# Stereoisomerization in Heterocyclic Hydrazones Derived from 2-Acylpyridines and their Oxidative Cyclization with Mercury(II) Acetate and Lead Tetra-acetate to Fused 1,2,4-Triazoles and 1,2,3-Triazolium Systems

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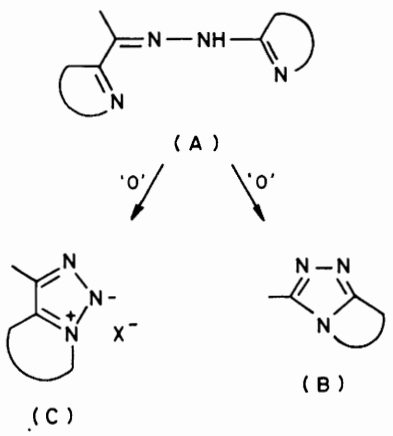
Hydrazones prepared by coupling 2-acylpyridines with arylhydrazines were isolated predominantly as *E*-isomers when the acyl substituent R was small (H or Me). When R was a phenyl group significant yields of *Z*-isomers, containing an intramolecular hydrogen bond, were also isolated. Oxidation reactions of these hydrazones were not influenced by the *E*- or *Z*-geometry of the substrate contrary to earlier reports. A common metallo intermediate with a *Z*-structure was encountered in the oxidations of the *E*- and *Z*-pyridine 2-carbaldehyde 2-pyridylhydrazone with mercuric acetate. In oxidations of a series of hydrazones with lead tetra-acetate the product controlling factor was the nature of the methine substituent R. For ketone derivatives (R ≠ H) oxidation to fused 1,2,3-triazolium systems occurred *via* a 5-*exo*-*tet* cyclization with *E*- and *Z*-hydrazone substrates. For aldehyde systems (R = H) the oxidation involved dehydrogenation to a nitrilimine and gave products by solvent addition or a 5-*endo*-*dig* cyclization to fused 1,2,4-triazolo systems.

Cyclizations of substituted hydrazone systems containing a 2-heterocyclic group on the amino nitrogen, (A), with metallic oxidizing agents [1-3] or by electrochemical methods [4] have been widely used for the synthesis of fused 1,2,4-triazolo compounds (B). Metallo intermediates have not previously been isolated or directly detected in these reactions. If the hydrazone substrate contains a 2-heterocyclic group on the methine carbon as in structure (A) the oxidation could also lead to fused 1,2,3-triazolium systems (C) (Scheme 1). There are only a few




**Scheme 1.**

examples of this latter reaction and it was reported earlier [5] that it occurs only with hydrazone *Z*-isomers. When both ends of the hydrazone chain contain 2-heterocyclic groups competition between products of type (B) and (C) is theoretically possible and the stereoisomerism of the hydrazone substrate could influence the outcome. We describe herein [6] a study of these factors for the competitive oxidations of a range of *E*- and *Z*-isomeric pairs of substituted hydrazones of 2-acylpyridines.

## Results and Discussion

(i) *Heterocyclic Hydrazone Isomers.*—(a) *Structure and spectra.* The series of hydrazones (Table 1) was prepared by direct coupling of the 2-acylpyridine with the appropriate hydrazine. When the methine substituent R was small (H or Me) the main isomer obtained was the *E*-form, the *Z*-form not being isolated [Table 1, compounds (**1**)—(**6**)]. However in some cases (with R = Me) small quantities of the *Z*-isomers were detected by careful t.l.c. and $^1$H n.m.r. analysis of the initial product mixture, although they were not isolated [Table 1, (**7**) and (**8**)]. The *Z*-isomer of pyridine-2-carbaldehyde 2-pyridylhydrazone *Z*-(**1**) was separately obtained in workable yields by u.v. irradiation of the *E*-form *E*-(**1**) in benzene followed by separation on a column of alumina. When the methine substituent R was a large phenyl group the increased steric interaction between R and the *cis*-NHAr group of the *E*-form resulted in the formation of significant yields of the *Z*-form [Table 1, (**9**)—(**14**)]. Interesting structural features were evident in these related isomeric pairs. Thus an intramolecular hydrogen-bond was detected between the hydrazone amino-NH and the methine pyridine nitrogen in the *Z*-forms and the methine phenyl substituent was twisted out of the plane containing the hydrazone chain in the *E*-forms derived from 2-benzoylpyridine. The intramolecular hydrogen bond was readily detected through the NH signals in the n.m.r. spectra (Table 2). These were deshielded by 2.5 to 4.5 p.p.m. in the *Z*-isomers relative to the *E*-isomers and on dilution with non-hydrogen bonding solvents such as $CCl_4$ the NH signals of the *E*-isomers moved upfield as expected for cleavage of

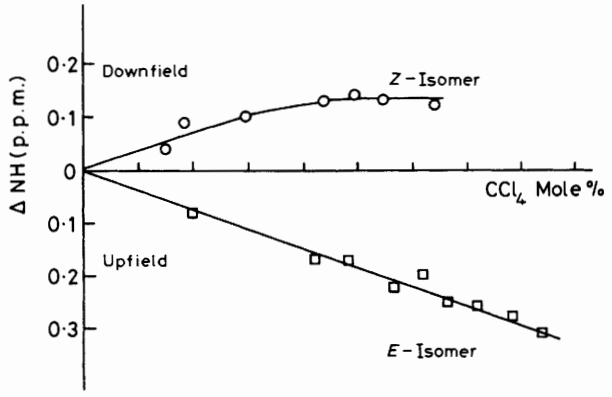
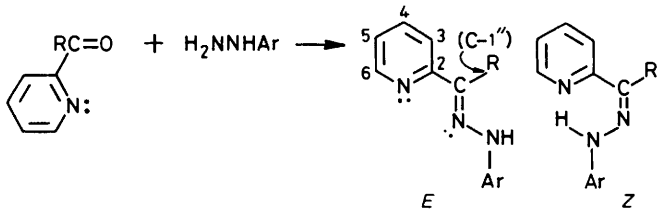



**Figure 1.** Relative shifts of the NH signals of the *E*- and *Z*-isomers of compound (**1**) on addition of $CCl_4$ to a solution in $(CD_3)_2SO$.

