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INVESTIGATIONS ON THE HINDERED ROTATION OF AMIDRAZONES

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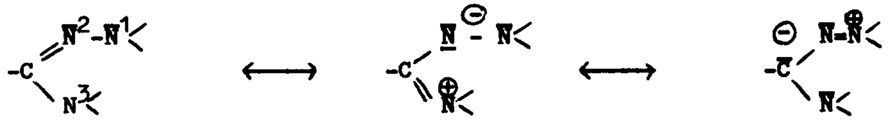
Introduction:

In a previous paper $^{1)}$ the structure of $N^1.N^1.N^3$-trisubstituted amidrazones (nomenclature of amidrazones see lit. $^{2)}$) has been discussed. IR-spectroscopic investigations have shown that these compounds exist only in the carbonic acid amide hydrazone form with a double bond between the carbon atom and the N^2-nitrogen atom. Another possible tautomeric carbonic acid hydrazide imide isomer could not be found. These results have recently been confirmed by other authors $^{3)}$.

Amidrazones are mesomeric systems, and like carboxylic acid amides they are planar due to the canonical formula II, which leads to a partial double bond character of the C-N^3 bond and, consequently, to a hindrance of internal rotation around this bond.



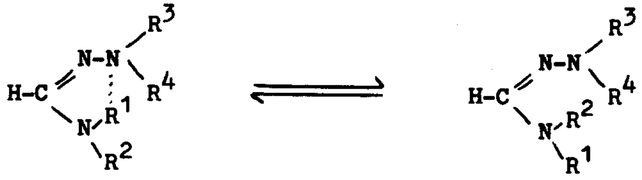
I II III

If rotamers exist in solution they can be detected by ^{1}HNMR spectroscopy and their rotation barriers $\Delta G^{\neq}$ can be calculated from the coalescence temperature T_c $^{4)}$.

Results:

IR-spectroscopic investigations showed that especially formic acid amidrazones 1 exist in solution as two isomers, containing an intramolecular hydrogen bond

(A) 1) (R^1=H) and (B) not.



A B

No.	R^1	R^2	R^3	R^4
1a	H	CH_3	CH_3	C_6H_5
1b	H	$CH_2C_6H_5$	CH_3	CH_3
1c	H	$CH_2C_6H_5$	$CH(CH_3)_2$	$CH(CH_3)_2$
1d	H	$CH_2C_6H_5$	$CH_2C_6H_5$	$CH_2C_6H_5$
1e	H	$CH_2C_6H_5$	CH_3	C_6H_5
1f	H	pyridyl-2	CH_3	CH_3
1g	H	pyridyl-2	CH_3	C_6H_5
2	CH_3	CH_3	CH_3	C_6H_5

The results of the ^{1}HNMR spectroscopical measurements and evaluations are shown in table 1.

Due to the coupling of the protons of the N^3-alkyl groups with the hydrogen atom, which prevented the measurement of the amidrazone 1d, the result of the N^3-deuterated are given additionally in order to confirm that the $\Delta G^{\neq}$ values are about equal for the N^3-H and N^3-D compounds.

Discussion:

The $\Delta G^{\neq}$ values are within the range of 14.5 to 15.6 kcal/mole for N^3-alkyl substituted formic acid amidrazones. Those of N^3-pyridyl-2 substituted amidrazones are significantly higher.

The tetrasubstituted amidrazone 2 shows a much lower $\Delta G^{\neq}$ value of 9.7 kcal/mole compared to 1a, the difference being about 5 kcal/mole.

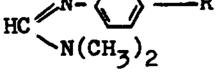
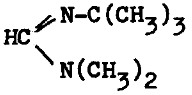
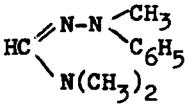
Table 2 shows that the hindered rotation in the trisubstituted amidrazones 1 is high, being comparable with those of N'-aryl amidines.

Table 1: Free activation enthalpies of the hindered rotation of some $N^1.N^1.N^3$-trisubstituted formic amidrazones (1) and the tetrasubstituted formic amidrazone 2

No.	R_2N^2	T_c (°C)	Δν (Hz)	ΔG$^{\neq}$ (kcal/mole)	Solv.	Signal
1a	H	5	5.5	14.9±0.2	$CDCl_3$	N^3-CH_3
	D	11	6.5	15.1±0.2	$CDCl_3$	N^3-CH_3
1b	H	0	6.5	14.5±0.2	$CDCl_3$	N^1-CH_3
	H	10	10	14.8±0.2	$CDCl_3$	N^3-CH_2
	D	2.5	4.5	14.8±0.2	$CDCl_3$	N^1-CH_3
	D	10	8	14.9±0.2	$CDCl_3$	N^3-CH_2
1c	H	23	8	15.6±0.2	$CDCl_3$	N^3-CH_2
	D	20	7.5	15.5±0.2	$CDCl_3$	N^3-CH_2
1d	D	11.5	6	15.2±0.2	$CDCl_3$	N^1-CH_2
1e	H	13	11	14.9±0.2	$CDCl_3$	N^3-CH_2
	H	7	7	14.8±0.2	$CDCl_3$	N^1-CH_3
	D	16.5	12	15.0±0.2	$CDCl_3$	N^3-CH_2
	D	10.5	7	15.0±0.2	$CDCl_3$	N^1-CH_3
1f	H	59	12	17.4±0.2	$CHBr_3$	N^1-CH_3
1g	H	61	12	17.5±0.2	$CHBr_3$	N^1-CH_3
2	CH_3	-86	9	9.7±0.2	HDA [a)]	N^3-CH_3

a) Hexadeuteroacetone

Table 2: Free activation enthalpies of N.N-dimethyl formic amide derivates

Compound		ΔG$^{\neq}$ (kcal/mole)	Solvent	Lit.
$HCS-N(CH_3)_2$		24.1	o-$C_6H_4Cl_2$	5)
$HCO-N(CH_3)_2$		21.0	w/o [a)]	6)
	R=NO_2	15.9	$CDCl_3$	7)
	R=CH_3	14.1	$CDCl_3$	7)
		12.4	Pyridine	8)
		9.7	CD_3COCD_3	X [b)]

a) w/o = without solvent   b) X = this paper

The higher $\Delta G^{\neq}$ values of the trisubstituted amidrazones 1a-1g compared with the tetrasubstituted compound 2 might be explained by the effect of intra- (isomer A) or intermolecular (isomer B) hydrogen bonding. The difference of about 5 kcal/mole, however, is much higher than that found in similar systems, e. g. thiohydroxamid acids, o-halogenphenols, where the additional energies caused by hydrogen bonds are about 2 kcal/mole 9),10),11). In fact, besides the influence of hydrogen bonding, the barrier to internal rotation in 2 compared with 1a-1g may be further lowered by steric interactions between the N^3-methyl groups and the amino group on N^2 in the planar ground state. The $\Delta G^{\neq}$ value of 2 is further lowered by a stronger contributation of the canonical formula III to the ground state. In 1a-1g hydrogen bonding involving the lone electron pair on the N^1-atom will diminish the importance of III.

Similarly, the difference of about 3 kcal/mole between 2 and trialkyl substituted amidines (table 2) is believed to result from the interaction of the lone electron pair of the amidrazone's N^1-nitrogen and the amidine system of 2 according to the canonical formula III in 2. It accounts for the lower $\Delta G^{\neq}$ value of 2 compared to N,N-dimethyl-N'-tert.-butyl-formamidine (table 2) contrary to the canonical formula II which is responsible for the hindered internal rotation around the $C-N^3$ bond.

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