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Mononuclear Heterocyclic Rearrangements. Part 16.[1] Kinetic Study of the Rearrangement of Some *ortho*-Substituted *Z*-Phenylhydrazones of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole into 2-Aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles in Dioxane-Water and in Benzene

Vincenzo Frenna* and Gabriella Macaluso

Dipartimento di Chimica Organica 'E. Paternò', Viale delle Scienze, Parco D'Orleans II, I-90128 Palermo, Italia

Giovanni Consiglio, Barbara Cosimelli and Domenico Spinelli

Dipartimento di Chimica Organica 'A. Mangini', Via S. Donato 15, I-40127 Bologna, Italia

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Abstract: The effects of six *ortho*-substituents (Me, Et, F, Cl, Br and NO_2), showing different electronic and proximity effects, on the rate of the title reaction have been studied at 313.15 K in dioxane/water at various pS^+ values (3.8–12.7) and in benzene at various piperidine concentrations. The kinetic data obtained have been treated by using a Fujita-Nishioka approach with a dissection of the *ortho*-substituent effect in 'ordinary polar effect', 'proximity polar effect' and 'primary steric effect'. The different contributions calculated have been discussed in the framework of the various mechanisms proposed for the studied rearrangement.

Keywords: Ring transformations; Heterocyclic rearrangements; Linear free energy relationships; Fujita-Nishioka equation; Dissection of polar and steric effects

For a long time our research group has been engaged in the study of the synthetic applications and of the mechanism of ring-ring interconversions[1,2] which we named *mononuclear heterocyclic rearrangements* (MHR).[3a] The results probably most representative have been obtained by using as substrates *meta*- and *para*-substituted *Z*-phenylhydrazones of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (**1a-m**), whose rearrangement into 2-aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles (**2a-m**) has been thoroughly investigated both in dioxane/water (D/W; 1:1, v:v) in the presence of buffers[4] and in benzene (PhH) in the presence of several amines.[5] In both systems we have observed that the structure of the transition state is substituent-dependent. Moreover in D/W it is also pS^+-dependent.

In this paper we report the results obtained in a study of the rearrangement of six

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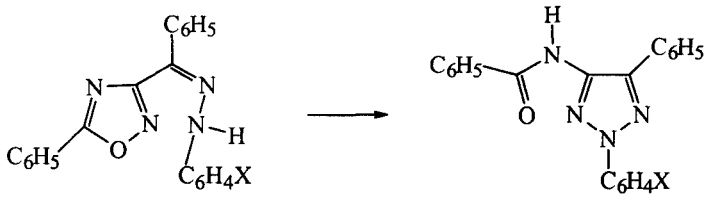
ortho-substituted *Z*-phenylhydrazones (**1o-t**) into the corresponding triazoles (**2o-t**) in W/D as well as in PhH to gain information about the influence of an *ortho*-substituent on the MHR reactivity also as a function of the used solvent. We have chosen substituents that show different electronic and steric effects: they range from alkyls (**o-p**: Me and Et) to halogens (**q-s**: F, Cl and Br) and nitrogroup (**t**: NO_2). Indeed, owing to the crowded nature of the transition state of MHR the present substituent could affect the reactivity by proximity effects. For the sake of comparison we have also determined the reactivity of *Z*-*p*-fluorophenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (**1n**) whose rearrangement into the corresponding triazole (**2n**) has not been examined before.



1 2

a : X = *p*-OMe
b : X = *p*-Me
c : X = *p*-Et
d : X = *m*-Me
e : X = *m*-Et
f : X = H
g : X = *p*-Cl
h : X = *p*-Br
i : X = *m*-Cl
j : X = *m*-Br
k : X = *m*-NO_2
l : X = *p*-CN
m : X = *p*-NO_2
n : X = *p*-F
o : X = *o*-Me
p : X = o-Et
q : X = *o*-F
r : X = *o*-Cl
s : X = *o*-Br
t : X = *o*-NO_2

Results and Discussion

MHR Reactivities of Z-Arylhydrazones 1o-t in D/W

The apparent first-order rate constants, k_A, for the studied rearrangements have been measured in the presence of buffers in a large range of pS^+ (3.8 - 12.7)[6] at various temperatures. The ratios of logarithmic kinetic constants at pS^+ 3.80 and 11.50, calculated at 313.15 K from activation parameters,[7] are collected in Table 1. Data for **1o**, **q** and **t** are plotted *versus* pS^+ values in Figure together with data concerning **1f**, *i.e.* the unsubstituted *Z*-phenylhydrazone.

