RELATIONSHIPS AMONG STRUCTURE, REACTIVITY TOWARDS THIOLS AND BASICITY OF PHENYLHYDRAZONOPROPANEDINITRILES

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Data required for characterization of reactivity of *ortho*-, *meta*-, and *para*-substituted derivatives by first and second order rate constants were obtained from spectrophotometric investigation of reaction kinetics of phenylhydrazonopropanedinitriles with model thiols. The reactivity has been found to be linearly dependent on Hammett constants of substituents. Similar dependence revealed the basicity characterized by pK_a values determined spectrophotometrically. Whilst reactivity and basicity of *meta*- and *para*-substituted derivatives is dependent, *ortho*-substituted derivatives did not obey any simple relation between reactivity and basicity. This finding is important for utilization of *ortho*-derivatives of phenylhydrazonopropanedinitrile when studying the uncoupling effect of these substances upon oxidative and photosynthetic phosphorylation.

Carbonylcyanidephenylhydrazones were reported[1-3] to be a new group of bioactive compounds. Bioeffects of these compounds, more correctly denoted as phenylhydrazonopropanedinitriles[4,5], involve their ability to uncouple the oxidative and photosynthetic phosphorylation in mitochondria and chloroplasts; this results in a failure of adenosine triphosphate synthesis as a universal cell fuel[6-8]. Even though many authors[9-15] utilize phenylhydrazonopropanedinitriles, the mechanism of this uncoupling effect has not been solved. Phenylhydrazonopropanedinitriles are weak acids ($pK_a \sim 6$) ref.[16]. In line with this fact and the Mitchell's chemiosmotic theory[17] phenylhydrazonopropanedinitriles are considered as proton translocators[18]. According to this conception these compounds disturb the proton gradient at the membrane, which is inevitable for the synthesis of adenosine triphosphate, by association–dissociation reactions in the lipidic components of membranes. The second conception considers phenylhydrazonopropanedinitriles as compounds chemically modifying membrane proteins involved in oxidative or photosynthetic phosphoryla-

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tion[19-21], receptors being first of all the SH groups of cysteine embodied in the respective structurally or catalytically active proteins. This follows from the fact that phenylhydrazonopropanedinitriles are characterized by a relatively high affinity just to SH groups in contrast to NH_2 and OH groups[21-23], and from the finding that the SH groups are important in the process of oxidative and photosynthetic phosphorylation[24-29].

This paper is aimed to characterize the reactivity of a series of phenylhydrazonopropanedinitriles towards thiols by the second order rate constants. Confrontation of the determined rate constants and pK_a values characterizing the basicity of phenylhydrazonopropanedinitriles with their uncoupling effect might help to solve the mechanism of effect of these substances.

EXPERIMENTAL

4-Trifluoromethoxy- and 3-chlorophenylhydrazonopropanedinitriles were products of Calbiochem, San Diego (USA), Boehringer, Mannheim (FRG) and Sigma, St. Luis (USA). The remaining phenylhydrazonopropanedinitriles were obtained by diazotization of the respective anilines and condensation of the intermediate diazonium salts with propanedinitrile[1,4,22]. 2-Mercaptoacetic acid, 2-mercaptoethylamine, L-cysteine, and its methyl ester were products of Sigma, St. Luis (USA). Spectrophotometers SP 30 UV VIS, Pye Unicam, Cambridge (Great Britain) and Specord UV VIS, Zeiss Jena (GDR) were used for spectrophotometric measurements.

