Mononuclear Heterocyclic Rearrangements. Part 2.[1a] Substituent Effects on the Rate of Rearrangement of Some Arylhydrazones of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole into 2-Aryl-4-benzoylamino-5-phenyl-1,2,3-triazole, at pS^+ 3.80 †

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The rates of the mononuclear heterocyclic rearrangement of some *meta*- and *para*-substituted phenylhydrazones of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (Ia—m) into 2-aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles (IIa—m) have been measured in dioxan–water (1 : 1 v/v) at pS^+ 3.80 and at various temperatures; the relevant activation parameters have also been determined. The results obtained, analysing the kinetic data by means of the Ingold–Yukawa–Tsuno equation (ρ -1.31, r^+ 0.10, r^- 0.25, correlation coefficient 0.9996), show that the reaction rate is moderately affected by the nature of the substituents present in the aryl fragments of phenylhydrazone and are consistent with an internal nucleophilic displacement by nitrogen on nitrogen.

IN the course of our research[1] on mononuclear heterocyclic rearrangements (m.h.r.s)[2] we recently reported[1a] results of a kinetic study of the rearrangement of the phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (Id) into 4-benzoylamino-2,5-diphenyl-1,2,3-triazole (IId) in the pS^+ range 3.8—12.2 and presented evidence for the occurrence of two different types of reaction, one (at high pS^+) base catalysed, the other pS^+ independent. In the pS^+ independent range (3.8—6.8) a single mechanism seems to operate, according to the constant values of the activation parameters. We proposed[1a] a mechanism of the S_Ni type with a highly solvated transition state (t.s.).

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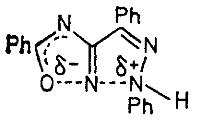
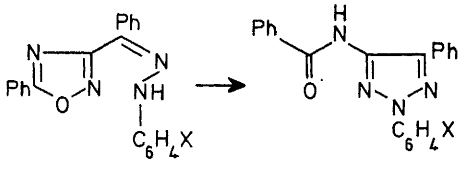
[2] A. J. Boulton, A. R. Katritzky, and A. M. Hamid, *J. Chem. Soc.* (*C*), 1967, 2005; A. S. Afridi, A. R. Katritzky, and C. A. Ramsden, *J.C.S. Perkin I*, 1976, 315; A. J. Boulton, 'Lectures in Heterocyclic Chemistry,' Hetero Corporation, Provo, 1973.

With the aim of obtaining further information on this point, we have now studied the m.h.r.s of a series of *meta*- and *para*-substituted phenylhydrazones (Ia—m) of 3-benzoyl-5-phenyl-1,2,4-oxadiazole in dioxan–water (1 : 1 v/v) at pS^+ 3.8.





(I) (II)

a; X = *p*-OMe
b; X = *p*-Me
c; X = *m*-Me
d; X = H
e; X = *p*-Cl
f; X = *p*-Br
g; X = *m*-Cl
h; X = *m*-Br
i; X = *m*-NO_2
l; X = *p*-CN
m; X = *p*-NO_2

SCHEME

EXPERIMENTAL

Synthesis and Purification of Compounds.—3-Benzoyl-5-phenyl-1,2,4-oxadiazole[3] gave the corresponding arylhydrazones (Ia—m) on treatment with the appropriate arylhydrazine in ethanol or ethanol–dioxan in the presence of acetic acid. The arylhydrazones (I) were thermally rearranged into the corresponding 2-aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles (II). The physical data of compounds (I) and (II) are collected in Table 1. Water and dioxan were purified according to the methods reported.[1a]

pS^+ *and Kinetic Measurements.*—An operational pH scale, pS^+,[4a] was established in aqueous dioxan by employing the pK_a values of acids determined by interpolation from the data reported by Harned and Owen.[4b] For dioxan–water (1 : 1 v/v) the meter reading after calibration against aqueous buffers was not significantly different from pS^+; in fact it was necessary to apply a correction of +0.16 to the meter reading.

pS^+ Measurements were made by using a Radiometer PHM63 digital pH meter. Variations of pS^+ values before and after any run in the buffered solutions of reaction were lower than 0.03 units; the mean value of pS^+ was used for calculations.