From an examination of the plots of Figure and the data of Table 1 the following comments can be made:

i) the shape of the curves pertaining to *ortho*-substituted *Z*-phenylhydrazones closely parallels that of the unsubstituted **1f**, pointing to the occurrence of two different reaction pathways, for which transition states with a different timing in bond breaking (N_α-H) and

bond forming (N_α-N_2) have been proposed as a function of the different electronic effects exerted by the substituents present.[4] The first, uncatalyzed and then pS^+-independent, occurs at low pS^+; the second, base-catalyzed and then pS^+-dependent, occurs at high pS^+;[9]

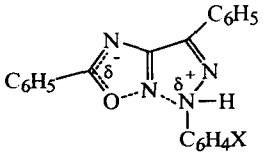
ii) in the whole range of pS^+ examined all the *ortho*-substituted *Z*-phenylhydrazones irrespective of the nature of the present substituent (feebly electron-repelling as alkyls; moderately or strongly electron-withdrawing, as halogens or nitrogroup, respectvely) are less reactive than **1f** and the corresponding *para*-isomers, as well. This clearly evidences the relevance of the proximity effects (both polar and steric in nature) determined by the *ortho*-substituent. In fact (see data in Figure and in Table 1) for X = Me, F and NO_2 in the uncatalyzed range $k_H/k_{o\text{-}X}$ ratios of 2.7, 5.9 and 1400 and $k_{p\text{-}X}/k_{o\text{-}X}$ ratios of 3.9, 3.6 and 95 have been calculated. Similar results have been observed in the base-catalyzed range at pS^+ 11.50 ($k_H/k_{o\text{-}X}$ 5.9, 1.7, 17; $k_{p\text{-}X}/k_{o\text{-}X}$ 7.5, 3.6, 4500, respectively);

iii) the curves pertaining to **1o** and **1q** intersect each other; therefore in pS^+-independent and -dependent ranges **1o** is less and more reactive than **1q**, respectively. This indicates that the relative weight of ordinary polar effect, proximity polar effect and primary steric effect is different at different pS^+ values and then depends on the different reaction mechanism operating. Moreover the pS^+ ranges where uncatalyzed and base-catalyzed pathways occur are substituent-dependent: *e.g.* at pS^+ 7 in the case of X = *o*-Me and *o*-NO_2 the reactions are uncatalyzed and base-catalyzed, respectively.

Linear Free Energy (lfe) Treatment of Kinetic Data in D/W

Meta- and *para*-substituents affect the reactivity in different ways depending on the pathway (*i. e.*, depending on the pS^+ range considered); then Hammett correlations gave different results that can be summarized as below.

At pS^+ 3.80 (*i.e.*, in the uncatalyzed range) electron-repelling and -withdrawing substituents increase and decrease, respectively, the reactivity: thus a good multiparameter correlation [Ingold-Yukawa-Tsuno,[10,11] *i. e.*, with (small) contributions of both r^+ (0.11) and r^- (0.26) parameters] has been obtained with a negative slope (ρ -1.29).[4b,12] The low susceptibility constant has been related to a balance between the opposite electronic effects (on the nucleophilicity of N_α and on the acidity of the proton of N_α-H bond) exerted by the substituent in the proposed S_{Ni}-like transition state (**3**).[4b]



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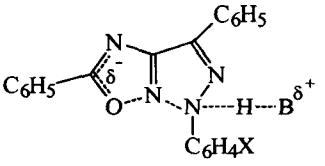

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Table 1. Parameters Used in Statistical Correlations for the Rearrangements 1→2 in D/W and in PhH

	in D/W				in PhH			Subst. Constants	
	pS^+ 3.80		pS^+ 11.50						
X	$\log(k_X/k_H)^a$	$\sigma_{calc}{}^b$	$\log(k_X/k_H)^a$	$\sigma_{calc}{}^c$	$\log(k)_X/(k)_H{}^d$	$\log(k)_X/(k)_H{}^e$	$\sigma_{calc}{}^f$	$E_S{}^g$	F^g
p-OMe	0.195[h]	-0.168	0.255[i]	-0.78[k]	0.282[l]	-0.003[l]	-0.268		
p-Me	0.155[h]	-0.124	0.102[i]	-0.31[k]	0.176[l]	-0.134[l]	-0.170		
p-Et	0.135[i]	-0.141	0.090[i]	-0.30[k]	0.153[l]	-0.150[l]	-0.150		
m-Me	0.053[h]	-0.069	0.023[i]		0.065[l]	-0.152[l]	-0.069		
m-Et	0.065[i]	-0.070	0.023[i]		0.093[l]	-0.119[l]	-0.07		
H	0.000[h]	0.000	0.000[i]		0.000[l]	0.000[l]	0.000		
p-Cl	-0.339[h]	0.269	0.646[i]	0.265		0.432[l]	0.227		
p-Br	-0.390[h]	0.282	0.689[i]	0.273		0.474[l]	0.232		
m-Cl	-0.498[h]	0.373	0.830[i]			0.725[l]	0.373		
m-Br	-0.526[h]	0.391	0.907[i]			0.771[l]	0.391		
m-NO_2	-0.945[h]	0.710	1.582[i]			1.329[l]	0.71		
p-CN	-1.015[h]	0.775	1.854[i]	0.858		1.213[l]	0.66		
p-NO_2	-1.173[h]	0.895	2.426[i]	1.048		1.571[l]	0.778		
p-F	-0.220[j]	0.151	0.320[j]	0.133		0.162[j]	0.062		
o-Me	-0.439[j]	-0.124	-0.774[j]	-0.31[k]		-0.549[j]	-0.170	-1.24	-0.04
o-Et	-0.491[j]	-0.141	-0.828[j]	-0.30[k]		-0. 555[j]	-0.150	-1.31	-0.05
o-F	-0.772[j]	0.151	-0.234[j]	0.133		0. 397[j]	0.062	-0.46	0.43
o-Cl	-1.258[j]	0.269	-0.728[j]	0.265		-0. 373[j]	0.227	-0.97	0.41
o-Br	-1.452[j]	0.282	-0.995[j]	0.273		-0. 585[j]	0.232	-1.16	0.44
o-NO_2	-3.153[j]	0.895	-1.231[j]	1.048		-0.653[j]	0.778	-2.52	0.67