The reaction kinetics of phenylhydrazonopropanedinitriles with thiols was investigated by a spectrophotometric measurement of absorbance changes in time at a wavelength corresponding to the greatest differences of absorption spectra of reactants and products. The initial concentrations of reactants were below the value of their solubility in the given solvent. The stock solutions of phenylhydrazonopropanedinitriles and thiols were methanolic and aqueous, respectively. The solutions for reactions contained up to 1% of methanol in Clark Lubs phthalate (pH 4–6), phosphate (pH 6–8) and borate (pH 8–10) buffer solutions[30]. The reactions were carried out at a minimum 40-fold excess of the thiol to phenylhydrazonopropanedinitrile. The reaction course is governed at these conditions by laws valid for the first order reaction. The first order rate constants k_{obs} (s^{-1}) were calculated from the line slope of the dependence $\log (A_\infty - A_t)$ on reaction time t, where A_∞ stands for the absorbance of the reaction solution after the reaction and A_t that in time t,

$$k_{obs} = 2{\cdot}303 \,.\, \mathrm{tg}\, \alpha \,. \qquad (1)$$

The rate constants are the average value of three measurements of kinetics and are reproducible with an accuracy up to 5%. The second order rate constants k ($l\, mol^{-1}\, s^{-1}$) were calculated according to[23]

$$k = \frac{(K_A + c_{H^+}) \,.\, (K_B + c_{H^+})}{c_B \,.\, c_{H^+} \,.\, K_B} \,.\, k_{obs} \,, \qquad (2)$$

where K_a is the dissociation constant of the respective phenylhydrazonopropanedinitrile, K_B the dissociation constant of the thiol, c_{H^+} the concentration of hydrogen ions, and c_B the analytical concentration of the thiol. The dissociation constants for thiols were taken from[31].

The dissociation constant values were determined by a spectrophotometric measurement of absorbances of compounds in undissociated and dissociated forms, and also in the pH region approximately corresponding to the pK_a value of the measured compound in buffer solutions of ionic strength $I = 0{\cdot}01$ (ref.[30]). Concentration of derivatives was $1 \cdot 10^{-5}$ mol l^{-1}. The absorbance was measured in a 30 mm-quartz cell at 25°C. The dissociation constants K_a were calculated according to[32],

$$K_a = \frac{\begin{vmatrix} c_{H_1+} \cdot A_1 & c_{H_1+} & 1 \\ c_{H_2+} \cdot A_2 & c_{H_2+} & 1 \\ c_{H_3+} \cdot A_3 & c_{H_3+} & 1 \end{vmatrix}}{\begin{vmatrix} c_{H_1+} & A_1 & 1 \\ c_{H_2+} & A_2 & 1 \\ c_{H_3+} & A_3 & 1 \end{vmatrix}}, \qquad (3)$$

where c_{H_1+} is the concentration of hydrogen ions and A_1 the corresponding absorbance of the compound in undissociated form, c_{H_2+} and A_2 are the same values for pH $\approx pK_a$, and c_{H_3+} and A_3 correspond to values of hydrogen ion concentration and absorbance for fully dissociated forms, respectively. The absorbance values were determined by three independent measurements at a constant wavelength.

The Hammett σ constants were taken from[33], for the nonlinear regression analysis EC-1025 computer was employed.

RESULTS AND DISCUSSION

Phenylhydrazonopropanedinitriles react with thiols in aqueous medium to furnish addition products of thiols at the electrophilic carbon atom of the cyano group[22]. These reactions can be spectrophotometrically monitored, since the reaction product can be distinguished from the starting compounds by its absorption spectrum (Fig. 1). Phenylhydrazonopropanedinitriles quantitatively react with thiols in at least 20-fold excess according to the first order reaction (Fig. 2). The first order rate constants

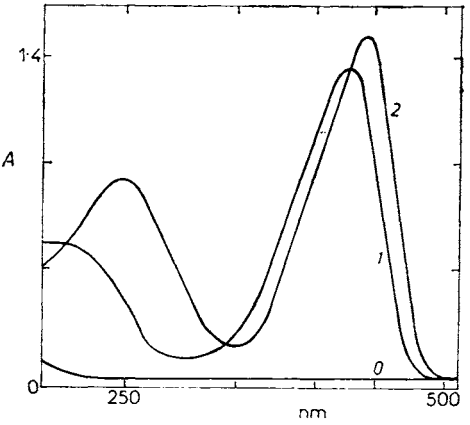

FIG. 1

Spectrophotometric indication of reaction of phenylhydrazonopropanedinitrile with cysteine. Reaction medium was the phosphate pH 7·0 buffer solution, temperature 25°C, initial concentrations of phenylhydrazonopropanedinitrile and cysteine: $5 \cdot 10^{-5}$ and $1 \cdot 10^{-3}$ mol l^{-1}, respectively. Curve *0* traces the spectrum of the thiol, *1* that of phenylhydrazonopropanedinitrile, and *2* that of the mixture after reaction