The kinetics (at constant ionic strength 0.05M) were followed spectrophotometrically, as previously reported,[1a] in the pS^+ independent range. The apparent first-order kinetic constants measured at pS^+ 3.8 and the relative activation parameters are collected in Table 2. The concentrations used were *ca.* 6×10^{-5}M. The wavelengths and log ε at the maximum used are reported in Table 2.

RESULTS AND DISCUSSION

Products of Reaction.—At pS^+ 3.8 compounds (Ia—m) in dioxan–water (1 : 1 v/v) rearranged into the corresponding triazoles (IIa—m) in high yield with virtually no by-products.

Kinetic Data.—According to the mechanism proposed by us[1a] in the pS^+ independent range, an increase in the rate of m.h.r. was observed on introduction of an electron-repelling substituent into the phenylhydrazone system. The introduction of an electron-withdrawing group reduced the reactivity as expected. Indeed, the rate of m.h.r. in the range considered depends on the electron density on the hydrazone nitrogen atom adjacent to the aryl group.

The correlation of the reactivity data at 40 °C ($\log k/k_H$) with Hammett substituent constants[5] gives, as foreseen, a negative ρ value (-1.33 ± 0.06; correlation coefficient 0.992) but the intercept is significantly different from zero (i -0.06 ± 0.03). The corresponding plot (see Figure 1) shows an apparently random dispersion of experimental points with respect to the calculated straight line, but a more careful examination of the results shows that (i) the *p*-cyanophenylhydrazone (Il) has a reactivity lower than that of the *m*-nitrophenylhydrazone (Ii) which is against the order expected on the basis of σ values;[5] (ii) the points for the *meta*-substituted phenylhydrazones (Ic, d, g—i) fall on a straight line

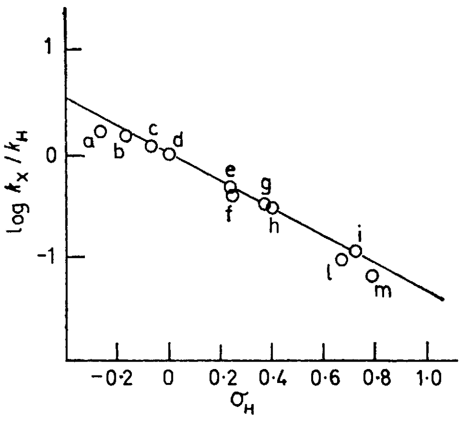


FIGURE 1 Plot of $\log k_X/k_H$ at 40 °C *versus* σ_m or σ_H. Least-square line (ρ_m) calculated using *meta*-substituents only

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(ρ_m −1.30, s_ρ 0.03, i −0.02, s_i 0.01, n 5, correlation coefficient 0.999 5, confidence level >99.9%) with an intercept of practically zero; (iii) *para*-substituted phenylhydrazones present a reactivity lower than that expected on the basis of their σ values and of ρ_m irrespective of the nature of the substituents. This behaviour is unexpected: in fact, for reactions which from a mechanistic viewpoint can be compared with the rearrangement studied by us, such as the reactions of anilines with acid chlorides[6] and with halogenonitro-aromatic[7] or -heteroaromatic derivatives,[8] it is well known that electron-withdrawing *para*-substituents lower reactivity more than is calculated from σ and ρ_m values, but electron-repelling *para*-substituents *never* cause a similar lowering, sometimes giving rise, on the contrary, to an increase in reactivity.[8b]

TABLE 1

Physical data for compounds (Ia—m)[a,b] and (IIa—m)[a,c]