[a] From k_A values calculated at 313.15 K by the activation parameters. k_H 1.24 x 10^{-6} s^{-1} at pS^+ 3.80 and 2.52 x 10^{-3} s^{-1} at pS^+ 11.50. [b] σ_{calc} for the rearrangements at pS^+ 3.80: $\sigma_{calc} = \sigma^n + 0.11\Delta\sigma_R{}^+ + 0.26\Delta\sigma_R{}^-$. [c] σ_{calc} for the rearrangements at pS^+ 11.50: $\sigma_{calc} = \sigma_H + 0.60\Delta\sigma^-$. [d] Kinetic constants for bimoleculat pathway (k_{II}, see equation 3). [e] Kinetic constants for termolecular pathway (k_{III}, see equation 3). [f] Values from Ref. 20. [g] Values from Ref. 18. [h] Values from Ref 4b and references therein. [i] Values from Ref 4e and references therein. [j] This work. [k] Values of σ^+. [l] Values from Ref. 5d; $(k_{II})_H$ 3.21 x 10^{-6} l mol^{-1} s^{-1}; $(k_{III})_H$ 7.65 x 10^{-5} l^{-2} mol^{-2} s^{-1}.

In contrast, at $pS^+ > 8.50$ (*i.e.*, in the base-catalyzed range) two lfe relationships have been observed, with the unsubstituted **1f** showing the lowest reactivity, and the electron-repelling and -withdrawing substituents both increasing the reactivity. This non-linear concave-upward lfe relationship clearly indicates a changeover of the mechanism with changing substituent.[4e,13]

As a matter of fact an electron-withdrawing substituent strongly increases the reactivity indicating that the abstraction of hydrogen atom of the *Z*-arylhydrazone plays a relevant role [e.g., at pS^+ 11.50 a good Yukawa-Tsuno correlation (ρ 2.22) has been observed with a significant r^- (0.60) contribution]; in contrast an electronic-repelling substituent, that reduces the acidity of the hydrogen atom, feebly increases the reactivity (ρ^+ -0.33). These observations agree with structures of the transition state (T.S., see **4**) which vary as a

function of the substituent present: thus the loosening of the N_α-H bond can be more advanced than the nucleophilic attack of N_α on N_2 bearing electron-withdrawing substituents on account of the low nucleophilicity of N_α and of the significant acidity of hydrogen atom of the arylhydrazone. Opposite effects are exerted by electron-repelling substituents. Therefore in the two cases the relative timing of N_α-N_2 formation and N_α-H breaking in the T.S.s is a function of the substituent electronic effects.[4e]

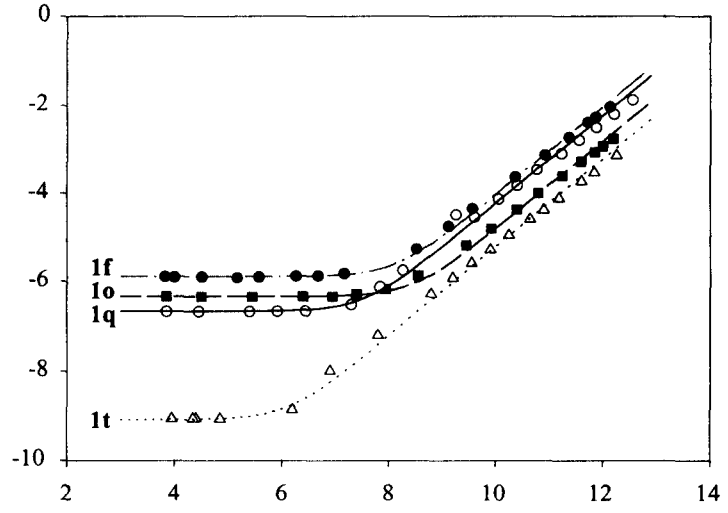


Figure. Plot of log k_A for the rearrangement (**1f, o, q, t**) → (**2f, o, q, t**) in D/W at 313.15 K *versus* pS^+

