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THE SYNTHESIS OF (2*H*)-PYRROLE-1-OXIDES BY RING CONTRACTION

Rudolph A. Abramovitch* and Berkeley W. Cue, Jr.

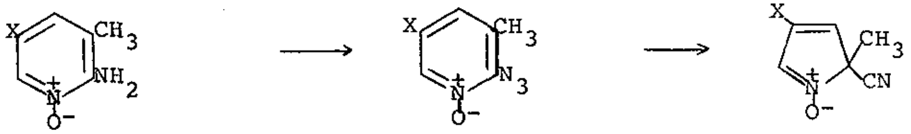
Department of Chemistry, University of Alabama,
University, Ala. 35486, U.S.A.

The ring contraction of 2-azido-3-alkylpyridine-1-oxides gives 2-alkyl-2-cyano-(2*H*)-pyrrole-1-oxides in good yield. Possible ambiguities in the nmr spectra of these compounds have been resolved.

We recently reported that the thermal decomposition of 2-azidopyridine-[1] and -quinoline-1-oxides[2] in non-protic solvents leads to 2-cyano-*N*-hydroxypyrroles and -indoles by ring-opening and recyclization to the five-membered compounds. It seemed likely, therefore, that if the 3-position in the pyridine ring were blocked, ring-opening and cyclization would lead to 2-substituted-2-cyano-(2*H*)-pyrrole-1-oxides since rearomatization would not be possible here. To find out if this is so we have examined the decomposition of some 3-alkyl-2-azidopyridine-1-oxides.

2-Azido-3-methylpyridine-1-oxide (**1a**), mp 89-91° (dec), was prepared as usual[1,3] from 2-amino-3-methylpyridine-1-oxide (**2a**).[4] Its thermolysis in benzene at 90° gave an oil (89%), bp 58-60°(0.06mm) whose analysis, mass spectrum, and infrared spectrum[5] were as expected for 2-cyano-2-methyl-(2*H*)-pyrrole-

1-oxide (**3a**). The *N*-oxide band appeared at 1525 cm^{-1}, which compares well with literature values for similarly constituted molecules.[7] *On the other hand, the nmr spectrum of the product* in $CHCl_3$ solution seemed inconsistent with structure **3a**, and exhibited a 1H low field triplet at δ7.7 (J = 2.5 Hz), a 2H doublet at δ6.0 (J = 2.5 Hz) and the methyl 3H singlet at δ1.82. Irradiation of the δ6.0 signal caused the δ7.7 one to collapse to a singlet, and the same happened to the δ6.0 signal when the δ7.7 one was irradiated. Addition of $Eu(fod)_3$ caused extensive shifts of all the peaks (the δ7.7 peak suffered the greatest shift and must be due to the proton closest to the complexed *N*-oxide function) but no resolution of possible peak degeneracy occurred. This led us to consider structures **4** and **5** for the product as these would fit the observed nmr data. These structures were, however, thought to be unlikely since (a) they would have



1

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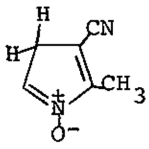
2: **a**; X = H
b; X = Br



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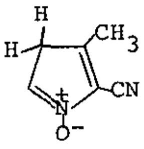


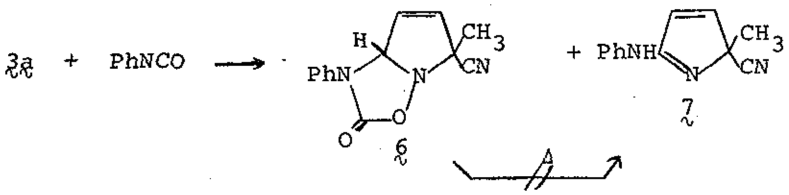
5

required multiple rearrangements to have occurred, which is difficult to visualize as taking place in benzene solution, and (b) **5**, for example, is a tautomer of the known[1] 2-cyano-1-hydroxy-3-

methylpyrrole in which the *N*-hydroxy form is known to be the preferred (if not exclusive) tautomer, so that **4** or **5** would have been expected to isomerize to the aromatic *N*-hydroxy form, which was not observed. The problem was resolved by determining the ^{13}C nmr spectrum of the ring-contracted product, and this agreed completely with structure **3a**: the nitrile carbon resonance occurred at 117.8 ppm (s), indicating that the -CN is attached to sp^3 carbon (cf. δ_{CN} in acetonitrile at 117.2 ppm); the CH_3 gave rise to a quartet at 24.7 ppm (sp^3-C-CH_3), and C_5, C_4, and C_3 gave rise to doublets at 147.4, 116.8, and 129.4 ppm, respectively. Finally, the accidental degeneracy of H_3 and H_4 in $CHCl_3$ was lifted by measuring the nmr spectrum of **3a** in DMSO-d_6. H_5 gave rise to a doublet of doublets at δ8.08 ($J_{4,5}$ = 4 Hz; $J_{3,5}$ = 2 Hz), H_4 to a doublet of doublets at δ6.24 ($J_{4,5}$ = 4 Hz; $J_{3,4}$ = 10 Hz), and H_3 to a doublet of doublets at δ6.39. The CH_3 group gave a sharp singlet at δ1.81.

The nitrone structure of **3a** was confirmed by its reaction with phenylisocyanate in boiling toluene to give the 1:1 adduct (**6**) (16%), mp 135-137°, and 5-anilino-2-cyano-2-methyl-(2*H*)-pyrrole (**7**) (11%), mp 145-148°, together with much tar. The spectral properties of **6** and **7** supported the assigned structures.[3] When pure **6** was heated in boiling chlorobenzene, it did not give **7**, probably because base-catalysis is necessary for CO_2 elimination, as has been found for the adduct of 3-picoline-1-oxide and phenyl isocyanate.[9]

A similar reaction sequence has been carried out with 2-azido-5-bromo-3-methylpyridine-1-oxide (**1b**), mp 96-98° (dec), prepared from **2b** hydrate, mp 152-153°. A 77% yield of **3b**, bp 125-127° (0.75mm), was thus obtained (lachrymatory gum).



It exhibited all the spectral properties expected. Preliminary results indicate that 2-azido-3-ethyl-6-methylpyridine-1-oxide also gives the corresponding (2*H*)-pyrrole-1-oxide.

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2. R. A. Abramovitch and B. W. Cue, Jr., *Heterocycles*, *1*, 227(1973).

3. All new compounds have been fully characterized (microanalysis, ir, nmr, and mass spectra).

4. E. V. Brown, *J. Amer. Chem. Soc.*, *79*, 3565(1957),

5. The nitrile band at 2248 cm^{-1} for this compound was very weak, which is not unexpected for a nitrile group adjacent to electron-withdrawing oxygen-containing substituents such as nitro or *N*-oxide.[6]

6. N. B. Colthup, L. H. Daly, and S. E. Wiberley, "Introduction to Infrared and Raman Spectroscopy", Academic Press, New York, 1964, p. 202.

7. R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. R. Todd, *J. Chem. Soc.*, 2094(1959).

8. The europium complex must be oriented in such a way as to deshield C_3-H and C_4-H equally.

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