Compound	M.p. (°C)	Compound	M.p. (°C)	I.r. spectra (Nujol) of compounds (II) ν_{NH}/cm^{-1}	ν_{CO}/cm^{-1}
(Ia)	145[d]	(IIa)	175—178[e]	3 165	1 656
(Ib)	144[d]	(IIb)	183[e]	3 125	1 656
(Ic)	145[d]	(IIc)	213[e]	3 145	1 650
(Id)	137[e]	(IId)	191[e]	3 226	1 650
(Ie)	150[e]	(IIe)	206[e]	3 145	1 656
(If)	146[f]	(IIf)	185—187[g]	3 175	1 650
(Ig)	143[d]	(IIg)	205[e]	3 106	1 645
(Ih)	140—142[f]	(IIh)	205[g]	3 086	1 645
(Ii)	173—175[d]	(IIi)	192[e]	3 175	1 658
(Il)	176—178[f]	(IIl)	205—208[g,h]	3 205	1 650
(Im)	180[d]	(IIm)	206[e]	3 165	1 656

[a] Satisfactory analytical data for C, H, and N were obtained for all new compounds (Ia—c, e—m), (IIa—c, e—m). [b] Compounds are yellow or pale yellow. [c] Compounds are colourless. [d] From benzene–ethanol. [e] From ethanol. [f] From dioxan–ethanol. [g] From benzene. [h] ν_{CN} 2 212 cm^{-1}.

TABLE 2

Rate constants and activation parameters for the rearrangement (I) ⟶ (II) in dioxan–water (1 : 1 v/v) at pS^+ 3.80

Compound	10^6k/s^{-1} (°C)[a]	−log k[b]	$\Delta H^{\ddagger}$[c]/ kcal mol^{-1}	$-\Delta S^{\ddagger}$[d]/ cal mol^{-1} K^{-1}	λ_{max}/nm	log ε
(Ia)	2.16 (41.00), 7.29 (51.20), 18.7 (60.30)	5.710	22.7	12.3	380	4.21
(Ib)	1.80 (40.10), 6.26 (51.00), 18.3 (61.00)	5.750	22.5	13.2	376	4.25
(Ic)	1.43 (40.10), 4.77 (50.60), 15.3 (61.00)	5.852	22.9	12.1	370	4.22
(Id)[e]	1.30 (40.05), 3.41 (50.10), 9.51 (60.20)	5.905	19.9	22.2	366	4.22
(Ie)	0.570 (40.10), 2.03 (50.00), 6.99 (61.00)	6.244	24.3	9.5	366	4.29
(If)	0.490 (39.90), 1.97 (50.50), 5.96 (60.20)	6.295	24.9	7.8	367	4.31
(Ig)	0.397 (40.00), 1.24 (50.00), 3.84 (60.20)	6.403	22.7	15.5	360	4.27
(Ih)	0.370 (40.00), 1.39 (50.40), 4.44 (60.20)	6.431	24.9	8.5	362	4.29
(Ii)	0.143 (40.10), 0.514 (50.40), 1.61 (60.20)	6.850	24.4	12.1	348	4.30
(Il)	0.122 (40.10), 0.433 (50.40), 1.35 (60.20)	6.920	24.2	13.0	364	4.48
(Im)	0.084 0 (40.10), 0.290 (50.20), 0.898 (60.20)	7.078	23.8	14.9	402	4.50

[a] The rate constants are accurate to within ±3%. [b] At 40°, values calculated from activation parameters and used for linear free energy relationship. [c] At 40°, the maximum error is 0.6 kcal mol^{-1}. [d] At 40°. [e] See ref. 1*a*.

In order to explain the deviations from the Hammett relationship observed for *para*-substituents we have used the Ingold–Yukawa–Tsuno (IYT) equation,[9] in the form proposed by Wepster *et al.*,[10] obtaining the relation (1) (Figure 2) * with an intercept near zero (i −0.01 ± 0.01) and correlation coefficient 0.9996.

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* Similar results have been obtained at 50 and 60 °C: a lowering of ρ and an increase in r^+ and r^- have been observed with increase of temperature. Moreover according to Exner[11] kinetic data at different temperatures are well correlated (correlation cofficient ⩾0.998, confidence level >99.9%).