k_{obs} are dependent under these conditions on temperature (Fig. 3), pH, and concentration of the thiol (Fig. 4). Dependence $\log k_{obs} = f(1/T)$ is at the same time linear for the temperature interval measured (5–35°C) and equation (*4*) holds for it

$$\log k_{obs} = -2\,349{\cdot}14 \,.\, T^{-1} + 6{\cdot}420\,. \qquad (4)$$

The correlation coefficient $r = 0{\cdot}998$ ($F = 498{\cdot}501$, $n = 7$). Calculated value of the activation energy $E_a = 4{\cdot}5 \,.\, 10^4$ J. The relation of logarithms k_{obs} upon the pH value has a trilinear shape (Fig. 4) and can be characterized by equation (*2*) which has, after logarithmic calculation and adaptation, the form

$$\log k_{obs} = \mathrm{pH} - \log\left(K_a \,.\, 10^{\mathrm{pH}} + 1\right) - \log\left(K_B \,.\, 10^{\mathrm{pH}} + 1\right) + \log\left(kK_B c_B\right). \qquad (5)$$

As shown in[23], this form of dependence k_{obs} on pH is given by the fact that the undissociated form of phenylhydrazonopropanedinitriles and dissociated form of thiols take part in the reaction which proceeds at the highest rate at a pH enabling the maximum concentration of reactive forms of both reactants. Concentration of the reactive form of phenylhydrazonopropanedinitrile increases in media of lower pH value; nevertheless, the amount of thiolate anion rapidly decreases. The situation in alkaline region of pH is just reverse. The second order rate constants k (pH inde-

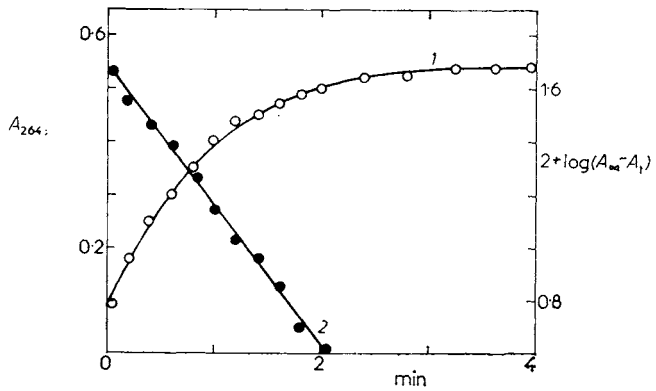

FIG. 2

Kinetics of the reaction of phenylhydrazonopropanedinitrile with cysteine in phosphate pH 7 buffer solution at 25°C. Initial concentrations of phenylhydrazonopropanedinitrile and cysteine: $5 \,.\, 10^{-5}$ and $1 \,.\, 10^{-3}$ mol l^{-1}, respectively. Blank represented the thiol solution; the left-hand scale for curve *1*, *A* at 264 nm, the right-hand scale for curve 2 shows $2 + \log(A_\infty - A_t)$

pendent) could be calculated employing equation (*5*) or (*2*) in various ways. The simpliest access employs k_{obs} determined for such a pH value which is at least by two units lower than the lowest pK_a in the phenylhydrazonopropanedinitrile series under investigation; here, the concentration of the reactive forms of phenylhydrazonopropanedinitriles is identical with their analytical concentration. The numerical value of the second and third members in equation (*5*) would be close to zero and could be, therefore, neglected. The second order constants k were determined from the simplified form of equation (*5*) $k = k_{obs} \cdot c_{H^+}/K_B \cdot c_B = k_{obs}/c_{RS^-}$. It is necessary to employ the complete equation (*2*) for determination of k if k_{obs} is estimated in a medium of higher pH. For this purpose two possibilities are at hand: *1*) k can be calculated for the particular pH values. As illustrated in Fig. 5, the second order rate constants are then the pH value independent. *2*) Equation (*5*) was fitted to experimental values by nonlinear regression analysis[34]. Its advantage is, when compared with the previous method, the simultaneous inclusion of all experimental points. Statistical significance of these curves (Fig. 5) is high: the lowest values of the correlation coefficient and F-test were $r = 0{\cdot}997$ and $F = 67{\cdot}9$, the highest standard

