NMR STUDY OF ANTIPYRINE ADDUCTS WITH LANTHANIDE SHIFT REAGENTS. MOLECULAR STRUCTURE OF 2,3-DIMETHYL -1-PHENYL-5-ETHOXYPYRAZOLE

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The complex formation of antipyrine with LSR in CCl_4 is studied. Recommendations for producing the limiting lanthanide induced shifts characteristic of the 1:1 complex are given and the geometry of the complex formed is determined. Results of an x-ray structure study of the adduct which is formed upon reaction of antipyrine and the ethyl ester of benzenesulfonic acid are presented.

Antipyrine (I) and its derivatives are known to have good complex-forming abilities with metal ions [1, 2].

Use of lanthanide induced shifts (LIS) in a few cases facilitates the discernment of the features of complex formation and the geometry of the adducts which are formed. In the general case, the experimental values of the LIS are determined as the combination of the diamagnetic (d), contact (c), and pseudocontact (pc) contributions:

$$\Delta(H_i)_{\text{ind}} = (\delta_i)^{\text{obs}} - (\delta_i)_0 = \\ = \Delta(H_i)_{\text{d}} + \Delta(H_i)_{\text{c}} + \Delta(H_i)_{\text{pc}},$$

where $(\delta_i)_0$ is the chemical shift of the absorption signal of the i-th resonating nucleus of the organic substrate molecule in the absence of LSR.

Besides this, the observed LIS under conditions of rapid exchange depends on the concentration of the various types of complexes which are formed in solution between reagent (R) and substrate (S):

$$\Delta(H_i)_{\text{ind}} = \sum_i (\Delta H_{i\infty})_{RS_n} - \frac{n[RS_n]}{[S_0]}$$

where n is the number of substrate molecules in the complex RS_n and $(\Delta H_{i\infty})_{RSn}$ is the limiting LIS value for the i-th resonating nucleus of this complex.

Proper separation of the pseudocontact component from the total induced shift is necessary for calculations which are carried out in order to determine the conformation of the adducts which are formed by the McConnell–Robertson formula:

$$\Delta(H_{i\infty})_{\text{pc}} = D(3\cos^2\Theta_i - 1)/r_i^3,$$

where r_i is the vector between the lanthanide atom and the nucleus for which the LIS is determined; θ_i is the angle between r_i and the main magnetic axis of an axially symmetric complex; and D is a constant whose value depends on the magnetic anisotropy of the complex [3].

$La(fod)_3$ was chosen for evaluation of the diamagnetic contribution to the experimental values of LIS. Figure 1 gives the results of the reaction of antipyrine with this reagent. The presence of inflection points near R/S = 0.5 is explained by a significant contribution to the induced shifts of a RS_2 complex in the experimental LIS. The negative changes in the induced shifts of the absorption signals of antipyrine upon complex formation between $0.0 \leq R/S \leq 0.5$ can be explained by a substantial change in the geometry of the antipyrine molecule

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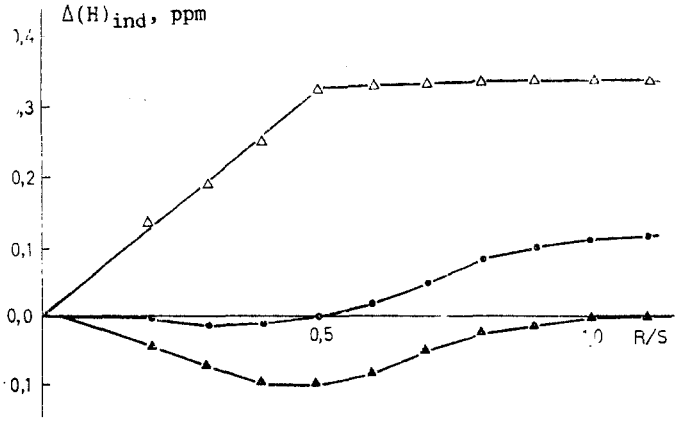

Fig. 1. Shifts of the antipyrine absorption signals induced by $La(fod)_3$. •) 2-Me; ▲) 3-Me; and Δ) 4-H.