The whole of results obtained with *meta*- and *para*-substituted phenylhydrazones **1a-n** allows the following discussion of the results collected with *ortho*-substituted *Z*-phenylhydrazones **1o-t** to be made.

Generally speaking the effects exerted by an *ortho*-substituent on the reactivity can be discussed using several approaches, between which the most fruitful are those proposed by Taft,[14] Charton,[15] Forthing and Nam,[16] Chapman and Shorter,[17] Fujita and Nishioka.[18] In our experience this last treatment is the most useful,[19] because it allows one to treat data concerning the total effect of an *ortho*-substituent as the sum of three contributions: the 'ordinary polar effect' (considered equal to that of the *para*-substituent and well expressed by Hammett or similar substituent constant),[11,20] the 'proximity polar effect' (represented by the Swain-Lupton *F* constant)[18,21] and the 'primary steric effect' (symbolized by the Taft E_s constant),[14,18] as indicated by equation 1, where ρ, δ and *f* are susceptibility constants and *i* is the intercept of the regression function with the ordinate.

$$\log k_o/k_H = \rho\sigma_o + \delta E_s + fF_o + i \qquad (1)$$

Interestingly this treatment allows to combine kinetic data for *ortho*-substituted (**1o-t**) with those for *meta*- and *para*-substituted (**1a-n**) *Z*-phenylhydrazones in equation 2

$$\log k_{o,m,p}/k_H = \rho\sigma_{o,m,p} + \delta E_s + fF_o + i \qquad (2)$$

By applying equations 1 and 2 to the MHR studied at pS^+ 3.80 and 11.50 the results reported in Table 2 are obtained: the levels of significance of correlations are better than 99.95% and all the terms in equations 1 and 2 are justified at better than 99.95% as examined by F tests.

A close correspondence between the susceptibility constants calculated for *meta*- and *para*-substituted *Z*-phenylhydrazones and for the whole of *ortho*-, *meta*- and *para*-substituted *Z*-phenylhydrazones has been observed: *e.g.*, at pS^+ 3.80 $\rho_{m,p} = -1.29 \pm 0.01$ and $\rho_{o,m,p} = -1.30 \pm 0.02$, and at p$S^+$ 11.50 for electron-withdrawing substituents $\rho_{m,p} = 2.22 \pm 0.05$ and $\rho_{o,m,p} = 2.23 \pm 0.04$ and for electron-repelling substituents $\rho^+_{m,p} = -0.33 \pm 0.01$ and $\rho^+_{o,m,p} = -0.33 \pm 0.01$, respectively. These results indicate that kinetic data for *ortho*-, *meta*- and *para*-derivatives can be confidently treated by means of a unique multiparameter lfe relationship, because the introduction of data concerning *ortho*-substituents does not affect the susceptibility constants of lfe relationships calculated for *meta*- and *para*-substituted *Z*-phenylhydrazones.

Let us now comment on the susceptibility constants calculated for the multiparameter lfe correlations.

At pS^+ 3.80 a large contribution of 'proximity polar effect' that significantly affects the reactivity has been observed: therefore *ortho* electron-withdrawing and -repelling substituents cause a decrease and an increase of the reactivity both for ordinary (ρ -1.4) and proximity polar (f -0.7) effects and this agrees with the effects exerted by *meta*- and *para*-substituents (ρ -1.3). Moreover, 'primary steric effect' of *ortho*-substituents influences the reactivity as expected: the higher the volume-filling factor of the substituent the higher the induced decrease of the reactivity (δ 0.55).

At pS^+ 11.50 two different lfe have been observed: one for electron-withdrawing and one for electron-repelling substituents (see above). Among the six *ortho*-substituents considered, four (F, Cl, Br and NO_2) have positive Hammett substituent constants (*i.e.* are electron-withdrawing substituents) and two (Me and Et) have negative Hammett substituent constants (*i.e.* are electron-repelling). Owing to the low number of points (four for the first and only two for the second relationship) it must be pointed out that these correlations are statistically less significant than those obtained at pS^+ 3.80.

With electron-withdrawing substituents a small contribution of 'proximity polar effect' (f 0.3-0.4; ρ 2.2-2.3) that hardly affects the reactivity and a large contribution of 'primary steric effect' (δ 1.5) that strongly decreases the reactivity have been found.