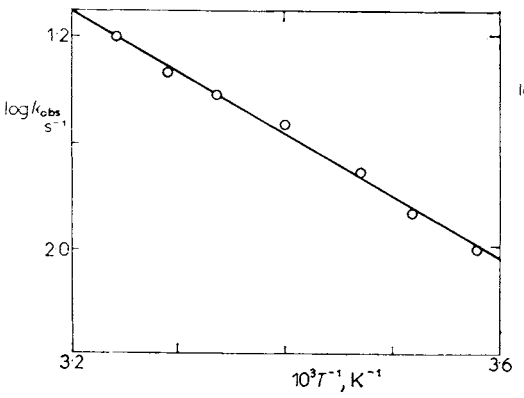

FIG. 3

Temperature dependence of reaction of phenylhydrazonopropanedinitrile with cysteine in pH 7·3 phosphate buffer solution. The reaction kinetics was spectrophotometrically monitored at 300 nm. The initial phenylhydrazonopropanedinitrile and cysteine concentration were $5 \cdot 10^{-5}$ and $2 \cdot 10^{-3}$ mol . l^{-1}, respectively

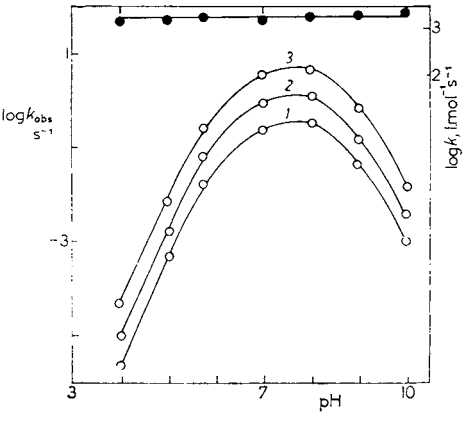

FIG. 4

Dependence of logarithms of the first order rate constants (log k_{obs}, s^{-1}, open circles), and second order rate constants (log k, l^{-1} mol s^{-1}, full circles) on the pH value of the reaction medium for the reaction of phenylhydrazonopropanedinitrile with cysteine at 25°C. The initial cysteine and phenylhydrazonopropanedinitrile concentrations: $1 \cdot 10^{-3}$ *1*, $2 \cdot 10^{-3}$ *2*, $4 \cdot 10^{-3}$ *3* and $2{\cdot}5 \cdot 10^{-5}$ mol l^{-1}; respectively

deviation $s = 0{\cdot}093$. The values of second order rate constants, determined by three above-mentioned methods, are in a good agreement (they differ by maximum $\pm 5\%$). Their values are listed in Table I.

Quantitative relation between reactivity (the average values k from Table I) and the structure of phenylhydrazonopropanedinitriles is characterized by equation (*6*):