**Table 1.**




| Compd. no. | R | Ar | Config'n. | M.p. (°C) | Yield or ratio of isomers in product mix | Isolated yield |
|---|---|---|---|---|---|---|
| (1) | H | 2-$C_5H_4N$ | *E* | 181—183 | 89% | 80% |
| | | | *Z* | 81—82 | <0.5 | 0% |
| (2) | H | *p*-$NO_2C_6H_4$ | *E* | 264 | 95% | 95% |
| | | | *Z* | | <0.5 | 0% |
| (3) | Me | Ph | *E* | 154—156 | 95% | 95% |
| | | | *Z* | | <0.5 | 0% |
| (4) | Me | *p*-$BrC_6H_4$ | *E* | 118 | 72% | 72% |
| | | | *Z* | | <0.5 | 0% |
| (5) | Me | *p*-$MeOC_6H_4$ | *E* | 98—99 | 51% | 51% |
| | | | *Z* | | <0.5 | 0% |
| (6) | Me | *p*-$MeC_6H_4$ | *E* | 96 | 50% | 50% |
| | | | *Z* | | <0.5 | 0% |
| (7) | Me | *p*-$NO_2C_6H_4$ | *E* | 199—201 | 78% | 80% |
| | | | *Z* | | 2% | 0% |
| (8) | Me | 2-$C_5H_4N$ | *E* | 69—70 [a] | 76% | 76% |
| | | | *Z* | | 2% | 0% |
| (9) | Ph | Ph | *E* | 143—144 | 72% | 70% |
| | | | *Z* | 86—87 | 24% | 21% |
| (10) | Ph | *p*-$BrC_6H_4$ | *E* | 146 | 51% | 47% |
| | | | *Z* | 133 | 27% | 22% |
| (11) | Ph | *p*-$MeOC_6H_4$ | *E* | | (1.3:1) | |
| | | | *Z* | 82 | (1:1.3) | 17% |
| (12) | Ph | *p*-$MeC_6H_4$ | *E* | 115 | (2.1:1) | 26% |
| | | | *Z* | 88—89 | (1:2.1) | 11% |
| (13) | Ph | *p*-$NO_2C_6H_4$ | *E* | 181—183 | 74% | (90%) [b] |
| | | | *Z* | 203—205 | 18% | (90%) [b] |
| (14) | Ph | 2-$C_5H_4N$ | *E* | Oil | (1:1.9) | |
| | | | *Z* | 145—146 | (1.9:1) | 88% [b] |

[a] M.p. of the hydrazone hydrate—the anhydrous hydrazone is a gum. [b] Because of ready interconversion of isomers high yields of either isomer could be isolated by varying the work-up procedure.

intermolecular hydrogen bonds but those of the *Z*-isomers moved downfield due to strengthening of the intramolecular hydrogen-bonding (Figure 1). The twisting of the methine phenyl ring in the *E*-series (**9**)—(**14**) (Table 2) was indicated by the phenyl C-1″ shifts which were in the range 137.5—138.5 p.p.m. for the *Z*-isomers, where the phenyl ring is conjugated with the hydrazone π-system, and in the range 131.8—133.0 in the *E*-isomers in which the phenyl ring is unconjugated and twisted out of the plane of the hydrazone π-system. In agreement with this the NH signals of the *E*-isomers (**9**)—(**14**) (Table 2) were consistently more shielded than those of the *E*-isomers (**3**)—(**8**) (Table 2) as expected if in the compounds *E*-(**9**)—*E*-(**14**) containing a methine Ph group the NH proton lies above the plane of this phenyl ring. An *X*-ray crystallographic structure of compound *E*(**9**) confirmed this configurational alignment in the crystalline state (Figure 2), where the phenyl ring, which is *cis*- to NHAr group, was twisted at an angle of 106.4° to the C(8)–C(1)–N(1) plane (Figure 2).* Other $^1H$ and $^{13}C$ chemical shifts which were sensitive to the stereoisomerism and of diagnostic value are included in Table 2. These were principally in the methine pyridine ring and were different due mainly to the electrostatic influence of the intramolecular hydrogen bond in the *Z*-form.

(b) *Stability and interconversions.* The *Z*-isomer *Z*-(**1**) was stable indefinitely in the solid state and in solution in deuteriodimethyl sulphoxide less than 25% conversion into the *E*-form occurred in 3 weeks at ambient temperatures. In deuterioacetic acid solution the isomerization to the *E*-form was more rapid but 50% of the *Z*-form still remained after 20 h. The *E*-hydrazones (**2**)—(**8**) derived from 2-acetylpyridine were stable and showed no changes. Interesting interconversions were observed with the series (**9**)—(**14**) containing sterically similar phenyl and pyridyl rings at the methine carbons. The preferred form was sensitive to solvent, the physical nature of the compound, and the electronic influence of the amino substituent. For the compounds (**9**)—(**12**) (Table 1) the *Z*-form

* The hydrazone dimensions (Figure 2) agreed well with recently reported cyrstal structures of hydrazones containing an amino NH in the *E*-configuration to a methine C=X substituent [where potential intramolecular H-bonding was absent as in compound *E*-(**9**)]. Thus for the *E*-form of butane-2,3-dione mono-*p*-nitrophenylhydrazone the C=N and N–N bond lengths were 1.289 and 1.344 Å respectively (G. R. Wiley and M. G. Drew, *Acta. Crystallogr., Sect. C.*, 1983 **39**, 403 and references therein) which values compare with 1.283 and 1.352 Å for the C(1)–N(1) and N(1)–N(2) bonds in Figure 2 (Table 4).

**Table 2.** Geometry-sensitive chemical shifts ($\delta_H$ and $\delta_C$)

| Hydrazone no. | Config'n. | N*H* | C*H*=N | *C*H=N | C-2 | 3-H | C-3 | 5-C | 6-H | C-1″ | *C*H$_3$ | *C*H$_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (1) | *E* | 11.3 | 8.16[b] | 139.2 | 156.7 | 7.98 | 118.8 | 122.9 | 8.58 | | | |
| (1) | *Z* | 13.9 | 7.33[b] | 130.6 | 152.9 | 7.45 | 123.6 | 125.0 | 8.72 | | | |
| (2) | *E* | 11.46 | 8.0 | 141.9 | 153.6 | 7.96 | 119.5 | 123.6 | 8.52 | | | |
| (3) | *E* | 9.48 | | 141.4 | 156.3 | 8.12 | 119.4 | 122.1 | 8.50 | | 2.38 | 11.0 |
| (4) | *E* | 9.64 | | 142.5 | 156.0 | 8.11 | 119.3 | 122.5 | 8.54 | | 2.37 | 11.2 |
| (5) | *E* | 9.29 | | 140.3 | 156.4 | 8.09 | 119.1 | 122.0 | 8.51 | | 2.32 | 11.0 |
| (6) | *E* | 9.29 | | 140.7 | 156.3 | 8.00 | 119.1 | 122.1 | 8.41 | | 2.32 | 11.0 |
| (7) | *E* | 10.45 | | 146.7 | 155.2 | 8.18 | 119.8 | 123.2 | 8.68 | | 2.45 | 11.6 |
| (8) | *E* | 9.76 | | 144.6 | 156.1 | 8.08 | 119.9 | 123.2 | 8.49 | | 2.34 | 11.5 |
| (9) | *E* | 9.07 | | 143.1 | 156.5 | 8.18 | 120.1 | 122.0 | 8.39 | 132.5 | | |
| (9) | *Z* | 12.32 | | 138.6 | 152.6 | 7.46 | 123.2 | 124.5 | 8.85 | 138.2 | | |
| (10) | *E* | 9.28 | | 143.5 | 155.9 | 8.16 | 119.7 | 121.8 | 8.4 | 132.1 | | |
| (10) | *Z* | 12.3 | | 139.4 | 152.6 | 7.27 | 123.6 | 124.7 | 8.92 | 138.4 | | |
| (11) | *E* | 8.83 | | 141.9 | 156.3 | | 119.9 | 121.8 | 8.65 | 133.0 | | |
| (11) | *Z* | 12.42 | | 136.8 | 152.8 | 7.39 | 123.9 | 124.2 | 8.76 | 138.5 | | |
| (12) | *E* | 8.95 | | 142.3 | 156.5 | 8.15 | 119.9 | 121.9 | 8.38 | 132.6 | | |
| (12) | *Z* | 12.26 | | 138.7 | 152.7 | 7.19 | 123.2 | 124.5 | 8.71 | 137.5 | | |
| (13) | *E* | 10.02 | | 148.0 | 155.8 | 8.14 | 120.8 | 123.1 | 8.41 | 132.2 | | |
| (13) | *Z* | 12.38 | | 143.8 | 151.9 | 7.54 | 124.0 | 125.0 | 9.00 | 137.5 | | |
| (14) | *E* | 8.5 | | 145.9 | 155.7 | 8.16 | 120.4 | 122.9 | 8.38 | 131.8 | | |
| (14) | *Z* | 12.93 | | 140.02 | 152.4 | 7.31—7.83 | 123.9 | 125.2 | 8.89 | 138.3 | | |