Table 2. Linear Free Energy Relationships[a] for the Rearrangements (1) → (2) at 313.15 K in D/W (1:1, v:v) at pS^+ 3.80 or 11.50 and in Benzene in the Presence of Piperidine

Equation used	$\rho \pm s_\delta$	$\delta \pm s_\rho$	$f \pm s_f$	$i \pm s_i$	R	n	Hydrazones
			in D/W, at pS^+ 3.80				
$\log k_{m,p}/k_H = \rho(\sigma^n + r^+\Delta\sigma^+ + r^-\Delta\sigma^-) + i$	-1.29 ± 0.01			-0.02 ± 0.01	0.9995	14	**1a-n**
$\log k_o/k_H = \rho\sigma_o + \delta E_S + fF + i$	-1.36 ± 0.17	0.55 ± 0.04	-0.87 ± 0.18	0.01 ± 0.05	0.9994	7	**1f,o-t**
$\log k_{o,m,p}/k_H = \rho\sigma_{o,m,p} + \delta E_S + fF + i$	-1.30 ± 0.02	0.54 ± 0.01	-0.90 ± 0.05	-0.01 ± 0.01	0.9994	20	**1a-t**
			in D/W, at pS^+ 11.50				
$\log k_{m,p}/k_H = \rho\sigma^+ + i$	-0.33 ± 0.01			0.00 ± 0.00	0.9997	6	**1a-f**
$\log k_{m,p}/k_H = \rho(\sigma^n + r^-\Delta\sigma^-) + i$	2.22 ± 0.05			0.03 ± 0.03	0.9983	9	**1f-n**
$\log k_o/k_H = \rho\sigma_o + \delta E_S + fF + i$	2.30 ± 0.01	1.55 ± 0.01	0.41 ± 0.01	0.00 ± 0.00	0.9999	5	**1f,q-t**
$\log k_{o,m,p}/k_H = \rho\sigma_{o,m,p} + \delta E_S + fF + i$	2.23 ± 0.04	1.51 ± 0.05	0.31 ± 0.16	0.02 ± 0.02	0.9994	13	**1f-n,q-t**
$\log k_{o,m,p}/k_H = \rho\sigma_{o,m,p} + \delta E_S + fF + i$	-0.33 ± 0.01	0.70 ± 0.03	0.18 ± 0.71	0.00 ± 0.00	0.9999	8	**1a-f,o,p**
$\log k_{o,m,p}/k_H = \rho\sigma_{o,m,p} + \delta E_S + i$	-0.33 ± 0.01	0.71 ± 0.00		0.00 ± 0.00	0.9999	8	**1a-f,o,p**
			in PhH				
$\log (k_{III})_{m,p}/(k_{III})_H = \rho\sigma + i$	1.92 ± 0.04			0.01 ± 0.02	0.9981	11	**1d-n**
$\log (k_{III})_{o,m,p}/(k_{III})_H = \rho\sigma_{o,m,p} + \delta E_S + fF + i$	1.96 ± 0.11	1.37 ± 0.13	1.73 ± 0.37	-0.01 ± 0.04	0.9897	15	**1d-n,q-t**
$\log (k_{III})_{o,m,p}/(k_{III})_H = \rho\sigma_{o,m,p} + \delta E_S + fF + i$	1.92 ± 0.04	0.83 ± 0.07	-0.09 ± 0.24	-0.01 ± 0.01	0.9988	14	**1d-n,r-t**
$\log (k_{III})_{o,m,p}/(k_{III})_H = \rho\sigma_{o,m,p} + \delta E_S + i$	1.92 ± 0.04	0.86 ± 0.01		0.01 ± 0.01	0.9988	14	**1d-n,r-t**

[a] s_ρ, s_δ, s_f, s_i represent standard errors, respectively, of ρ, δ, f and i; i, intercept; R, correlation coefficient; n, number of data points. The values of σ_{calc}, E_S, F and $\log (k_X/k_H)$ used in correlations are shown in Table 1.

Only two *ortho* electron-repelling substituents with similar E_s and F values have been examined, thus the value of 'proximity polar effect' (f 0.2 ± 0.7) has no statistical meaning while that of 'steric effect' (δ 0.70 ± 0.03) is only qualitatively indicative of a relevant effect. Thus, a recalculation of the relationship by excluding the 'proximity polar contribution' has been carried out, giving excellent results (n 8, R 0.9999) with the same ρ and δ susceptibility constants. On the basis of the $k_{p\text{-}alk}/k_{o\text{-}alk}$ ratios (7.4) calculated the global proximity effects can be considered significant.