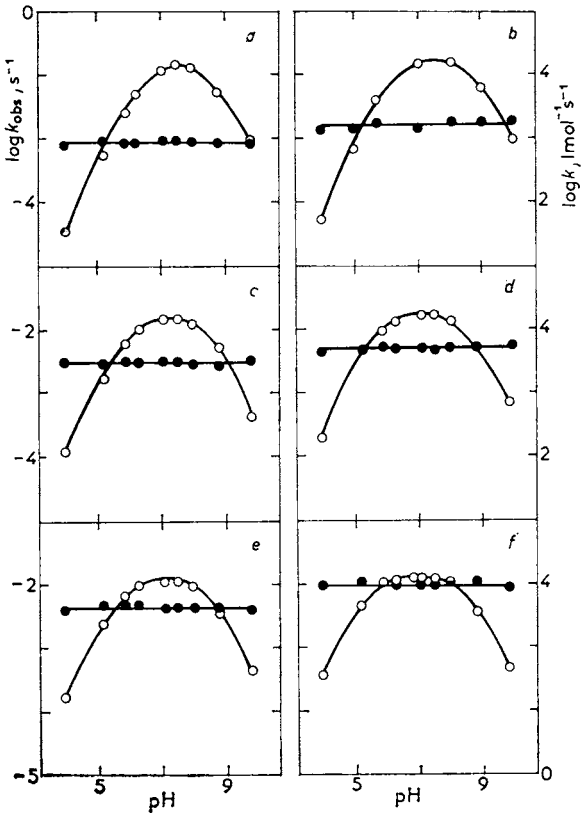

FIG. 5

Dependence of logarithms of the first order rate constants (log k_{obs}, s^{-1}, open circles) and second order rate constants (log k, l mol^{-1} s^{-1}, full circles) on the pH value of reaction medium for the reaction of cysteine with 4-methylphenylhydrazonopropanedinitrile (*a*), phenylhydrazonopropanedinitrile (*b*), 4-chlorophenylhydrazonopropanedinitrile (*c*), 4-trifluoromethoxyphenylhydrazonopropanedinitrile (*d*), 4-acetophenylhydrazonopropanedinitrile (*e*), and 4-nitrophenylhydrazonopropanedinitrile (*f*). Temperature 25°C, initial concentration of cysteine and phenylhydrazonopropanedinitriles: $1 \cdot 10^{-3}$ and $1 \cdot 10^{-5}$ mol l^{-1}, respectively

$$\log k = 1{\cdot}112\sigma + 3{\cdot}149\,, \qquad (6)$$
$$F = 36{\cdot}442\,, \quad r = 0{\cdot}976\,, \quad n = 8\,.$$

Similar linear dependences between reactivity and Hammett σ constants were found even for reactions of phenylhydrazonopropanedinitrile with further thiols, *e.g.* with 2-mercaptoacetic acid (*7*), mercaptoethylamine (*8*), and cysteine methyl ester (*9*):

$$\log k = 1{\cdot}112\sigma + 4{\cdot}752\,, \qquad (7)$$
$$F = 41{\cdot}055\,, \quad r = 0{\cdot}976\,, \quad n = 7\,;$$

$$\log k = 1{\cdot}029\sigma + 3{\cdot}114\,, \qquad (8)$$
$$F = 93{\cdot}164\,, \quad r = 0{\cdot}989\,, \quad n = 7\,;$$

$$\log k = 1{\cdot}052\sigma + 2{\cdot}572\,, \qquad (9)$$
$$F = 146{\cdot}431\,, \quad r = 0{\cdot}993\,, \quad n = 7\,.$$

The second order rate constants for reactions with model thiols and the σ and pK_a constants are listed in Table II. The spectrophotometric determination of pK_a

TABLE I

The first order (k_{obs}, s^{-1}) and second order (k, $l\,mol^{-1}\,s^{-1}$) rate constant values for reactions of phenylhydrazonopropanedinitriles with cysteine

R	$k_{obs}{}^a \cdot 10^5$	$k^b \cdot 10^3$	$k^c \cdot 10^3$	$k^d \cdot 10^3$	σ
4-CH_3	8·2	0·8	0·78	0·79	−0·17
H	17·7	1·7	1·8	1·6	0·00
3-OH	15·6	1·5	—	—	0·12
4-Cl	30·1	2·8	2·7	2·7	0·23
4-OCF_3	48·3	4·7	4·7	4·7	0·35
3-Cl	42·1	4·1	—	—	0·37
4-$COCH_3$	41·1	4·1	4·0	4·1	0·50
4-NO_2	97·0	9·8	9·6	9·8	0·78

[a] Determined for reactions of phenylhydrazonopropanedinitriles with cysteine in phthalate pH 4·0 buffer solution at 25°C, the initial cysteine and individual derivative concentrations were $2{\cdot}5 \cdot 10^{-3}$ mol l^{-1} and $1{\cdot}0 \cdot 10^{-5}$ mol l^{-1}; [b] calculated from k_{obs} according to relationship $k = k_{obs}/c_{RS^-}$; [c] average values from data in Fig. 5; [d] as fitted by experimental data from Fig. 5 according to Eq. (*5*).