[a] For numbering system *cf.* Table 1. [b] In $CD_3CO_2D$ these shifts were *E* δ 8.31 and *Z* δ 8.08.

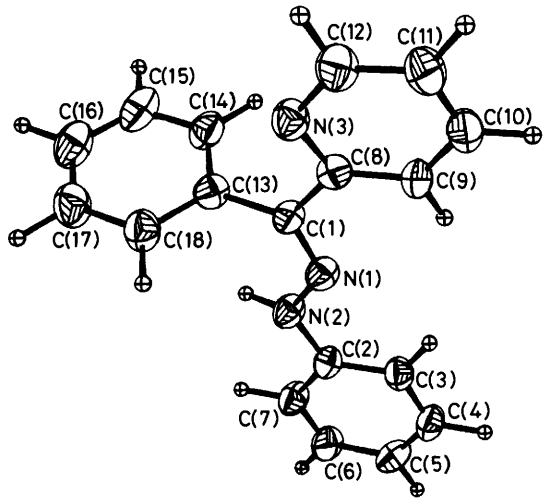
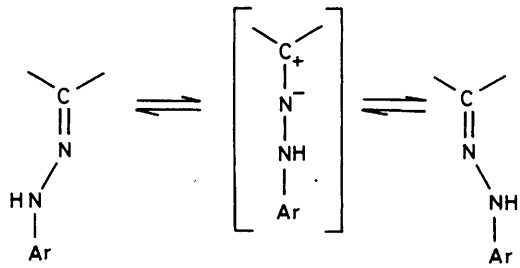



**Figure 2.** *X*-Ray structure of compound *E*-(**9**)

changed completely to the *E*-form during 7 h in deuterioacetic acid solution. For the compounds (**13**) and (**14**), containing strongly deactivating substituents on the amino nitrogen, the *Z*-forms crystallized preferentially from acetic acid solution. The compound *E*-(**14**), which could only be obtained as an impure oily residue changed slowly to the crystalline *Z*-form *Z*-(**14**) with time. This unusual *E*→*Z* isomerization[7] also occurred in $(CD_3)_2SO$ and $CD_3CO_2D$ solutions with compounds (**13**) and (**14**) giving an equilibrium mixture from the pure *E*-form. Only compounds (**13**) and (**14**) showed easily reversible isomerizations to give equilibrium mixtures starting from either the *E*- or *Z*-isomer. The ease of isomerization with these compounds is consistent with a rotational mechanism[8–10] where electron-withdrawing groups on the imine N atom may significantly lower the barrier to isomerization of a C=N bond and rate enhancements of the order $10^4$ have been reported from substituent effects.[11]

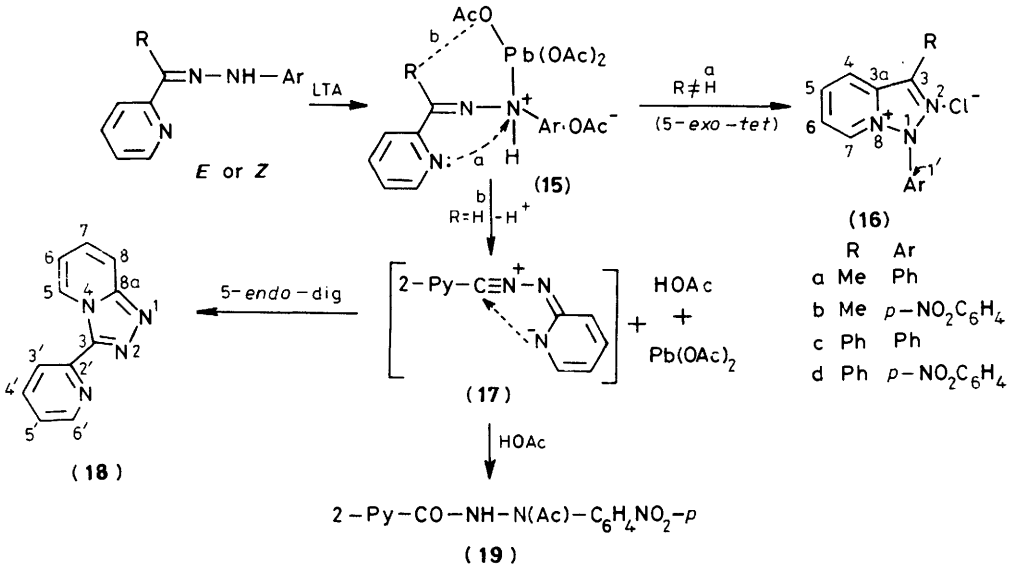



(ii) *Oxidation Reactions.*—(a) *Lead tetra-acetate.* Results for the oxidation of a series of hydrazones with lead tetra-acetate (LTA) are summarized in Table 3. The *s*-triazolopyridine (**18**) was obtained in high yield from oxidation of compounds *E*-(**1**) and *Z*-(**1**) and cyclization at the hydrazone amino group to a 1,2,3-triazolium system (path a, Scheme 2) was not encountered. When the hydrazone amino pyridyl ring was replaced by a non-heterocyclic moiety as in the substrate *E*-(*2*), in order to encourage cyclization by path (a) this still did not occur and the reaction followed path (b) giving the product (**19**). The formation of such products in the LTA oxidation of aldehyde phenylhydrazones has been shown[12–14] to arise from solvent addition to a nitrilimine intermediate. However when the methine hydrogen was replaced by a methyl or phenyl group the reaction readily followed path (a) exclusively. Thus treatment of the series *E*-(**3**), *E*-(**7**), *E*-(**9**), *Z*-(**9**), *E*-(**13**), and *Z*-(**13**) with LTA in acetic acid gave the corresponding 1,2,3-triazolium salts (**16**) in high yields (Table 3). The same products in smaller yields were obtained from the *E* and *Z* isomer pairs (**9**) and (**13**) and, as with the aldehyde derivatives (**1**), the geometrical configuration of the substrate did not influence the products formed. In earlier work[5] on compounds of type (**9**) this oxidation was used to assign the isomeric structures, on the basis that since only one of the isomers readily cyclized this was likely to have the *Z*-structure. We have found that the compound involved was, in fact, the *E*-isomer *E*-(**9**). Compound *Z*-(**9**) also underwent a similar cyclization but the