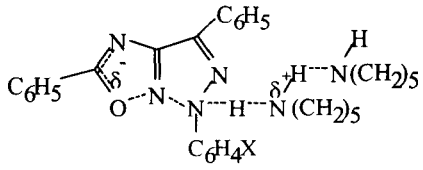
A comparison of thermodynamic parameters of *ortho*- and *para*-substituted *Z*-phenylhydrazones is restricted to halogens (fluorine, chlorine and bromine) and the nitrogroup. A similar trend has been observed: the lower reactivities of *ortho*- with respect to *para*-isomers in the uncatalysed and in the catalyzed ranges are entropy and enthalpy dependent, respectively. The comparison for alkyls is not significant on account of the small differences in the reactivities between *ortho*- and *para*-isomers.

MHR Reactivities of Z-Arylhydrazones 1n-s in PhH

The apparent first-order kinetic constants for the studied rearrangements have been measured at various piperidine concentrations ([PIP] 0.12-1M). A strong dependence of the reactivity on piperidine concentration has been observed. The plots of k_A/[PIP] (k_A measured at 313.15 K) *versus* [PIP] (see equation 3) gave excellent statistical results (n 7 or 8; $r \geq 0.9997$: see Experimental) with an intercept statistically not different from zero, indicating that for both electron-withdrawing and -repelling substituents the bimolecular

$$k_A/[PIP] = k_{II} + k_{III}\,[PIP] \qquad (3)$$

reaction pathway is not operating and that the reaction occurs only through the termolecular reaction pathway (catalysis of catalysis mechanism, see **5**).



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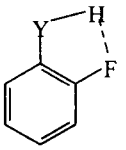
Moreover as already observed for *meta*- and *para*-substituted *Z*-phenylhydrazones the contribution of the uncatalysed pathway is not significant. All the *ortho*-substituted *Z*-phenylhydrazones, but *ortho*-fluoro derivative [$(k_{III})_H/(k_{III})_{o\text{-}F}$ 0.4; $(k_{III})_{p\text{-}F}/(k_{III})_{o\text{-}F}$ 0.6] are less reactive than the unsubstituted one [$(k_{III})_H/(k_{III})_{o\text{-}X}$ 2.5–170] and the corresponding

para-substituted *Z*-arylhydrazones [$(k_{III})_{p\text{-}X}/(k_{III})_{o\text{-}X}$ 2.4–4.5], indicating that also in PhH steric effects can play a relevant role (see data in Table 1).

Lfe Treatment of Kinetic Data in PhH and Comparison with Data in D/W at pS$^+$ 11.5

k_{III} values for *meta*- and *para*-substituted *Z*-phenylhydrazones in PhH gave two lfe relationships: the non-linear concave-upward Hammett plot has a minimum between *p*-ethyl (**1c**) and *m*-alkyl (**1d-e**) *Z*-phenylhydrazones (indeed, a very similar situation has been observed in D/W at pS^+ 11.5). Therefore including the four electron-withdrawing substituents (X = *o*-F, *o*-Cl, *o*-Br and *o*-NO_2; **1q-t**) in the multiparameter correlation (equation 2) with *ortho*-substituted **1** (see above lfe relationship in D/W at pS^+ 11.5) does not give good statistical results (*n* 15, *R* 0.9897). On the other hand on exclusion of kinetic data of *o*-fluorophenylhydrazone (**1q**) an excellent correlation has been obtained (*n* 14, *R* 0.9988) and this agrees with the observation that **1q** is the only *ortho*-substituted *Z*-phenylhydrazone more reactive than **1f**. In this situation (the small number of *ortho*-isomers considered) the relationship seems able to give only qualitative information: the 'proximity polar effect' does not appear detectable (*f* -0.09 ± 0.24), while 'primary steric effect' appears relevant (δ 0.8). Thus, a recalculation of the relationship by excluding the 'proximity polar contribution' has been carried out, once more giving excellent results (*n* 13, *R* 0.9988) with the same ρ and δ susceptibility constants. It is interesting to observe that by using the susceptibility constants of line 12 of Table 2 we have calculated for *ortho*-fluorophenylhydrazone (**1q**) a value of k_{III} *ca.* $4.2\cdot10^{-5}$ $l^2mol^{-2}s^{-1}$, *i.e.* about 4.5 times lower than that measured. The peculiar behaviour of **1q** can be ascribed to the well established formation of a strong intramolecular hydrogen bond in apolar solvents with fluorine atom in systems like **6** (where a five-membered ring is involved) as observed in *ortho*-fluoro phenols (Y = O)[22] and anilines or anilino derivatives (Y = NR).[22] This effect favours the transition state formation, significantly affecting (increasing) the reactivity.