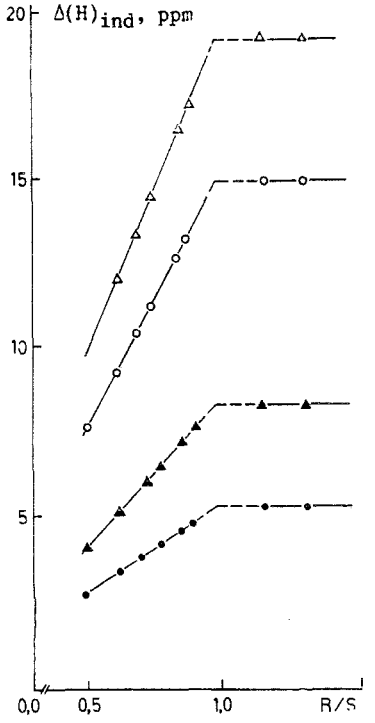

Fig. 2. Shifts of antipyrine absorption signals induced by $Yb(fod)_3$. •) 2-Me; ▲) 3-Me; o) α-Ph; and Δ) 4-H.

as a result of rearrangement of the electronic structure which agrees with the x-ray structure study of antipyrine [4] and its adducts with metals [1]. Further addition of the reagent leads to a disproportionation of the RS_2 complex: $RS_2 + R \rightleftarrows 2RS$. Small positive changes in the induced shifts at $R/S > 0.5$ allow a hypothesis about the insignificant change in the geometry of the organic substrate in the LSR–antipyrine adducts with 1:1 and 1:2 composition to be made. Thus, the experimental values of LIS at $R/S = 1.0$, which are characteristic of the stable 1:1 complex, can be determined by extrapolation of the LIS obtained between $0.5 < R/S < 1.0$.

The experimental values of the LIS of antipyrine induced in the $0.5 < R/S < 1.5$ range by $Yb(fod)_3$, for which contact contributions to the LIS are absent, are given in Fig. 2. The presence of a sharp break at $R/S = 1.0$ and the constancy of the values of LIS in the $R/S > 1.0$ range indicate coordination of ytterbium to the oxygen atom of antipyrine and are consistent with the formation of a predominantly 1:1 adduct with a high value for the equilibrium constant. The limiting values of the pseudocontact components of LIS accounting for the change of geometry of antipyrine upon complex formation are defined as the difference in the signals induced by $Yb(fod)_3$ and $La(fod)_3$ at $R/S = 1.0$.

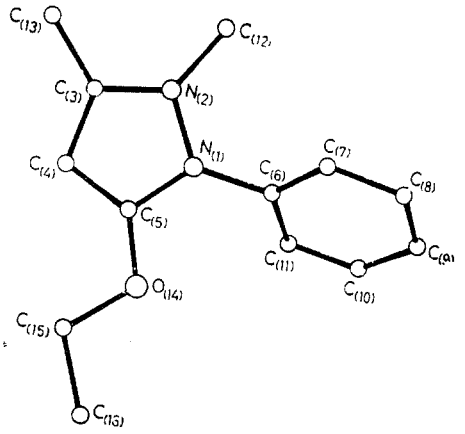

Fig. 3. Structure of the 2,3-dimethyl-1-phenyl-5-ethoxypyrazole·cation.

In order to determine the geometry of the 1:1 adducts which are formed in solution, a program was developed for the IBM by which a correlation between the results of calculations obtained upon variation of the ytterbium atomic coordinates relative to the chosen geometry of the organic substrate and the limiting values of the pseudocontact component of the experimental LIS was sought. The possibility of using antipyrine for calculating the geometry of the adducts which are formed was eliminated as a result of the changes in the geometry upon complex formation. Therefore, the results of the x-ray structural study of 2,3-dimethyl-1-phenyl-5-ethoxypyrazole (II), which is formed upon reaction of antipyrine and the ethyl ester of benzenesulfonic acid, were used for calculation of the geometric factors ($G_i = (3\cos^2\theta_i - 1)/r_i^3$). The oxygen atom of the pyrazole was placed at the Cartesian coordinate origin, the $C{-}O_{(5)}$ bond was directed along the abscissa, and the $C_{(5)}{-}C_{(4)}$ bond was placed in the first quadrant of the XY plane. It was assumed that the principle magnetic axis of the axially symmetric 1:1 complex passes through the lanthanide atom and oxygen. Calculation of the complex geometry was carried out over all proton-containing groups of antipyrine. The geometrical factors for the protons of the methyl and phenyl groups were the average values for 24 positions with free rotation of these groups. The optimal coordinates for ytterbium were determined at the minimal values of the RR or SR factors [5]:

