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Some Stereochemical Aspects of the Pellizzari Rearrangement

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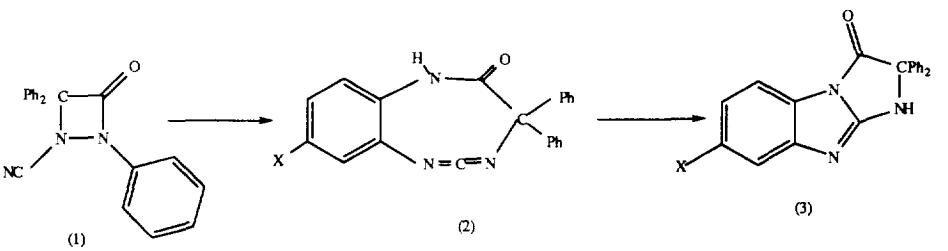
Abstract: Variable temperature nmr spectroscopy and X-ray crystallography have been employed to study the stereochemistry of 2-cyano-3,3-dimethyl-1-phenylpyrazolidin-5-one which thermally rearranges to 2,3-dihydro-2,2-dimethylpyrimido[1,2-a]benzimidazol-4(1H)-one.

Following our original discovery [1,2] of the facile thermal rearrangement of the diazetidinone (1) to the imidazo[1,2-a]benzimidazole (3) we have progressively investigated the mechanism and scope of this unusual transformation. Isotopic labelling studies [3] are only compatible with the mechanistic patthway indicated for the conversion of (1) to (3).



Parallel isotopic labelling experiments[4] indicate a similar mechanism for the conversion of α-cyanophenylhydrazine into 1-cyano-2-cyanaminobenzimidazole originally discovered by Pellizzari.[5] Substituents present in the 2- and 6-positions of the N-aryl group undergo what can be considered as [1,9]sigmatropic shifts [3,6]. Analogous rearrangements have been observed with the indazolone (4) which gives (5) [7,8], and the pyrazolidinone (6) which yields (7) [7,9]. More recently Viehe and his colleagues [10] have observed the rearrangement of (8) to (9), and of (10) to (11). In order for the requisite bond breaking and bond making to occur in a concerted fashion it is essential for the N-aryl and N-cyano groups to adopt a *cis* relationship rather than the stereochemically preferred *trans* arrangement. In the case of the diazetidinones (1) the measured energies of activation for conversion to (3) are around 20 to 25 Kcal/mole depending on X.[11] Free energies of N-inversion as high as 17 Kcal/mole have been observed for 1,2-dibenzyl-3,3-dimethyldiazetidinone[12]. So far all of our attempts to detect such inversion processes, or the putative intermediate (2), by differential

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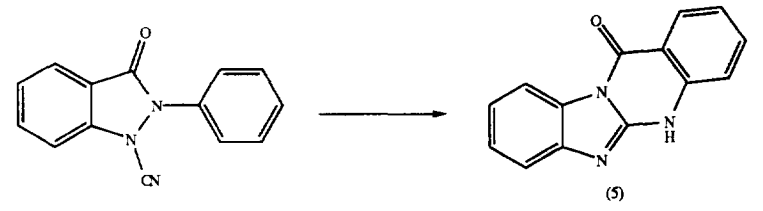
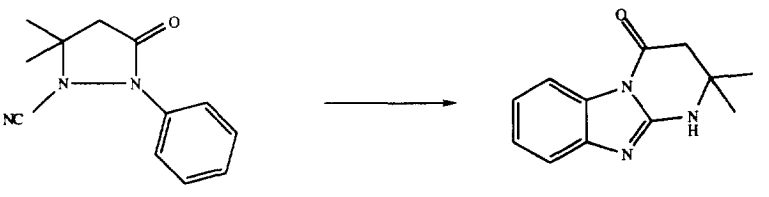
Professor Hans Suschitzky zu seinem achtzigen Geburtstag mit herzlichen Glückwünschen gewidmet.

scanning calorimetric studies have failed.

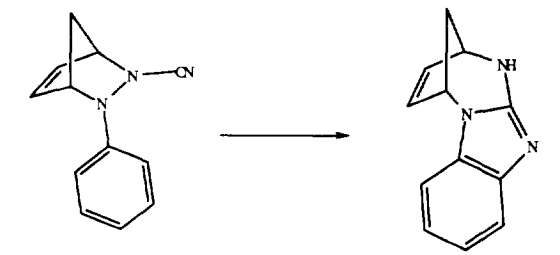


(4) (5)



(6) (7)

A more promising candidate for such investigations is the pyrazolidinone (6) with an energy of activation of 36.7 Kcal/mole for its conversion to (7) [11]. Previous studies [13] have shown that N-inversion in the pyrazolidinone (12) may be easily detected by ^{1}H nmr studies. Thus, cooling a hexadeuterioacetone solution of (12) to -91°C provides a spectrum containing *inter alia* 2 signals for the 3,3-dimethyl group which coalesce on warming to -49° corresponding to a value of 10.7 Kcal/mole for the free energy of inversion.