6

Moreover a plot of kinetic data in PhH *versus* data in D/W at pS^+ 11.5 for **1f-n, q-t** does not show a good correlation (*n* 13, *R* 0.9895 *i* 0.13): *vice-versa* by excluding data for **1q** the correlation coefficient increases to 0.9988 (*n* 12, *i* 0.08) confirming that the outlier point in the correlation is that for **1q**. The slope of the plot (*s* 0.65, *i* 0.08) confirms a lower effect of

substituents in PhH as compared to D/W in line with the previous results obtained with *meta*- and *para*-substituted *Z*-phenylhydrazones in different solvents.

Conclusions

The Fujita-Nishioka treatment of kinetic data concerning MHR of six *ortho*-substituted (**1o-t**) and of fourteen *meta*- and *para*-substituted phenylhydrazones (**1a-n**) has allowed the dissection of substituent effects in 'ordinary polar effect', 'proximity polar effect' and 'primary steric effect', whose contributions have been explained on the basis of the different mechanisms proposed for MHR.

Experimental

Synthesis and Purification of Compounds

Compounds **1n-t** were prepared from 3-benzoyl-5-phenyl-1,2,4-oxadiazole[23] and the appropriate arylhydrazine in ethanol in the presence of acetic acid. Purification was achieved by chromatography [silica gel: cyclohexane/ethyl acetate (20/1)] and crystallization from ethanol.

The *Z*-arylhydrazones **1n-t** were rearranged into the corresponding 2-aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles **2n-t** by standing in ethanol in the presence of aqueous KOH (10%) at room temperature until disappearance of the starting product (tlc analysis). Compounds **2n-t** were purified by crystallization from ethanol.

1n – yellow, m.p. 142-4 °C; [Found: C, 70.5; H, 4.2; N, 15.7. $C_{21}H_{15}N_4OF$ requires C, 70.38; H, 4.22; N, 15.63%]; ν_{max}(Nujol) 3220 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 11.42 (1H, s, NH), 8.24-7.18 (14H, m, 2Ph, Ar); HMRS (EI): M^+ found 358.12245. $C_{21}H_{15}N_4OF$ requires 358.12299.

1o – yellow, m.p. 143-5 °C; [Found: C, 74.6; H, 5.2; N, 15.9. $C_{22}H_{18}N_4O$ requires C, 74.56; H, 5.12 N, 15.81%]; ν_{max}(Nujol) 3235 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 11.55 (1H, s, NH), 8.26-6.91 (14H, m, 2Ph, Ar), 2.48 (3H, s, CH_3); HMRS (EI): M^+ found 354.14749. $C_{22}H_{18}N_4O$ requires 354.14806.

1p – yellow, m.p. 121-3 °C; [Found: C, 75.1; H, 5.5; N, 15.3. $C_{23}H_{20}N_4O$ requires C, 74.98; H, 5.47 N, 15.21%]; ν_{max}(Nujol) 3245 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 11.67 (1H, s, NH), 8.27-6.98 (14H, m, 2Ph, Ar), 2.85 (2H, q, *J* 7.5 Hz, CH_2CH_3), 1.45 (3H, t, *J* 7.5 Hz, CH_2CH_3); HMRS (EI): M^+ found 368.16632. $C_{23}H_{20}N_4O$ requires 368.16371.

1q – yellow, m.p. 161-3 °C; [Found: C, 70.5; H, 4.3; N, 15.7. $C_{21}H_{15}N_4OF$ requires C, 70.38; H, 4.22; N, 15.63%]; ν_{max}(Nujol) 3230 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 11.85 (1H, s, NH), 8.26-6.87 (14H, m, 2Ph, Ar); HMRS (EI): M^+ found 358.12211. $C_{21}H_{15}N_4OF$ requires 358.12299.

1r – yellow, m.p. 155-7 °C; [Found: C, 67.3; H, 4.1; N, 15.0. $C_{21}H_{15}N_4OCl$ requires C, 67.29; H, 4.03; N, 14.95%]; ν_{max}(Nujol) 3225 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 12.10 (1H, s, NH), 8.31-6.90 (14H, m, 2Ph, Ar); HMRS (EI): M^+ found 374.09278. $C_{21}H_{15}N_4OCl$ requires 374.09344 (Cl-35 isotope).

1s – yellow, m.p. 147-8 °C; [Found: C, 60.3; H, 3.7; N, 13.5. $C_{21}H_{15}N_4OBr$ requires C, 60.16; H, 3.61; N, 13.36%]; ν_{max}(Nujol) 3220 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 11.98 (1H, s, NH), 8.33-6.87 (14H, m, 2Ph, Ar); HMRS (EI): M^+ found 418.04233. $C_{21}H_{15}N_4OBr$ requires 418.04292 (Br-79 isotope).

1t – yellow, m.p. 162-4 °C; [Found: C, 65.6; H, 4.0; N, 18.3. $C_{21}H_{15}N_5O_3$ requires C, 65.45; H, 3.92; N, 18.17%]; ν_{max}(Nujol) 3190 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 13.80(1H, s, NH), 8.40-6.98 (14H, m, 2Ph, Ar); HMRS (EI): M^+ found 385.11720. $C_{21}H_{15}N_5O_3$ requires 385.17749.