TABLE II

Values of second order rate constants (k, l mol^{-1} s^{-1}) for reaction of *para*- and *meta*-R-phenylhydrazonopropanedinitriles with 2-mercaptoacetic acid (MAA), 2-mercaptoethylamine (MEA), cysteine methyl ester (MEC) and pK_a constants of phenylhydrazonopropanedinitriles and Hammett constants σ of substituents R. Reactions progressed in phosphate buffer solutions of pH 7·0, (MAA), 7·5 (MEA), and 7·6 (MEC) at 25°C; the initial concentration of phenylhydrazonopropanedinitriles was 2·5 . 10^{-5} mol l^{-1}, that of thioles 1 . 10^{-3} (MAA), 2·5 . 10^{-3} (MEA), and 1 . 10^{-3} mol l^{-1} (MEC)

R—C_6H_5—NH—N=C(CN)(CN)	MAA	MEA	MEC	σ	pK_a
4-CH_3	3·4 . 10^4	8·8 . 10^2	2·4 . 10^2	−0·17	6·75
H	5·3 . 10^4	1·3 . 10^3	3·8 . 10^2	0·00	6·55
3-OH	—	1·5 . 10^3	4·6 . 10^2	0·12	6·45
4-Cl	1·2 . 10^5	2·7 . 10^3	7·4 . 10^2	0·23	6·15
4-OCF_3	1·0 . 10^5	—	—	0·35	6·00
3-Cl	1·5 . 10^5	2·8 . 10^3	1·0 . 10^3	0·37	6·00
4-$COCH_3$	2·5 . 10^5	4·6 . 10^3	1·1 . 10^3	0·50	5·85
4-NO_2	3·9 . 10^5	8·0 . 10^3	2·5 . 10^3	0·78	5·50

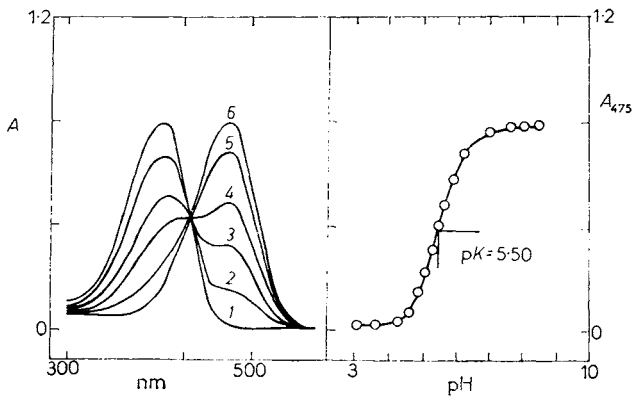

FIG. 6

a) Electronic absorption spectra of 4-nitrophenylhydrazonopropanedinitrile in buffer solutions of various pH and at constant ionic strength (I = 0·01). Curve *1* traces the absorption spectrum at pH 3·0, *2* at pH 4·8, *3* at pH 5·3, *4* at pH 5·7, *5* at pH 6·3, *6* at pH 9·0. Concentration of the compound was 2·5 . 10^{-5} mol l^{-1}, temperature 25°C. *b*) Dependence of absorbance of 4-nitrophenylhydrazonopropanedinitrile at 475 nm on the pH values of the medium and mode of the pK_a value readings. Conditions as for *a*

constants is seen in Fig. 6. Regression analysis of relations between the second order rate constants k and pK_a values afforded following equations:

$$\log k = -0{\cdot}824\, pK_a + 10{\cdot}115 \qquad (10)$$
$$F = 32{\cdot}149\,, \quad r = 0{\cdot}970\,, \quad n = 7$$