$$RR = \left[\sum_{ij} \omega_{ij} (R_{ij}^{\text{obs}} - R_{ij}^{\text{calc}})^2 \Big/ \sum_{ij} (R_{ij}^{\text{obs}})^2 \right]^{1/2},$$

where $R_{ij}^{obs} = (\Delta H_{j\infty})_{pc}/(\Delta H_{j\infty})_{pc}$; and ω_{ij} are the weighting coefficients, proportional to the R_{ij}^{obs} values. Upon summation, the values R_{ij} as well as R_{ji} are considered, R_{ij}^{calc} is G_i/G_j:

$$SR = \left[\sum_{i} ((\Delta H_{i\infty})_{pc} - kG_i)^2 \Big/ \sum_{i} (\Delta H_{i\infty})_{pc}^2 \right]^{1/2},$$

where $k = \sum_i ((\Delta H_{i\infty})_{pc} \cdot G_i)/\sum_i G_i^2$ is the proportionality coefficient, and G_i is the geometrical factor.

The following minimal values of the factors were obtained as a result of the calculations carried out, RR = 0.02 and SR = 0.03, for which the O–Yb distance is 2.5 Å, the C_5–O–Yb angle is 144°, and the torsion angle C_4–C_5–O–Yb is 44°. The values obtained for the lanthanide coordinates agree well with the results of the x-ray study of the antipyrine adducts with metals [1].

At the same time, these coordinates do not correspond to the results of calculation of the geometry of the antipyrine–$Pr(fod)_3$ complex [6], apparently, because of the method used in this work for determination of the limiting LIS, obtained as a result of extrapolation of

TABLE 1. Atomic Coordinates ($\times 10^4$, for H atoms $\times 10^3$) and Their Equivalent Isotropic Temperature Factors in the Structure of 2,3-Dimethyl-1-phenyl-5-ethoxypyrazole (II) Benzenesulfonate

Atom	x	y	z	B_{iso}^{eq} (Å²)	Atom	x	y	z
$N_{(1)}$	4365(4)	5450(2)	5681(5)	3,4(2)	$H_{(4)}$	196	638	652
$N_{(2)}$	4945(4)	5959(2)	5115(6)	3.6(2)	$H_{(7)}$	679	513	692
$C_{(3)}$	4045(6)	6385(2)	5353(7)	3.8(2)	$H_{(8)}$	780	420	658
$C_{(4)}$	2872(5)	6163(2)	6092(7)	3.8(2)	$H_{(9)}$	667	341	528
$C_{(5)}$	3118(5)	5588(2)	6298(7)	3,5(2)	$H_{(10)}$	429	357	429
$C_{(6)}$	5021(5)	4895(2)	5617(6)	2.9(2)	$H_{(11)}$	335	457	400
$C_{(7)}$	6291(5)	4806(2)	6285(7)	3.7(2)	$H_{(12.1)}$	643	643	393
$C_{(8)}$	6843(5)	4256(3)	6205(8)	4,5(2)	$H_{(12.2)}$	653	552	407
$C_{(9)}$	6142(7)	3817(3)	5461(9)	5,0(2)	$H_{(12.3)}$	724	597	364
$C_{(10)}$	4862(6)	3921(3)	4774(8)	4,6(2)	$H_{(13.1)}$	456	697	355
$C_{(11)}$	4292(5)	4460(2)	4840(6)	3.3(2)	$H_{(13.2)}$	500	726	500
$C_{(12)}$	6211(6)	5963(2)	4192(8)	4,1(2)	$H_{(13.3)}$	357	726	536
$C_{(13)}$	4314(7)	6983(3)	4835(9)	5,6(2)	$H_{(15.1)}$	128	575	854
$O_{(14)}$	2415(4)	5168(2)	6974(5)	4,6(2)	$H_{(15.2)}$	36	559	714
$C_{(15)}$	1029(5)	5363(2)	7635(8)	4,3(2)	$H_{(16.1)}$	100	469	902
$C_{(16)}$	390(7)	4846(3)	8328(11)	6,5(3)	$H_{(16.2)}$	−36	500	913
S*	1408(1)	3470(1)	2304	3.44(3)	$H_{(16.3)}$	54	447	755
$C_{(17)}$*	527(5)	3246(2)	4099(7)	3,2(2)	$H_{(18)}$*	143	381	571
$C_{(18)}$*	905(6)	3469(3)	5589(7)	4,6(2)	$H_{(19)}$*	36	345	786
$C_{(19)}$*	247(8)	3287(3)	6969(7)	5,6(2)	$H_{(20)}$*	−135	276	792
$C_{(20)}$*	−796(7)	2897(3)	6887(8)	5,2(2)	$H_{(21)}$*	−179	238	536
$C_{(21)}$*	−1162(6)	2680(3)	5355(10)	5,3(2)	$H_{(22)}$*	−93	271	268
$C_{(22)}$*	−517(5)	2852(2)	3993(8)	4,0(2)				
$O_{(23)}$*	412(4)	3428(2)	1026(5)	4,4(2)				
$O_{(24)}$*	1838(4)	4058(2)	2617(5)	4.5(2)				
$O_{(25)}$*	2545(4)	3077(2)	2125(6)	5,4(2)				