**Table 3.** Oxidations with LTA

| Substrate compd. no. | Product Compd. | M.p. (°C) | Yield[b] (%) | N.m.r. shifts ($\delta_H$ and $\delta_C$)[c] C-3 | C-3a | C-1′ | 4-H | C-4 | 7-H | C-7 | $CH_3$ | $CH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *E*-(1) | (18) | 125 | 73 | *d* | *d* | *d* | | | 7.18 | 114.8 | | |
| *Z*-(1) | (18) | 125 | 86 | *d* | *d* | *d* | | | 7.18 | 114.8 | | |
| *E*-(2) | (19) | 60 | 72 | | | *e* | | | | | | |
| *E*-(3) | (16a)[a] | 196 | 62 | 135.2 | 142.1 | 130.5 | 9.04[f] | 120.4 | 9.41[g] | 125.4 | 2.86 | 10.5 |
| *E*-(7) | (16b) | 205 | 78 | 135.9 | 141.8 | 148.8 | 8.81[f] | 120.6 | 9.5[g] | 125.8 | 2.85 | 10.4 |
| *E*-(9) | (16c)[a] | 204 | 64 | 133.4 | 141.5 | 130.7 | 8.99[f] | 120.8 | 9.34[g] | 125.3 | | |
| *Z*-(9) | (16c)[a] | 204 | 70 | 133.4 | 141.5 | 130.7 | 8.99[f] | 120.8 | 9.34[g] | 125.3 | | |
| *E*-(13) | (16d) | 228 | 80 | 134.1 | 142.5 | 149.8 | 9.2[f] | 121.0 | 9.78[g] | 125.8 | | |
| *Z*-(13) | (16d) | 228 | 80 | 134.1 | 142.5 | 149.8 | 9.2[f] | 121.0 | 9.78[g] | 125.8 | | |

[a] Hygroscopic. [b] Isolated yield. [c] Numbering system, *cf.* Scheme 2. [d] C(5)-H: $\delta_H$ 9.7 (d, *J* 7 Hz), $\delta_C$ 128.6; C(6)-H: $\delta_H$ 7.18 (t, *J* 7 Hz), $\delta_C$ 114.8; C(7)-H: $\delta_H$ 7.44—7.62 (m), $\delta_C$ 126.6; C(8): $\delta_C$ 115.5; C(8a): $\delta_C$ 147.6. [e] *Cf.* Experimental section. [f] (d, *J* 8—9 Hz). [g] (d, *J* 6—7 Hz).



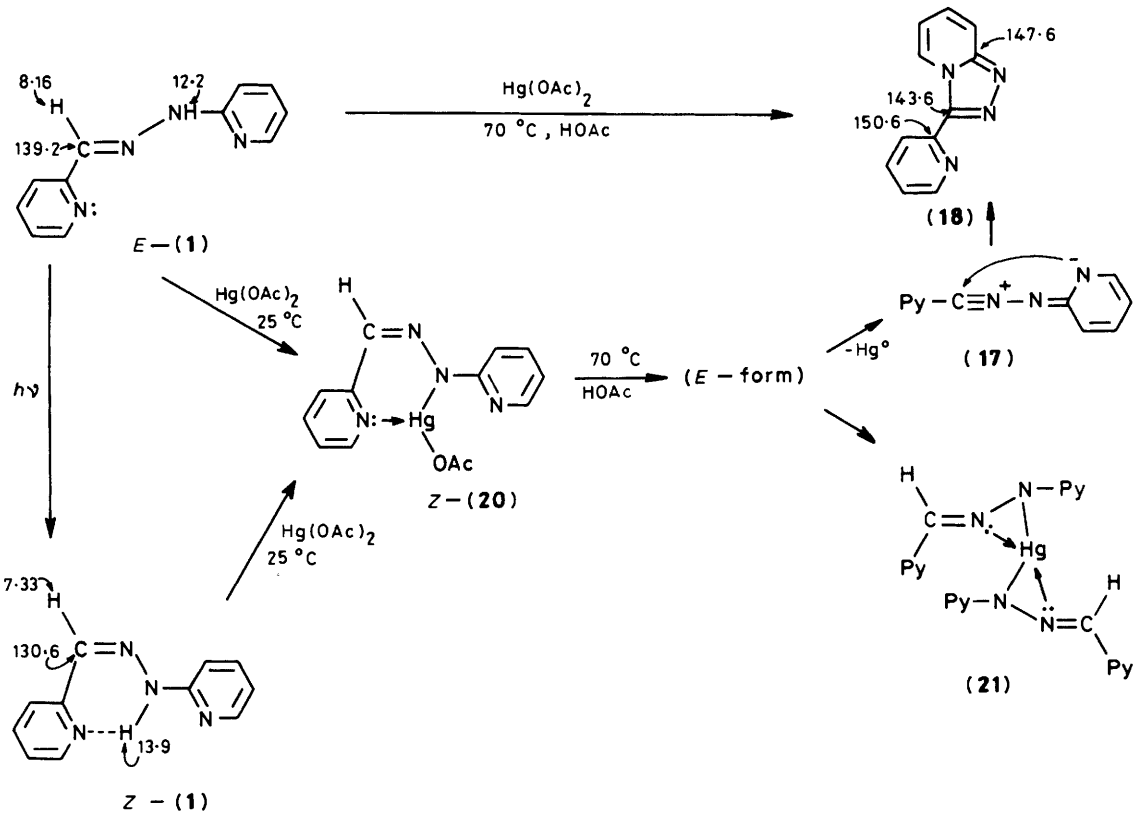

**Scheme 2.**

reaction was less clean and the product, (**16c**), was isolated initially as a sticky viscous hydrochloride complex (from chloride added in the work-up to exchange the acetate anion) giving the impression of decomposition. In each of these reactions (Table 3) $^1$H n.m.r. analysis of the product mixtures showed that the cyclization had occurred in yields of $\geqslant$90% but because of difficulties in work-up and purification of the products the isolated yields (Table 3) were somewhat lower. The structures of the products were established from their $^1$H and $^{13}$C n.m.r. spectra which showed all the expected signals and, in the case of compounds (**16**), the expected deshielding of the protons in the pyridinium ring relative to the parent substrate (Table 3). In compounds (**16**) the methyl $^1$H signal was also deshielded by *ca.* 0.5 p.p.m. relative to the parent.