[6] E. G. Williams and C. N. Hinshelwood, *J. Chem. Soc.*, 1934, 1079; C. N. Hinshelwood, W. B. S. Newling, and L. A. K. Staveley, *Trans. Faraday Soc.*, 1934, **30**, 597; F. J. Stubbs and C. N. Hinshelwood, *J. Chem. Soc.*, 1949, 571; A. N. Bose and C. N. Hinshelwood, *ibid.*, 1958, 4085; H. S. Venkataraman and C. N. Hinshelwood, *ibid.*, 1960, 4977, 4986; G. V. Semenyuk, M. V. Oleinik, and L. M. Litvinenko, *Reakts. Sposobnost Org. Soedinenii*, 1967, **4**, 760 (*Chem. Abs.*, 1969, **70**, 2931); *Zhur. obshchei Khim.*, 1968, **38**, 2009 (*Chem. Abs.*, 1969, **70**, 19475); E. Tommila and T. Vihavaien, *Acta Chem. Scand.*, 1968, **22**, 322; A. Arcoria, S. Fisichella, G. Scarlata, and D. Sciotto, *J. Org. Chem.*, 1973, **38**, 32; G. Borkent, P. A. T. Jijssen, J. P. Roos, and J. J. Van Aartsen, *Rec. Trav. chim.*, 1976, **95**, 84.

[7] H. J. Van Opstall, *Rec. Trav. chim.*, 1933, **52**, 901; A. Singh and D. H. Peacock, *J. Phys. Chem.*, 1936, **40**, 669; N. B. Chapman and R. E. Parker, *J. Chem. Soc.*, 1951, 3301; T. A. Emokpae, I. M. Dosunmu, and J. Hirst, *J.C.S. Perkin II*, 1974, 1860; J. Kavalek, J. Haasovà, and V. Stĕrba, *Coll. Czech. Chem. Comm.*, 1972, **37**, 3333; J. Kavalek, T. M. Chinh, V. Mikan, V. Stĕrba, and M. Vecera, *ibid.*, 1973, **38**, 1935; J. J. Ryan and R. A. Humffray, *J. Chem. Soc.* (*B*), 1967, 1300.

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[9] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' 1969, Cornell University Press, Ithaca, 2nd edn., p. 1217; Y. Tsuno, T. Ibata, and Y. Yukawa, *Bull. Chem. Soc. Japan*, 1959, **32**, 960; Y. Yukawa and Y. Tsuno, *ibid.*, pp. 965, 971; Y. Yukawa, Y. Tsuno, and M. Sawada, *ibid.*, 1966, **39**, 2274; 1972, **45**, 1198.

[10] B. M. Wepster, *J. Amer. Chem. Soc.*, 1973, **95**, 102; A. J. Hoefnagel, J. C. Monshouwer, E. C. G. Snorn, and B. M. Wepster, *ibid.*, p. 5350; A. J. Hoefnagel and B. M. Wepster, *ibid.*, p. 5357.

[11] O. Exner, *Progr. Phys. Org. Chem.*, 1973, **10**, 411 and references therein.

These results give useful information about the reaction mechanism. The low values of ρ, r^+, and r^- seem to indicate that the rate-determining transition state requires little help from substituents in charge dispersion.

$$\log k_X/k_H = (-1.31 \pm 0.01)[\sigma^n + (0.10 \pm 0.02)\Delta\sigma_R^+ + (0.25 \pm 0.01)\Delta\sigma_R^-] \quad (1)$$

The r^+ value observed (*ca.* 0.1) indicates through-resonance interactions [10,12] between the reaction centre and the substituent which are less important than those for the dissociation of benzoic acids. Such a low r^+ value for a reaction in a polar solvent which involves an atom (nitrogen) directly linked to an aromatic ring has no precedent.