*Atoms of the benzenesulfonate anion.

TABLE 2. Bond Distances, d(Å), in the Structure of (II)

Bond	d	Bond	d
$N_{(1)}$—$N_{(2)}$	1,394(6)	$C_{(10)}$—$C_{(11)}$	1,371(8)
$N_{(1)}$—$C_{(5)}$	1,358(6)	$C_{(14)}$—$C_{(15)}$	1,476(7)
$N_{(1)}$—$C_{(6)}$	1,441(7)	$C_{(15)}$—$C_{(16)}$	1,497(9)
$N_{(2)}$—$C_{(3)}$	1,338(7)	S—$C_{(17)}$	1,794(6)
$N_{(2)}$—$C_{(12)}$	1,451(7)	S—$O_{(23)}$	1,439(4)
$C_{(3)}$—$C_{(4)}$	1,396(8)	S—$O_{(24)}$	1.452(4)
$C_{(3)}$—$C_{(13)}$	1,477(8)	S—$O_{(25)}$	1,446(4)
$C_{(4)}$—$C_{(5)}$	1,367(8)	$C_{(17)}$—$C_{(18)}$	1,388(8)
$C_{(5)}$—$O_{(14)}$	1,319(7)	$C_{(17)}$—$C_{(22)}$	1,373(7)
$C_{(6)}$—$C_{(7)}$	1,372(7)	$C_{(18)}$—$C_{(19)}$	1,376(9)
$C_{(6)}$—$C_{(11)}$	1,393(7)	$C_{(19)}$—$C_{(20)}$	1,364(9)
$C_{(7)}$—$C_{(8)}$	1,388(8)	$C_{(20)}$—$C_{(21)}$	1,41(1)
$C_{(8)}$—$C_{(9)}$	1,374(9)	$C_{(21)}$—$C_{(22)}$	1,351(9)
$C_{(9)}$—$C_{(10)}$	1,393(9)		

the experimental LIS from the R/S < 0.5 to R/S = 1.0 region, which, as shown above, is prohibited for a system in which the conformation changes upon complex formation.

An x-ray structure confirmed that the product from reaction of antipyrine with the ethyl ester of benezenesulfonic acid is 2,3-dimethyl-1-phenyl-5-ethoxypyrazole. The structure of the cation is shown in Fig. 3. The atomic coordinates and their temperature factors are given in Table 1, and the bond distances and angles are in Table 2 and 3, respectively.

The pyrazole ring in the cation is planar within 0.012 Å in contrast to the neutral antipyrine [4], in which it has the envelope conformation. The distances of the endocyclic bonds $N(_1)$—$N(_2)$, 1.394(6); $N(_2)$—$C(_3)$, 1.338(3); $C(_3)$—$C(_4)$, 1.396(8);$C(_4)$—$C(_5)$, 1.367(8); and $N(_1)$—$C(_5)$, 1.358(6) Å naturally differ form those found for antipyrine (1.412, 1.381, 1.349, 1.431, ana 1.400 Å, respectively) and are intermediate between the values corresponding to double and single bonds, which agrees with the results of studies of other pyrazole salts [7, 8]. Such a redistribution of bond distances is explained by the formation in the cation of a heterocyclic aromatic system. Of the exocyclic bonds, it should be noted that $C(_5)$—$O(_{14})$,