2n – colourless, m.p. 190-1 °C; [Found: C, 70.5; H, 4.2; N, 15.8. $C_{21}H_{15}N_4OF$ requires C, 70.38; H, 4.22; N, 15.63%]; ν_{max}(Nujol) 3320, 1680 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.05-7.16 (15H, m, 2Ph, Ar, NH); HMRS (EI): M^+ found 358.12248. $C_{21}H_{15}N_4OF$ requires 358.12299.

2o – colourless, m.p. 159-61 °C; [Found: C, 74.7; H, 5.2; N, 15.9. $C_{22}H_{18}N_4O$ requires C, 74.56; H, 5.12 N, 15.81%]; ν_{max}(Nujol) 3170, 1645 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.95-7.48 (15H, m, 2Ph, Ar, NH), 2.51 (3H, s, CH_3); HMRS (EI): M^+ found 354.14759. $C_{22}H_{18}N_4O$ requires 354.14806.

2p – colourless, m.p. 130-2 °C; [Found: C, 75.1; H, 5.5; N, 15.3. $C_{23}H_{20}N_4O$ requires C, 74.98; H, 5.47 N, 15.21%]; ν_{max}(Nujol) 3190, 1652 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.08-7.45 (15H, m, 2Ph, Ar, NH), 2.83 (2H, q, *J* 7.5 Hz, CH_2CH_3), 1.21 (3H, t, *J* 7.5 Hz, CH_2CH_3); HMRS (EI): M^+ found 368.16305. $C_{23}H_{20}N_4O$ requires 368.16371.

2q – colourless, m.p. 157-9 °C; [Found: C, 70.5; H, 4.2; N, 15.8. $C_{21}H_{15}N_4OF$ requires C, 70.38; H, 4.22; N, 15.63%]; ν_{max}(Nujol) 3215, 1652 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.92-7.45 (15H, m, 2Ph, Ar, NH); HMRS (EI): M^+ found 358.12207. $C_{21}H_{15}N_4OF$ requires 358.12299.

2r – colourless, m.p. 173-5 °C; [Found: C, 67.4; H, 4.1; N, 15.1. $C_{21}H_{15}N_4OCl$ requires C, 67.29; H, 4.03; N, 14.95%]; ν_{max}(Nujol) 3215, 1652 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.92-7.48 (15H, m, 2Ph, Ar, NH); HMRS (EI): M^+ found 374.09299. $C_{21}H_{15}N_4OCl$ requires 374.09344 (Cl-35 isotope).

2s – colourless, m.p. 154-6 °C; [Found: C, 60.3; H, 3.7; N, 13.5. $C_{21}H_{15}N_4OBr$ requires C, 60.16; H, 3.61; N, 13.36%]; ν_{max}(Nujol) 3160, 1648 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.91-7.48 (15H, m, 2Ph, Ar, NH); HMRS (EI): M^+ found 418.04211. $C_{21}H_{15}N_4OBr$ requires 418.04292 (Br-79 isotope).

2t – colourless, m.p. 143-5 °C; [Found: C, 65.6; H, 4.0; N, 18.3. $C_{21}H_{15}N_5O_3$ requires C, 65.45; H, 3.92; N, 18.17%]; ν_{max}(Nujol) 3160, 1655 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.05-7.40 (15H, m, 2Ph, Ar, NH); HMRS (EI): M^+ found 385.11698. $C_{21}H_{15}N_4OCl$ requires 385.17749.

pS⁺ and Kinetic Measurements

Piperidine,[24] benzene[24] and dioxane[24] were purified according to the methods previously reported.

Details on operational pH scale used (pS^+) have already been reported.[4a,d]

The kinetics were followed spectrophotometrically as previously described[4] by measuring the disappearance of **1n-t** at the wavelengths of their absorption maxima, where the absorption of **2n-s** was minimal. The rate constants are accurate to within ± 3%. Tables of the apparent first-order kinetics constants in PhH at 313.15 K in the presence of piperidine and of the relevant linear regression analyses according to equation 3 as well as data in D/W calculated at 313.15 K at various pS^+ together with thermodynamic parameters are available on request from the authors (V. F. or D. S.). In Table 1 are collected ratios of logarithmic kinetic constants at pS^+ 3.80 and 11.50 in D/W and in PhH.

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13. Calculation for the Yukawa-Tsuno correlation at pS^+ 11.50 reported in ref. 4e was concerned with reactivity of *Z*-arylhydrazones **1f-m**. Now we have added kinetic data for **1n**: no significant change in the calculated parameters has been observed.
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