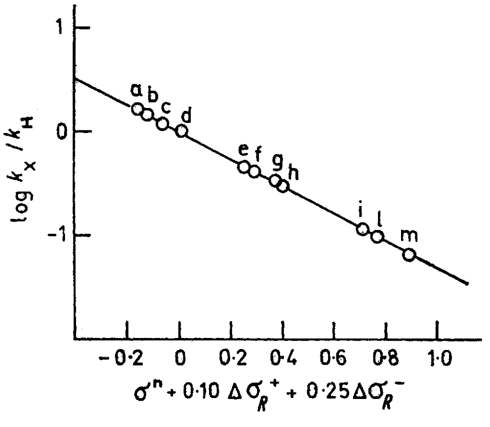

FIGURE 2 Least-square line using the ' overall ' IYT equation (ρ −1.31)

Also the absolute ρ value appears low if compared with that measured for the protonation equilibrium of arylhydrazines (in water, ρ −1.21).[13,*] Because the effect of a substituent in the benzene ring on a side-chain reaction decreases with increasing chain length, the reaction studied (which occurs on the α-nitrogen atom) should display substituent effects larger than those observed in protonation of arylhydrazines (which involves the β-nitrogen atom).

Let us consider the possible reasons for this behaviour. With regard to structure of the t.s., the correlation data observed can be related to a low degree of formation of the new nitrogen–nitrogen bond or to a balancing of opposite electronic effects exerted by substituents in the states preceding the rate-determining step. The high values observed for activation enthalpies ($\Delta H^\ddagger \geq 20$ kcal mol^{-1}) and the influence of the nature of the substituent present in the 5-position of the oxadiazole ring [1a] lead us to exclude the possibility of a low degree of formation of the new nitrogen–nitrogen bond. On the other hand, taking into account the reactivity [1a] of (Id) at p$S^+ \geq 6.8$ (occurrence of general base catalysis), we think that in the pS^+ independent range, nitrogen–hydrogen bond breaking (probably assisted by solvent molecules) also controls the reaction rate. The results obtained can easily be rationalized on this basis.

Because of the electronic effect an electron-repelling substituent increases the nucleophilic strength of the nitrogen atom and favours the formation of the new nitrogen–nitrogen bond, but it opposes the breaking of the nitrogen–hydrogen bond which determines the evolution of the t.s. The balancing of the effects exerted causes a low net electronic effect, as indicated by the ρ and r^+ values. Similar observations can be made for an electron-withdrawing substituent, *i.e.* it reduces the nucleophilic strength of the nitrogen atom, but favours nitrogen–hydrogen bond breaking, thus leading to low r^- and ρ values.

TABLE 3

Parameters involved in the calculation of ρ values at 40 °C

Substituent	σ_H [a]	σ^n [b]	$\Delta\sigma_R^+(\Delta\sigma_R^-)$ [b]	log k/k_H	σ_{obs} [c]
p-OMe	−0.268	−0.09	−0.71	0.195	−0.164
p-Me	−0.170	−0.10	−0.22	0.155	−0.133
m-Me	−0.069	−0.069		0.053	
H	0.000	0.000		0.000	
p-Cl	0.227	0.29	−0.19	−0.339	0.247
p-Br	0.232	0.30	−0.16	−0.390	0.286
m-Cl	0.373	0.373		−0.498	
m-Br	0.391	0.391		−0.526	
m-NO_2	0.710	0.710		−0.945	
p-CN	0.660	0.70	0.29	−1.015	0.768
p-NO_2	0.778	0.778	0.45	−1.173	0.889

[a] Values defined by Hammett.[5] [b] Values from ref. 10. [c] Calculated as in ref. 10.

Thus our results on the reaction mechanism of m.h.r. confirms the superiority of the IYT equation with respect to the simple Hammett relation in evaluating the through-resonance interactions.

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[*] Moreover, taking into account the difference in solvent, to make a comparison with the above mentioned protonation equilibrium, the ρ value for the reaction studied should be greatly reduced.[14]

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