In the light of previous mechanistic studies[12–15] on substituted phenylhydrazones these oxidations may be rationalized in terms of the initial formation of an *N*-metallo-intermediate (**15**) (Scheme 2). This may react by path (a) (a 5-*exo-tet* cyclization[16]) or (b) (Scheme 2), and the only structural constraint is the nature of the methine substituent R. When this is aliphatic or aromatic the reaction is exclusively by path (a) and if R is H, *i.e.* for aldehyde derivatives, path (b) is the exclusive route.

(b) *Mercury*(II) *acetate.* Support for this mechanistic picture was obtained when mercury(II) acetate was used as oxidizing agent. Thus treatment of the *E*-isomer *E*-(**1**) with mercury(II) acetate in acetic acid at 70 °C gave the *s*-triazolopyridine (**18**) (37%) along with the bis(hydrazonato)mercury compound (**21**) (Scheme 3). In this case it was possible to isolate the *N*-metallo intermediate (**20**) by stirring the reactants at room temperature in acetic acid followed by addition of light petroleum (b.p. 60—80 °C) which caused compound (**20**) to separate. Interestingly, the n.m.r. spectra of the metallo compound (**20**) displayed methine pyridine shifts similar to those of the hydrogen-bonded *Z*-structures suggesting a mercury-complexed *Z*-structure for the intermediate (Scheme 3). This was confirmed when the same metallo-intermediate was obtained on similar treatment of the *Z*-hydrazone *Z*-(**1**) with mercury(II) acetate. Isomerization of the hydrazones did not occur under these mild conditions in the absence of mercury(II) acetate. When a solution of compound (**20**) in acetic acid was heated at 70 °C it readily gave the same yields of the *s*-triazolopyridine (**18**), the bis(hydrazonato)-mercurial (**21**), and metallic mercury as observed in the direct cyclization at 70 °C.

Direct $^1$H n.m.r. monitoring of the conversion of compound (**20**) into the cyclized product (**18**) at 70 °C in deuterioacetic acid




**Scheme 3.** $^1H$ and $^{13}C$ N.m.r. δ values are given in p.p.m. for selected atoms

showed a further isomerization back to the *E*-form. As the temperature was raised to 60 °C for a few minutes the methine CH=N signal of the *Z*-form (δ 8.06) gradually changed to a signal due to the methine CH=N of the *E*-form (δ 8.37) and the full spectrum resembled that of the parent *E*-structure in deuterioacetic acid. The spectrum reverted to that of the original *Z*-structure on re-cooling. When the temperature was raised further to 70 °C the methine CH signal moved further downfield to δ 8.8 and began to disappear concomitant with the appearance of signals due to the products, after *ca.* 1 h, and no further intermediates were detected. Interestingly, the overall reaction for the normal *E*-substrate, *E*-(**1**), had involved a series of *E*→*Z*→*E* isomerizations prior to the cyclization. The final step of the reaction probably involved a 5-*endo-dig* cyclization[16] of a nitrilimine intermediate (**17**) since it has previously been shown[12,13] that nitrilimines are generated in LTA oxidation of phenylhydrazone substrates. Nitrilimines with the potential for intramolecular cyclization appear to be particularly shortlived and attempts[17] to trap them by intermolecular trapping with normal 1,3-dipolarophiles were not successful. However their involvement is now supported by the presence of intermediates such as *E*-(**20**) from which they could be readily formed.

## Experimental

M.p.s were measured with an Electrothermal apparatus. I.r. spectra were measured for either films or mulls with a Perkin-Elmer 377 spectrophotometer. $^1H$ and $^{13}C$ N.m.r. spectra were measured for solutions in $(CD_3)_2SO$, with $SiMe_4$ as internal reference, on JEOL JNM-100 and CFT-20 spectrometers. All of the compounds reported gave satisfactory microanalyses [data provided as Supplementary material SUP. No. 56000 (5 pp.)].* Carbon-13 n.m.r. signals were assigned using off-resonance proton decoupling and also selective individual proton decoupling.

*Heterocyclic Hydrazone Substrates.*—In general, the hydrazones were prepared by carefully adding the carbonyl compound to a solution of the appropriate hydrazine in ethanol containing acetic acid or hydrochloric acid. The following are typical examples:

(a) *Pyridine-2-carbaldehyde 2-pyridylhydrazones* E-(**1**) *and* Z-(**1**). Pyridine-2-carbaldehyde (1 ml, 1.126 g) was added to a solution of 2-hydrazinopyridine (1.1 g) in ethanol (20 ml) and the mixture was treated with acetic acid (0.3 ml); it was then stirred at 50 °C for 30 min after which it was diluted with water (5 ml) and cooled to give yellow crystals of compound *E*-(**1**), m.p. 181—183 °C (from ethanol). Fractional evaporation of the filtrate gave successive crops (1.58 g, 80%). The *Z*-isomer, *Z*-(**1**), was obtained by irradiation of a solution of the *E*-isomer (3 g) in benzene (300 ml) with a water-cooled Hanovia medium-pressure arc lamp. The solution was reduced to 75 ml when, with time, unchanged compound *E*-(**1**) separated; the soluble *Z*-isomer was separated from remaining *E*-(**1**) on an alumina column (activity II-III) with chloroform as eluant. The separation was monitored by t.l.c.: *Z*-(**1**), $R_F$, 0.79; *E*-(**1**), $R_F$, 0.32 in $CHCl_3$–MeOH (9:1, v/v) and the compound *Z*-(**1**), m.p. 81—82 (from diethyl ether (590 mg, 20%) was obtained from the early fractions; $\nu_{max.}$ 3 170 and (NH) 1 585 $cm^{-1}$ (C=N); n.m.r. results are given in Table 2).

(b) 2-*Benzoylpyridine* p-*Nitrophenylhydrazones*, E-(**13**) *and* Z-(**13**). A solution of *p*-nitrophenylhydrazine (1.86 g) in ethanol (25 ml) was treated with 2-benzoylpyridine (1.86 g) and acetic

* For details of the Supplementary publications scheme see Instructions for Authors (1984), *J. Chem. Soc., Perkin Trans. 1*, 1984, Issue 1.

acid (0.3 ml) at 50 °C; the mixture was stirred for 30 min and then diluted with water (10 ml) to give a solid mixture (2.91 g, 92%) of the *E*- and *Z*-isomers (**13**) (*E*:*Z*, 4.2:1). This mixture was dissolved in hot acetic acid (solution A). When solution (A) was rapidly treated with an equal volume of ice-cold water *exclusive* precipitation of the *E*-isomer, *E*-(**13**), occurred, m.p. 205 °C (dull yellow blocks from $CHCl_3$). Alternatively, the *Z*-isomer, *Z*-(**13**), m.p. 196 °C (orange needles) was obtained exclusively by slow and careful cooling of the acetic acid solution (A). When the *Z*-isomer was dissolved in acetic acid an equilibrium mixture dominated by the *E*-isomer was formed in solution.

