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THE KINETICS OF SYN-ANTI INTERCONVERSIONS IN ARYLIDENE SEMICARBAZONES[1]

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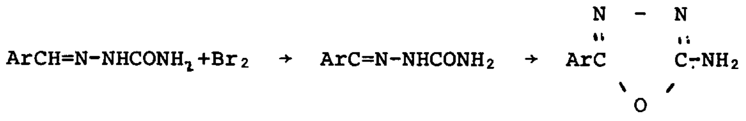
Reaction of arylidene semicarbazones (I) with bromine in aqueous acetic acid leads to the oxadiazoles (II) (Scheme 1). Despite the clear intervention of bromine in this process we have found that rate-determining step in this reaction follows a kinetic law zeroth order in bromine. The rate-determining process is in fact the syn-anti isomerisation of the substrate semicarbazone. The present report is the first recorded kinetic study of such semicarbazone interconversions.



(I) (II)

Scheme 1

The kinetics of the reaction of the substrates (I) with bromine were measured in 70% aqueous acetic acid containing 0.1M KBr using the electrochemical techniques we have described elsehwere.[3] These rate constants (Table 1) correspond to first-order kinetics in hydrazone (I) and were found to be independent of the concentration of bromine (i.e. zero order in bromine). Variation in the concentration of potassium bromide used (at constant ionic strength) by a factor of ten - a process which substantially alters the relative amounts of the two possible electrophiles. Br_2 and Br_3^- - did not change the observed rate of bromine uptake.

These rate data apply then to some transformation in the semicarbazones prior to bromination. Azo-alkane formation (i.e. of $ArCH_2N{=}NCONH_2$) can be ruled out because (a) Simon and Moldenhauer

TABLE 1

Rates of Syn-Anti Interconversion of Semicarbazones ($XC_6H_4CH{=}NNHCONH_2$)
(Solvent : 70% H_2O - acetic acid, containing 0.1M KBr, 20°C, k in $sec.^{-1}$)

X	10^4k	X	10^4k	X	10^4k
p-MeO	4.6	p-Cl	2.15	o-F	1.8
p-Me	4.05	p-Br	2.05	o-Cl	1.55
p-iPr	3.9	m-Br	1.8	o-I	1.17
pH	3.2	$o\text{-}CH_3$	1.9		

TABLE 2

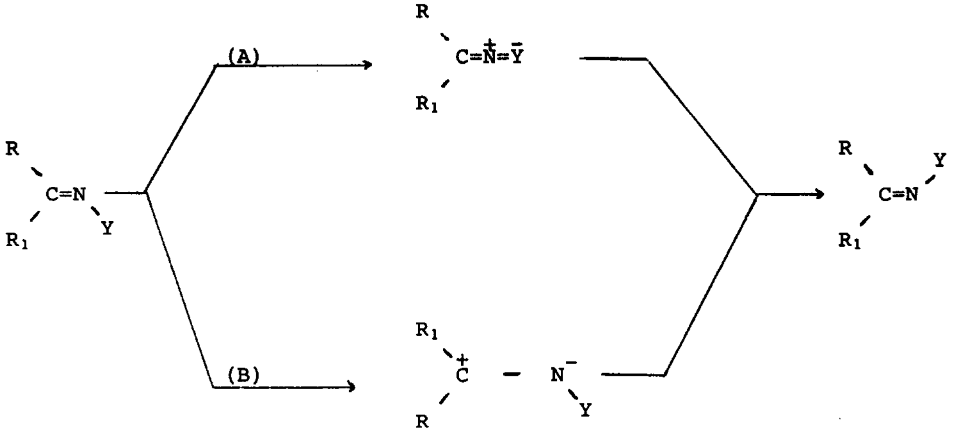
Data on the isomerisations of various systems of type (R) ArCH=N-Y

System, Y =	ρ	δ	$\Delta G^{\pm}$ k.cal/mole	k_1, ranges (temp.)
$-NHC_6H_3(NO_2)_2$	0.0 $(\rho)^*$	0.49	-	5-30 x 10^{-4} (20°)
$-NCH_3C_6H_4NO_2p$	-0.29	0.15	23	1-4 x 10^{-5} (20°)
$-NHCN_4-CH_2C_6H_5$ [a]	-0.69	+0.44	-	1-4 x 10^{-4} (25°)
$-NHCONH_2$	-0.65	.29	22.05	1-4 x 10^{-4} (20°)

[a] CN_4 represents the tetrazolyl ring

have shown that azoalkane formation is very slow compared to the rate constants we have measured here, and, (b) the rate of bromination of the model compound ($C_6H_5CH{=}N{-}NCH_3CONH_2$) wherein such a transformation is impossible under our experimental conditions, was found to be both fast (k, 3.0×10^{-5} $sec.^{-1}$), and like its unmethylated analogue also observed zeroth order rate in bromine. Our present kinetic data best fit, a rate-determining geometric isomerisation of the semicarbazones prior to halogenation. While there has been some controversy[5] about which isomer (syn or anti) predominates in such acidic media as 70% acetic acid, our data leads to the conclusion that the minor isomer present must brominate very rapidly and, therefore, it is the rate of conversion of the less reactive isomer to the reactive form which is rate-determining.

The rate data apply to a steric change of the type depicted in Scheme 2 for which there are two extremes of mechanism, inversion path (A) or rotation path (B).



Scheme 2

We have examined a number of such migrations involved in the above transformation where Y is a substituted amino group, for example Y = $-NHC_6H_3(NO_2)_2$;[1a,b] $-NCH_3C_6H_4NO_2$-p;[1c,d] or -NH-5-(1 or 2 benzyl-) tetrazolyl,[1e] and the data obtained best fitted a transition state which contained considerable torsional character, i.e. similar to path B.[6] On the basis of this data, we had concluded that special circumstances, e.g. ring size, ring type etc. were responsible for such isomerisation kinetics.

It is surprising then that semicarbazones fit the same pattern. The comparison of results (Table 2) shows the similar pattern of Y migration throughout the various systems studied.[7] We again ascribe a mechanism of type B as playing a major role in the isomerisation of the semicarbazones. This accords with the results obtained, e.g. (a) a small negative ρ (partial carbonium ion character on the imine carbon in the transition state), and (b) the observed steric effects (δ = .29) (the more bulky ortho groups slow down the reaction) - results which are inconsistent with an inversion mechanism.

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