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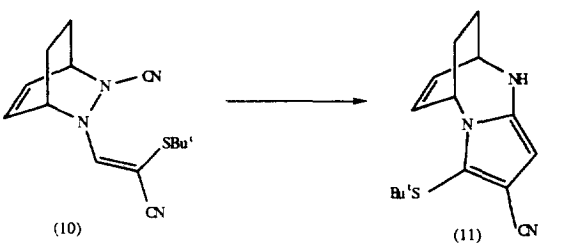

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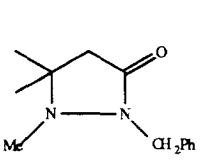

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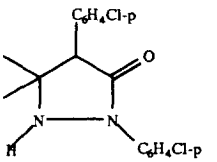

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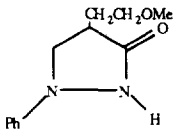
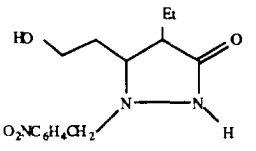


(14)



(15)

However, we have found that the ^{1}H nmr spectrum of the cyanopyrazolidinone (6) in hexadeuterioacetone at room temperature consists of a singlet at δ1.62 for the *gem* dimethyl group, a singlet at δ3.11 for the methylene protons, a doublet at δ7.35 for the *ortho*-phenyl protons, a doublet at δ7.72 for the *para*-phenyl proton and a double doublet at δ7.59 for the *meta*-phenyl protons with J = 7.4 and 7.6 Hz. This spectrum remained unchanged on cooling to -93°. Identical behaviour was observed in deuteriomethanol as solvent down to -80°C.

These observations raised the question as to the stereochemistry of (6) as the above nmr spectra are consistent with a planar configuration about the cyano bearing nitrogen. X-ray crystallographic structures of three pyrazolidinones (13) [14], (14)[15] and (15)[16] are reported in the literature and all have a buckled five-membered ring. While the amide nitrogen N(2) (numbering as in ORTEP drawing) is planar in each case the sum of the bond angles around N(1) is 318° in the case of (13) and 334° in the case of (14). No dimensions are presently available for (15)[16]. However, in the case of (6) it seemed possible that the N-cyano nitrogen might adopt a planar configuration due to conjugative interaction between the nitrogen lone pair and the cyano group. This possibility received some support from structural information on cyanamide for which bond angle sums of 344.7 [17], 356.4 [18], 349.6 [19] and 349.3 [19] at the amino-nitrogen have been derived from microwave, X-ray and neutron diffraction studies. Consequently the structure of the pyrazolidinone (6) was determined by X-ray crystallography. An ORTEP drawing of the molecule with thermal ellipsoids and crystallographic numbering is shown in Figure I. Bond lengths and bond angles are listed in Tables I & II. The sum of the angles around the N-cyano nitrogen is 333.96 attesting to a pyramidal configuration in keeping with (13) and (14), but in contrast to the almost flat cyanamide. A further feature of note is the non-linearity of the N-cyano moiety, N1-C1-N3, with an NCN bond angle of 173.9° slightly smaller than the 175° observed for cyanamide [18,19].

The five-membered ring has closely comparable bond lengths and angles to those observed for the pyrazolidinones (13)[14] and (14)[15] and a similarly puckered conformation. This latter aspect is most clearly seen by comparing the displacements of the individual ring atoms from the best plane as listed in Table III for all three compounds.

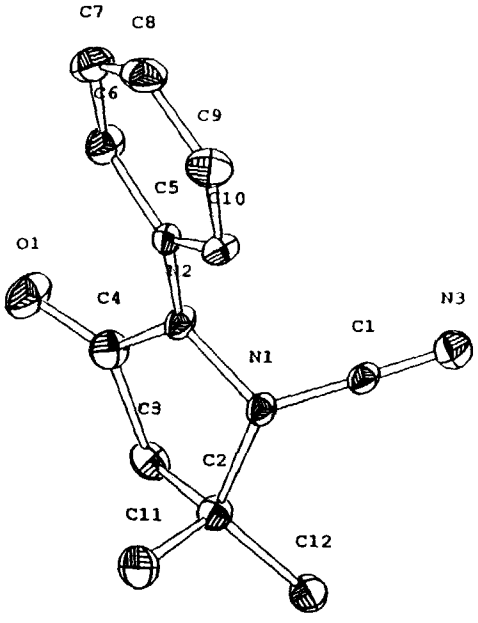


Table I Bond Lengths (Å) , Compound 6

C!-N1	1.339(9)	C5-C6	1.368(10)
C1-N3	1.141(9)	C5-C10	1.388(11)
C2-C3	1.528(10)	C5-N2	1.409(8)
C2-C11	1.521(10)	C6-C7	1.385(12)
C2-C12	1.503(9)	C7-C8	1.377(15)
C2-N1	1.510(7)	C8-C9	1.378(13)
C3-C4	1.513(10)	C9-C10	1.384(12)
C4-N2	1.363(9)	N1-N2	1.426(7)
C4-O1	1.209(9)		

Table II Bond Angles (°), Compound 6

N1-C1-N3	173.9(6)	C10-C5-N2	120.0(6)
C3-C2-C11	112.5(6)	C5-C6-C7	120.4(8)
C3-C2-C12	114.9(6)	C6-C7-C8	120.7(7)
C3-C2-N1	100.3(5)	C7-C8-C9	119.3(7)
C11-C2-C12	110.1(6)	C8-C9-C10	119.7(8)
C11-C2-N1	107.3(5)	C5-C10-C9	120.9(8)
C12-C2-N1	111.1(5)	C1-N1-C2	117.2(5)
C2-C3-C4	103.2(6)	C1-N1-N2	110.8(4)
C3-C4-N2	107.2(6)	C2-N1-N2	106.0(4)
C3-C4-O1	127.1(6)	C4-N2-C5	128.5(5)
N2-C4-O1	125.7(6)	C4-N2-N1	111.3(5)
C6-C5-C10	118.8(7)	C5-N2-N1	118.3(5)
C6-C5-N2	121.2(7)		