(c) *2-Benzoylpyridine 2-pyridylhydrazones* E-(**14**) *and* Z-(**14**). A solution of 2-hydrazinopyridine (1 g) and 2-benzoylpyridine (1.7 g) in ethanol (20 ml) and acetic acid (0.3 ml) was heated at 40 °C and stirred for 30 min; the solvent was then removed under reduced pressure. N.m.r. analysis showed the residue to contain a mixture (*Z*:*E*, 1.9:1) of the hydrazones (**14**). Crystallization of the residue from ethanol gave compound *Z*-(**14**) as yellow plates, m.p. 145 °C (2.21 g, 88%). When a solution of the mixture in acetic acid was fractionated between water and ether evaporation of the ethereal extract gave an oily residue containing 90% of compound *E*-(**14**) which was not, however, isolated pure. With time the oil changed to the crystalline *Z*-isomer.

The other hydrazones were prepared similarly. Compounds *E*-(**4**), *E*-(**5**), and *E*-(**6**) were obtained as hydrochlorides by using the appropriate substituted phenylhydrazine hydrochloride in the coupling reaction. The free hydrazones (Table 1) were obtained by treating aqueous solutions of the hydrochlorides with an excess of dilute aqueous sodium carbonate causing precipitation of the hydrazones; these decomposed over a few days and were best stored as their hydrochloride derivatives. Data on the hydrazones are summarized in Tables 1 and 2 and in the Supplementary publication.

*Oxidation Reactions.*—The following reactions are typical examples.

(a) *Lead tetra-acetate.* (i) A solution of *E*-2-pyridinecarbaldehyde 2-pyridylhydrazone *E*-(**1**) (500 mg) in acetic acid (30 ml) containing acetic anhydride (0.1 ml) was treated by careful dropwise addition, during 1 h, of a solution of LTA (1.76 g) in acetic acid (70 ml) at ambient temperature; the mixture was then stirred for 30 min, poured into water (100 ml) and extracted with chloroform (4 × 50 ml). The combined chloroform extract was washed with aqueous $Na_2CO_3$ and evaporated under reduced pressure. The residue was leached with hot, light petroleum (b.p. 60—80 °C) (3 × 30 ml) and 5-(2′-*pyridyl*)-s-*triazolo*[4,3-a]*pyridine* (**18**), m.p. 125 °C (Found: C, 67.1; H, 4.2; N, 28.6. $C_{11}H_8N_4$ requires C, 67.3; H, 4.1; N, 28.55%) separated from the pentane extracts (total yield, 365 mg, 73%); $\delta_H$ 7.18 (t, *J* 7 Hz, 6-H), 7.44—7.62 (2 H, m, 7- and 5′-H), 7.86—8.18 (2 H, m, 8- and 4′-H), 8.42 (1 H, d, *J* 7 Hz, 3′-H), 8.8 (1 H, d, *J* 5 Hz, 6′-H), and 9.7 (1 H, d, *J* 7 Hz, 5-H); $\delta_C$ 114.8 (C-6), 115.5 (C-8), 121.9 (C-3′), 124.0 (C-5′), 126.6 (C-7), 128.6 (C-5), 137.7 (C-4′), 143.6 (C-3), 147.6 (C-8a), 149.05 (C-6′), and 150.6 (C-2′).

For the oxidation of the *Z*-isomer the compound *Z*-(**1**) (360 mg) was added to a solution of LTA (1.3 g) in acetic acid (30 ml) and a similar work-up also gave compound (**18**) (84%).

(ii) A mixture of pyridine-2-carbaldehyde 4′-nitrophenylhydrazone (0.6 g) in acetic acid (15 ml) and acetic anhydride (0.1 ml) was treated with LTA (0.9 g) stirred at ambient temperature for 5 min and then treated with water (20 ml) and extracted with chloroform (3 × 15 ml). The combined chloroform extract was evaporated and the residue, a brown gum, was purified by passage though an alumina column (II-III activity) using chloroform as eluant to give N′-*acetyl*-N′-(4-*nitrophenyl*)-*pyridine*-2-*carbohydrazide* (**19**) (440 g, 72%) as a brown waxy solid, m.p. 60 °C (Found: C, 55.6; H, 4.05; N, 18.4. $C_{14}H_{12}N_4O_4$ requires C, 56.0; H, 4.05; N, 18.65%); $\nu_{max.}$ 3 355 (NH), 1 710 (CO non-conjugated), 1 685 $cm^{-1}$ (CO conjugated); $\delta_H$ 2.29 (3 H, s, Ac), 7.65 (1 H, dd, $J_{4,5}$ 7 Hz, $J_{2,6}$ 5 Hz, pyridyl 5-H), 8.02 (1 H, t, *J* 7 Hz, pyridyl 4-H), 8.69 (1 H, d, *J* 5 Hz, pyridyl 6-H), 7.79 and 8.26 ($A_2B_2$-$J_{AB}$ 9 Hz, 4′-$NO_2C_6H_4$ and pyridyl 3-H; under δ 8.26 signal), and 10.38 (1 H, br, NH); $\delta_C$ 149.3 (pyridyl C-2), 123.5 (C-3), 137.9 (C-4), 127.7 (C-5), 148.7 (C-6); 147.8 (C−1′), 123.3 (C-2′, C-6′), 124.5 (C-3′, C-5′), 126.1 (C-4′), 22.35 and 171.0 (Ac), 163.0 (CO).

(iii) For the ketone hydrazone derivatives the substrate was stirred with LTA in dry acetic acid at ambient temperature for 30 min. The resulting mixture was treated with dilute HCl to precipitate $PbCl_2$ which was removed; the acetic acid mother liquor was then evaporated under reduced pressure. The residue was dissolved in ethanol and the various compounds (**16**) were precipitated by careful addition of ethyl acetate or chloroform. For example 2-benzoylpyridine 4′-nitrophenylhydrazone *E*-(**13**) (500 mg) was added to LTA (840 mg) in acetic acid (10 ml) and worked up as described to give 1-(4′-*nitrophenyl*)-3-*phenyl*-[1,2,3]*triazolo*[1,5-a]*pyridinium chloride* (**16d**) (440 mg, 80%), m.p. 226—228 °C (from ethanol–chloroform, 1:1 v/v) (Found: C, 61.0; H, 3.9; N, 15.7. $C_{18}H_{13}ClN_4O_2$ requires C, 61.3; H, 3.7; N, 15.9%); $\delta_H$ 8.44—8.79 (m, Ar), 4.47 and 8.79 (pair ds, $A_2B_2$, $J_{AB}$ 9 Hz, 4′-$NO_2C_6H_4$), 9.2 (d, *J* 9 Hz, 4-H), and 9.78 (d, *J* 7 Hz, 7-H); $\delta_C$ 134.1 (C-3), 121.0 (C-4), 135.9 (C-5), 124.2 (C-6), 125.8 (C-7), 142.5 (C-3a), 149.8 (C-1′), 127.9 (C-2′), 125.8 (C-3′), 136.8 (C-4′), 128.3, 129.7, 131.1 (C-4″), and 126.4 (C-1″) (Ph). When the *Z*-isomer *Z*-(**13**) (370 mg) was added to a solution of LTA (840 mg) in acetic acid (15 ml) and worked up as described compound (**16d**) was obtained in 77% yield.

