorosulphonyl isocyanate (3·687 g. *cf* ref 6) during 25 min with stirring. The resultant soln was stirred 13 hr at 22°, then refluxed for 3 hr. Triethylamine (3·5 ml) in methylene chloride was added at 0° over the course of 25 min, stirring was continued at 22° for 2·5 hr. the mixture was poured onto crushed ice and the organic phase separated. The aqueous phase was extracted with ether, the combined organic phases were dried over $MgSO_4$, the solvents removed and the residue was distilled under reduced pressure. the product (1·66 g, 72%) was in all respects indentical with that from pyrolysis of 1-cyano-3,5-dimethylpyrazole. Physical data are reported under 2 above.

6. *Tetrolonitrile* (XIII)

A mixture of propargyl bromide (11·9 g, 0·1 mole) and KCN (7·0 g, 0·108 mole) in dry DMF (50 ml) was stirred at 20° for 14 hr. filtered, diluted with water and extracted with pentane. Removal of the solvent and distillation at 50–60°/50 mm gave a 10% soln (2 g) of tetrolonitrile in propargyl bromide. The nitrile was isolated and identified (m.p. 17–18°) by GLC. Physical data are reported under 3 above. Optimal reaction conditions were not investigated.

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