TABLE 3. Bond Angles, ω, in the Structure of (II)

Angle	ω, °	Angle	ω, °
$C_{(5)}N_{(1)}N_{(2)}$	106.7(5)	$C_{(7)}C_{(8)}C_{(9)}$	120.9(6)
$N_{(1)}N_{(2)}C_{(3)}$	108.2(5)	$C_{(8)}C_{(9)}C_{(10)}$	119.9(6)
$N_{(2)}C_{(3)}C_{(4)}$	109.2(5)	$C_{(9)}C_{(10)}C_{(11)}$	120.4(6)
$C_{(3)}C_{(4)}C_{(5)}$	105.8(5)	$C_{(10)}C_{(11)}C_{(6)}$	118.3(5)
$C_{(4)}C_{(5)}N_{(1)}$	110.0(5)	$C_{(17)}SO_{(23)}$	105.4(2)
$C_{(5)}N_{(1)}C_{(6)}$	129.6(5)	$C_{(17)}SO_{(24)}$	105.3(2)
$N_{(2)}N_{(1)}C_{(6)}$	124.7(5)	$C_{(17)}SO_{(25)}$	105.6(2)
$N_{(1)}N_{(2)}C_{(12)}$	121.8(5)	$O_{(23)}SO_{(24)}$	113.0(2)
$C_{(3)}N_{(2)}C_{(12)}$	129.1(5)	$O_{(23)}SO_{(25)}$	113.5(2)
$N_{(2)}C_{(3)}C_{(13)}$	122.4(6)	$O_{(24)}SO_{(25)}$	113.0(2)
$C_{(4)}C_{(3)}C_{(13)}$	128.4(6)	$SC_{(17)}C_{(18)}$	120.0(4)
$C_{(4)}C_{(5)}O_{(14)}$	133.3(5)	$SC_{(17)}C_{(22)}$	119.7(4)
$N_{(1)}C_{(5)}O_{(14)}$	116.6(5)	$C_{(18)}C_{(17)}C_{(22)}$	120.2(5)
$C_{(5)}O_{(14)}C_{(15)}$	112.6(5)	$C_{(17)}C_{(18)}C_{(19)}$	119.9(6)
$O_{(14)}C_{(15)}C_{(16)}$	107.1(5)	$C_{(18)}C_{(19)}C_{(20)}$	120.7(6)
$N_{(1)}C_{(6)}C_{(7)}$	121.3(5)	$C_{(19)}C_{(20)}C_{(21)}$	118.1(6)
$N_{(1)}C_{(6)}C_{(11)}$	116.1(5)	$C_{(20)}C_{(21)}C_{(22)}$	121.8(6)
$C_{(11)}C_{(6)}C_{(7)}$	122.5(5)	$C_{(21)}C_{(22)}C_{(17)}$	119.2(6)
$C_{(6)}C_{(7)}C_{(8)}$	118.0(6)		

1.319(7) Å, is greatly shortened by comparison to the standard bond distance of a C(Ar)–O bond (for example, 1.36 Å in phloroglucine [9]). Apparently, this is related to a significant conjugation of the unshared electron pair of the oxygen atom with the π-system of the pyrazole ring. This conjugation is aided by the fortuitous coplanarity (relative to the heterocyclic ring) of the ethoxy substituent (torsion angle $C_{(4)}C_{(5)}O_{(14)}C_{(15)}$ of 0.1(7)°). The phenyl ring, $C_{(6)}...C_{(11)}$, is planar within 0.007 Å and forms an angle of 55.9(2)° with the plane of the heterocycle.

The geometric parameters of the benzenesulfonate are normal (Tables 2 and 3) [10]. The SO_3 group is oriented relative to the phenyl ring with a torsion angle $C_{(18)}C_{(17)}SO_{(25)}$ of 89.3(7)°.

EXPERIMENTAL

NMR spectra were recorded on a BS-467 spectrometer (60 MHz) in CCl_4 with a TMS internal standard. LSR were dried for 12 h in vacuum (133.3 Pa) over P_2O_5 at 56°C before use.