(b) *Mercury*(II) *acetate.* (i) A solution of either isomer, *E*-(**1**) or *Z*-(**1**), of pyridine-2-carbaldehyde 2-pyridylhydrazone (2 g) in acetic acid (20 ml) was treated with mercury(II) acetate (3.2 g) and the mixture heated at 80 °C for 8 h. Globules of mercury were removed and the mixture treated with water (30 ml) and then extracted with ether (3 × 15 ml). The combined ethereal extract (aqueous solution A) was washed with dilute aqueous sodium carbonate, dried, and evaporated. The residue was leached with hot, light petroleum (b.p. 60—80 °C) and compound (**18**) (identical with the sample from LTA oxidation) (0.7 g, 37%) separated from the cooled pentane. The aqueous solution (A) was evaporated at 60 °C under reduced pressure and the residue heated at 60 °C with ethanol–dimethyl sulphoxide (4:1 v/v). Insoluble *bis*(*pyridine*-2-*carbaldehyde* 2-*pyridylhydrazonato*)*mercury* (**21**), m.p. 201—202 °C (3.5 g, 58%) was collected and purified by washing with ethanol (Found: C, 44.2; H, 3.05; N, 18.5. $C_{22}H_{18}HgN_8$ requires C, 44.4; H, 3.05; N, 18.8%); $\delta_C$ methine pyridyl, 152.2; C-2, 127.7 (C-3), 142.8 (C-4), 127.7 (C-5), 146.6 (C-6), 136.8 (CH=N), 147.9 (C-2′ of aminopyridyl), 119.2 (C-3′), 142.0 (C-4′), 113.2 (C-5′), and 150.6 (C-6′); $\delta_H$ 8.45 (s, CH=N), and 7.14—7.98 (m, pyridyl Ar).

(ii) When light petroleum (b.p. 60—80 °C) was added to the reaction mixture prior to the latter being heated the *N*-mercurioacetato hydrazone (**20**) separated (82%). The same compound(**20**) was also obtained (97%) when either compound *E*-(**1**) or *Z*-(**1**) was treated with mercury(II) acetate in dichloromethane, m.p. 146 °C (washed with diethyl ether) (Found: C, 34.65; H, 3.3; N, 10.6. $C_{13}H_{12}HgN_4O_2$·HOAc requires C, 34.85; H, 3.1; N, 10.8%); $\delta_H$($CD_3COOD$) 8.08 (s, CH=N), 7.98 (t, *J* 7 Hz, 4-H of methine pyridyl), 7.42—7.81 (m, 3-, 5-H), and 8.66 (d, *J* 5 Hz, 6-H); $\delta_C$ 133.9 (CH=N), 151.9 (C-2 of methine pyridyl), 127.3 (C-3), 141.9 (C-4), 127.3 (C-5), 147.2 (C-6), 151.5, (C-2′ of amino pyridyl), 112.0 (C-3′), 141.2 (C-4′), 119.0 (C-5′), and 148.9 (C-6′). When compound (**20**) was heated in acetic acid solution the products (**18**) (37%) and (**19**) (56%) were isolated by the work-up described. The corresponding

**Table 4.** Bond lengths (Å) and bond angles (°)

| | | | |
|---|---|---|---|
| C(1)–N(1) | 1.283(6) | C(9)–H(9) | 1.080(0) |
| C(1)–C(8) | 1.487(6) | C(9)–C(10) | 1.384(8) |
| C(1)–C(13) | 1.488(7) | C(10)–H(10) | 1.080(0) |
| N(1)–N(2) | 1.352(6) | C(10)–C(11) | 1.379(8) |
| N(2)–H(1) | 1.008(10) | C(11)–H(11) | 1.080(0) |
| N(2)–C(2) | 1.400(6) | C(11)–C(12) | 1.350(8) |
| C(2)–C(3) | 1.398(7) | C(12)–H(12) | 1.080(0) |
| C(2)–C(7) | 1.387(7) | C(12)–N(3) | 1.343(7) |
| C(3)–H(3) | 1.080(0) | C(13)–C(14) | 1.390(8) |
| C(3)–C(4) | 1.372(7) | C(13)–C(18) | 1.393(8) |
| C(4)–H(4) | 1.080(0) | C(14)–H(14) | 1.080(0) |
| C(4)–C(5) | 1.399(9) | C(14)–C(15) | 1.393(8) |
| C(5)–H(5) | 1.080(0) | C(15)–H(15) | 1.080(0) |
| C(5)–C(6) | 1.388(9) | C(15)–C(16) | 1.373(10) |
| C(6)–H(6) | 1.080(0) | C(16)–H(16) | 1.080(0) |
| C(6)–C(7) | 1.403(7) | C(16)–C(17) | 1.370(11) |
| C(7)–H(7) | 1.080(0) | C(17)–H(17) | 1.080(0) |
| C(8)–C(9) | 1.388(7) | C(17)–C(18) | 1.394(9) |
| C(8)–N(3) | 1.345(6) | C(18)–H(18) | 1.080(0) |

| | | | |
|---|---|---|---|
| C(8)–C(1)–N(1) | 115.8(4) | H(6)–C(6)–C(5) | 119.5(3) |
| C(13)–C(1)–N(1) | 124.9(4) | C(7)–C(6)–C(5) | 121.0(5) |
| C(13)–C(1)–C(8) | 119.3(4) | C(7)–C(6)–H(6) | 119.5(3) |
| N(2)–N(1)–C(1) | 120.1(4) | C(6)–C(7)–C(2) | 119.2(5) |
| H(1)–N(2)–N(1) | 114.4(4.3) | H(7)–C(7)–C(2) | 120.4(3) |
| C(2)–N(2)–N(1) | 118.1(4) | H(7)–C(7)–C(6) | 120.4(3) |
| C(2)–N(2)–H(1) | 121.7(3.8) | C(9)–C(8)–C(1) | 121.0(4) |
| C(3)–C(2)–N(2) | 117.9(4) | N(3)–C(8)–C(1) | 116.3(4) |
| C(7)–C(2)–N(2) | 122.0(4) | N(3)–C(8)–C(9) | 122.7(4) |
| C(7)–C(2)–C(3) | 120.1(4) | H(9)–C(9)–C(8) | 120.5(3) |
| H(3)–C(3)–C(2) | 120.0(3) | C(10–C(9)–C(8) | 119.0(4) |
| C(4)–C(3)–C(2) | 119.9(5) | C(10)–C(9)–H(9) | 120.5(3) |
| C(4)–C(3)–H(3) | 120.1(3) | H(10)–C(10)–C(9) | 120.7(3) |
| H(4)–C(4)–C(3) | 119.4(3) | C(11)–C(10)–C(9) | 118.7(5) |
| C(5)–C(4)–C(3) | 121.3(5) | C(11)–C(10)–H(10) | 120.7(3) |
| C(5)–C(4)–H(4) | 119.4(3) | H(11)–C(11)–C(10) | 120.9(3) |
| H(5)–C(5)–C(4) | 120.8(3) | C(12)–C(11)–C(10) | 118.2(5) |
| C(6)–C(5)–C(4) | 118.5(5) | C(12)–C(11)–H(11) | 120.9(3) |
| C(6)–C(5)–H(5) | 120.8(3) | H(12)–C(12)–C(11) | 117.2(3) |
| N(3)–C(12)–C(11) | 125.6(5) | C(16)–C(15)–H(15) | 120.2(4) |
| N(3)–C(12)–H(12) | 117.2(3) | H(16)–C(16)–C(15) | 119.8(4) |
| C(12)–N(3)–C(8) | 115.9(5) | C(17)–C(16)–C(15) | 120.5(6) |
| C(14)–C(13)–C(1) | 121.5(5) | C(17)–C(16)–H(16) | 119.7(4) |
| C(18)–C(13)–C(1) | 121.0(5) | H(17)–C(17)–C(16) | 120.0(4) |
| C(18)–C(13)–C(14) | 117.5(5) | C(18)–C(17)–C(16) | 119.9(6) |
| H(14)–C(14)–C(13) | 119.2(3) | C(18)–C(17)–H(17) | 120.1(4) |
| C(15)–C(14)–C(13) | 121.5(5) | C(17)–C(18)–C(13) | 121.1(6) |
| C(15)–C(14)–H(14) | 119.2(4) | H(18)–C(18)–C(13) | 119.5(3) |
| H(15)–C(15)–C(14) | 120.3(4) | H(18)–C(18)–C(17) | 119.4(4) |
| C(16)–C(15)–C(14) | 119.5(6) | | |