for reaction of phenylhydrazonopropanedinitriles with 2-mercaptoacetic acid,

$$\log k = -0{\cdot}799\, pK_a + 8{\cdot}070\,, \qquad (11)$$
$$F = 198{\cdot}501\,, \quad r = -0{\cdot}995\,, \quad n = 7$$

for that with mercaptoethylamine,

$$\log k = -0{\cdot}820\, pK_a + 8{\cdot}500\,, \qquad (12)$$
$$F = 57{\cdot}011\,, \quad r = -0{\cdot}978\,, \quad n = 8$$

for that with cysteine,

$$\log k = -0{\cdot}774\, pK_a + 7{\cdot}629\,, \qquad (13)$$
$$F = 277{\cdot}394\,, \quad r = -0{\cdot}995\,, \quad n = 7$$

for that with cysteine methyl ester.

These equations show that the reactivity towards thiols and the basicity of *meta*- and *para*-substituted phenylhydrazonopropanedinitriles are linearly dependent values. It is, therefore, impossible to use the *meta*- and *para*-substituted fenylhydrazonopropanedinitriles for the study of relationships between physico-chemical properties and the uncoupling effect of these substances on oxidative or photosynthetic phosphorylation. Aim of such a study would be to decide whether basicity or reactivity of phenylhydrazonopropanedinitriles are substantial for the afore-mentioned effect.

Aiming to find a suitable series of phenylhydrazonopropanedinitriles, which would not exhibit linear dependence between reactivity and basicity, 15 *ortho*-substituted derivatives of phenylhydrazonopropanedinitriles was synthesized and the second order rate constants for reaction with 2-mercaptoacetic acid and pK_a values were determined analogously as for *para*- and *meta*-derivatives; these are presented in Table III. Comparison of reactivity with basicity (Fig. 7) showed that no simple dependence could be found between these parameters. This fact is due to a direct interaction of substituents at aromatic ring with the imino group, as the centre of basicity in the phenylhydrazonopropanedinitrile molecule. Consequently, the *ortho*-effect disconnects the linearity of the relation reactivity–basicity; this makes it possible to employ the *ortho*-substituted phenylhydrazonopropanedinitriles for the

TABLE III

The second order rate constants (k) for reaction of *ortho*-phenylhydrazonopropanedinitriles with 2-mercaptoacetic acid and the pK_a values. Reactions were carried out in Clark–Lubs pH 4·0 to 10·0 solutions at 25°C and initial concentrations of phenylhydrazonopropanedinitriles and 2-mercaptoacetic acid $2{\cdot}5 \cdot 10^{-5}$ and $2{\cdot}5 \cdot 10^{-3}$ mol l^{-1}, respectively

Compound	R—C_6H_5—NH—N=C(CN)(CN)	k, l mol^{-1} s^{-1}	pK_a
1	H	$4{\cdot}5 \cdot 10^4$	6·55
2	2-CH_3	$2{\cdot}1 \cdot 10^5$	6·90
3	2-Br	$4{\cdot}8 \cdot 10^4$	6·35
4	2-CF_3	$1{\cdot}9 \cdot 10^6$	5·00
5	2-COOH	$2{\cdot}5 \cdot 10^4$	6·70
6	2-OH	$4{\cdot}0 \cdot 10^5$	6·10
7	2-Cl	$8{\cdot}8 \cdot 10^5$	5·85
8	2-NO_2	$0{\cdot}6 \cdot 10^5$	5·80
9	2-Cl, 4-NO_2	$5{\cdot}4 \cdot 10^6$	4·15
10	2-NO_2, 4-CH_3	$6{\cdot}7 \cdot 10^5$	6·00
11	2-CH_3, 4-NO_2	$1{\cdot}1 \cdot 10^6$	5·50
12	2-CH_3, 5-CH_3	$6{\cdot}3 \cdot 10^4$	6·60
13	2-CH_3, 5-CH_3	$2{\cdot}6 \cdot 10^5$	6·90
14	2-Cl, 6-Cl	$7{\cdot}9 \cdot 10^5$	4·70
15	2-Cl, 3-Cl	$2{\cdot}3 \cdot 10^6$	5·15