Solutions with various concentrations of reagent and substrate were prepared such that the total concentration was 0.05 M (equimolar method).

2,3-Dimethyl-1-phenyl-5-ethoxypyrazole benzenesulfonate. To a melt (120°C) of 9.4 g (0.05 mole) of antipyrine was added dropwise 9.3 g (0.05 mole) of the ethyl ester of benzenesulfonic acid so that the temperature of the reaction mixture did not exceed 160°C. Then the mixture was cooled to room temperature, dissolved in dry acetone, and left for a day in a refrigerator. The precipitate which formed was filtered and dried at room temperature. Yield of (II) was 80%. PMR spectrum ($CDCl_3$): 8.03-7.13 (10H, m, arom.); 6.22 (1H, s, 4-H); 4.34 (2H, q, J = 9.0 Hz, CH_2–CH_3); 3.70 (3H, s, 2-CH_3); 2.62 (3H, s, 3-CH_3); 1.33 ppm (3H, t, J = 9.0 Hz, CH_2–CH_3).

Crystals of (II) are rhombic, at 20°C, a = 9.7506(8), b = 23.249(2), c = 8.2775(5) Å, d_{calc} = 1.326 g/cm³, Z = 4, space group $Pna2_1$.

Unit cell constants and intensities of 1274 independent reflections with $F^2 \geq 2\sigma$ were measured on a Hilger–Watts automatic four-circle diffractometer (20°C, λMoK_α, graphite monochromator, $\theta/2\theta$ scanning, $\theta \leq 28°$).

The structure was solved by direct methods and refined by least squares method initially isotropically and then anisotropically. All hydrogen atoms were found in a difference Fourier synthesis and were included in the refinement with fixed coordinates and isotropic temperature factors B_{iso} = 5 Å. The final R factor was 0.047 (R_w = 0.052). All calculations were done on an IBM Eclipse S/200 using INEXTL programs [11].

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DIRECT $^{13}C-^{13}C$ SPIN–SPIN COUPLING CONSTANTS IN THE VINYL GROUP OF N-VINYLAZOLES

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The unshared electron pair of the dicoordinated nitrogen atom introduces a stereospecific contribution to the $^{13}C-^{13}C$ spin–spin coupling constant (SSCC) in the vinyl group of a series of N-vinylazoles, the value of which depends on the energetics of the unshared pair.

Studies of direct $^{13}C-^{13}C$ SSCC showed their sensitivity to electronic effects of the surroundings and also stereospecificity allowing these parameters to be used for conformation and analysis [1-4]. The electronegativity of the substituent is the basic factor determining the value of $^1J_{CC}$ in the vinyl group. In monosubstituted ethylene, this constant changes in the range 54.7-82.2 Hz, increasing with an increase in the electronegativity of the substituent [5]. The spatial proximity to the interacting carbon nuclei of an unshared electron pair (UEP) of a heteroatom (nitrogen or oxygen) can introduce an additional contribution to the $^1J_{CC}$ value [1-4]. The increase in $^1J_{CC}$ of the vinyl group in S-trans-conformers of alkylvinyl esters, reaching 4 Hz [2], serves as an example of this effect. In this work, $^1J_{CC}$ of the vinyl group in a series of N-vinylazoles (I-XIX) are determined and their relation to the electronic and spatial structure of this class of compounds is analyzed.

The $^1J_{CC}$ values in the vinyl group of N-vinylazoles (Table 1) changes in the range 76.5-79.7 Hz and the obvious tendencies in the changes in $^1J_{CC}$ upon increasing the number of nitrogen atoms in the azole ring are not followed. For example, for N-vinylpyrrole (77.5 Hz [5]) and 1-vinyl-5-methyltetrazole, XV, they coincide. More noticeable changes in $^{13}C-^{13}C$ SSCC (up to 2 Hz) are observed for the pairs of compounds IV and V, XII and XIII, upon introducing substituents in the 5 position of the azole ring. The data of [6, 7] allow the assumption to be made that such a substituent leads to a stabilization of the S-cis-conformer due to steric reasons (relative to the $N(_2)$ atom of N-vinylazoles (A), where the UEP of $N(_2)$ is in the spatial proximity to the vinyl C=C bond), while N-vinylazoles unsubstituted in the

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