trifluoroacetate derivative (**20**; $CF_3CO$ for Ac) (m.p. 172 °C) was also prepared for spectroscopic comparisons.

X-*Ray Crystal Structure of Compound* E-(**9**).—*X*-Ray crystallographic studies on $C_{18}H_{15}N_3$. A crystal with dimensions 0.31 × 0.43 × 0.52 mm was used.

*Crystal data.* Monoclinic $a$ = 10.820(3), $b$ = 9.335(3), $c$ = 14.940(4) Å, $\beta$ = 73.87(6), $U$ = 1 449.61Å$^3$, $Z$ = 4, Space group $P2_{1/c}$, Mo-$K_\alpha$ radiations ($\bar{\lambda}$ = 0.710 69 Å), $\mu$(Mo-$K_\alpha$) = 0.42 cm$^{-1}$, $F(000)$ = 576.

Data were collected on a Hilger Y-290 diffractometer. The method used for data collection was that previously described by Ferguson *et al.*[18]

Data were collected within the range $2° < \theta < 22°$, using the $\theta$—$2\theta$ technique; 1 793 unique reflections were examined of which 1 015 had $I > 4\delta I$. The structure was solved by direct methods (MULTAN) and refined using (SHLX). The final $R$ factors were $R$ = 5.91 and $R_w$ = 7.82. The weighting scheme used as $w = 1/(G^2F + 0.013F^2)$. All non-hydrogen atoms were anisotropic and hydrogen atoms were included at reasonable positions. The number of variable parameters included in the full matrix least-squares cycles was 196 and in the final cycle the maximum shift/ESD in a parameter was 0.003. Bond lengths and angles are listed in Table 4 and the atomic co-ordinates in Table 5. The thermal parameters are part of the Supplementary publication (see p. 2113) and the structure factors are available from the editorial office on request.

**Table 5.** Atomic co-ordinates with e.s.d.s in parentheses

| Atom | *x/a* | *y/b* | *z/c* |
|---|---|---|---|
| C(1) | 0.370 0(4) | 0.432 5(4) | 0.752 9(3) |
| N(1) | 0.296 7(4) | 0.492 7(3) | 0.825 6(3) |
| N(2) | 0.347 2(4) | 0.583 1(4) | 0.876 9(3) |
| H(1′) | 0.433 4(32) | 0.624 5(62) | 0.842 6(49) |
| C(2) | 0.262 6(4) | 0.655 7(4) | 0.950 9(3) |
| C(3) | 0.315 6(5) | 0.740 4(5) | 1.008 0(4) |
| H(3) | 0.418 8(5) | 0.749 4(5) | 0.993 7(4) |
| C(4) | 0.236 5(6) | 0.812 2(5) | 1.082 1(4) |
| H(4) | 0.278 4(6) | 0.876 4(5) | 1.126 3(4) |
| C(5) | 0.102 5(6) | 0.803 5(5) | 1.101 7(4) |
| H(5) | 0.040 9(6) | 0.861 9(5) | 1.159 5(4) |
| C(6) | 0.050 6(5) | 0.718 5(5) | 1.045 1(4) |
| H(6) | −0.052 6(5) | 0.707 6(5) | 1.060 6(4) |
| C(7) | 0.130 1(5) | 0.646 1(5) | 0.968 1(4) |
| H(7) | 0.088 6(5) | 0.583 9(5) | 0.922 7(4) |
| C(8) | 0.304 5(5) | 0.337 4(5) | 0.700 5(3) |
| C(9) | 0.172 8(5) | 0.346 9(5) | 0.712 6(4) |
| H(9) | 0.115 3(5) | 0.422 7(5) | 0.761 4(4) |
| C(10) | 0.116 4(6) | 0.257 7(5) | 0.661 3(4) |
| H(10) | 0.014 2(6) | 0.262 8(5) | 0.669 1(4) |
| C(11) | 0.193 1(6) | 0.162 2(5) | 0.600 0(4) |
| H(11) | 0.152 8(6) | 0.091 3(5) | 0.558 3(4) |
| C(12) | 0.320 1(5) | 0.159 9(5) | 0.593 3(4) |
| H(12) | 0.378 7(5) | 0.083 8(5) | 0.545 3(4) |
| N(3) | 0.379 8(4) | 0.243 9(4) | 0.641 3(3) |
| C(13) | 0.511 2(5) | 0.456 0(4) | 0.716 8(4) |
| C(14) | 0.596 8(5) | 0.398 6(5) | 0.761 3(4) |
| H(14) | 0.560 2(5) | 0.333 9(5) | 0.822 9(4) |
| C(15) | 0.7288 (6) | 0.422 5(6) | 0.728 3(5) |
| H(15) | 0.793 3(6) | 0.378 9(6) | 0.765 0(5) |
| C(16) | 0.776 2(6) | 0.501 9(6) | 0.648 8(6) |
| H(16) | 0.878 7(6) | 0.517 5(6) | 0.621 6(6) |
| C(17) | 0.694 4(7) | 0.561 5(6) | 0.603 7(5) |
| H(17) | 0.732 3(7) | 0.626 0(6) | 0.542 2(5) |
| C(18) | 0.562 3(6) | 0.538 7(5) | 0.637 5(4) |
| H(18) | 0.498 4(6) | 0.586 2(5) | 0.601 6(4) |

## Acknowledgements

The *X*-ray crystal structure was carried out by Drs. P. McArdle and D. Cunningham of the Inorganic Section of this Department.

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*Received 25th January* 1984; *Paper* 4/142