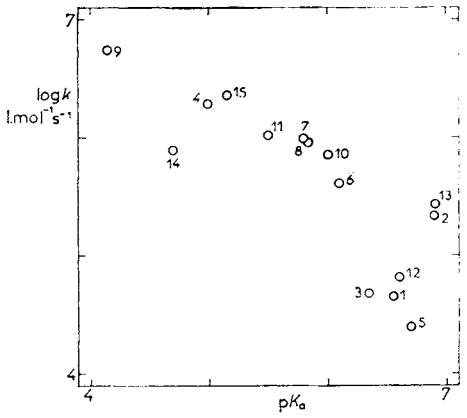

FIG. 7

Comparison of basicity (pK_a constants) and reactivity (log k, l mol^{-1} s^{-1}) for reaction of 2-mercaptoacetic acid with *ortho*-substituted phenylhydrazonopropanedinitriles (Table III). Conditions for determination of pK_a and k values are the same as in Fig. 6, or Table III

investigation of relations between physico-chemical properties and bioactivity of these substances.

The second order rate constants k calculated according to equation (*2*) or (*5*) enable a mutual reactivity comparison not only of phenylhydrazonopropanedinitriles, but also of thiols. Table IV summarizes data characterizing the reactivity of some thiols towards phenylhydrazonopropanedinitrile and its *para*-nitro derivative. This Table also lists the basicity of thiols (pK_a constants). Regression analysis disclosed that equation (*14*) holds for the fundamental derivative:

$$\log k = 0{\cdot}578\ pK_{RSH} - 1{\cdot}484\,, \qquad (14)$$
$$F = 16{\cdot}076\,,\quad r = 0{\cdot}943\,,\quad n = 7\,.$$

Dependence of reactivity of 4-nitrophenylhydrazonopropanedinitrile on pK_a constants could also be expressed by equation (*15*):

$$\log k = 0{\cdot}602\ pK_{RSH} - 0{\cdot}783\,, \qquad (15)$$
$$F = 24{\cdot}206\,,\quad r = 0{\cdot}961\,,\quad n = 7\,.$$

Reactivity of phenylhydrazonopropanedinitriles towards further nucleophiles (RNH_2, ROH) will be unlike under physiologic conditions, since differences in nucleophilicity of RS^- when compared with those of RNH_2 and ROH are extremely high (3–4 orders of magnitude[35]).

TABLE IV

The second order rate constants (k, l mol^{-1} s^{-1}) for reaction of phenylhydrazonopropanedinitrile (PHPD) and 4-nitrophenylhydrazonopropanedinitrile (4-NO_2PHPD) with various thiols and the pK_a values of thiols. Reactions were carried out in a phosphate pH 7·0 buffer solution at 25°C; initial phenylhydrazonopropanedinitriles and thiols concentration was $2{\cdot}5 \cdot 10^{-5}$ and $1 \cdot 10^{-3}$ mol l^{-1}, respectively

Thiol	PHPD	4-NO_2PHPD	pK_a
Cysteine methyl ester	$3{\cdot}8 \cdot 10^2$	$2{\cdot}5 \cdot 10^3$	6·50
2-Mercaptoethylamine	$7{\cdot}0 \cdot 10^2$	$7{\cdot}9 \cdot 10^3$	8·15
Cysteine	$1{\cdot}6 \cdot 10^3$	$9{\cdot}7 \cdot 10^3$	8·39
2-Mercaptoethanol	$7{\cdot}0 \cdot 10^3$	$7{\cdot}8 \cdot 10^4$	9·40
Benzylmercaptan	$7{\cdot}9 \cdot 10^3$	$6{\cdot}3 \cdot 10^4$	9·43
N-Acetylcysteine	$1{\cdot}3 \cdot 10^4$	$1{\cdot}2 \cdot 10^5$	9·52
2-Mercaptoacetic acid	$5{\cdot}3 \cdot 10^4$	$3{\cdot}9 \cdot 10^5$	10·22

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