Solvent Effects on the Rate of the Reaction of 2,4-Dinitrofluorobenzene with the Ethyl Ester of Tyrosine

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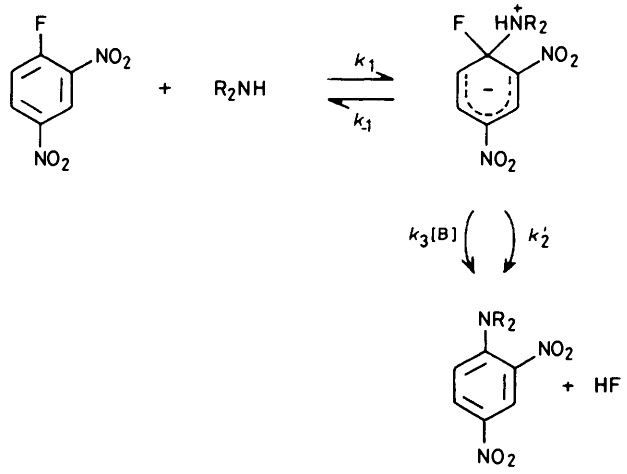
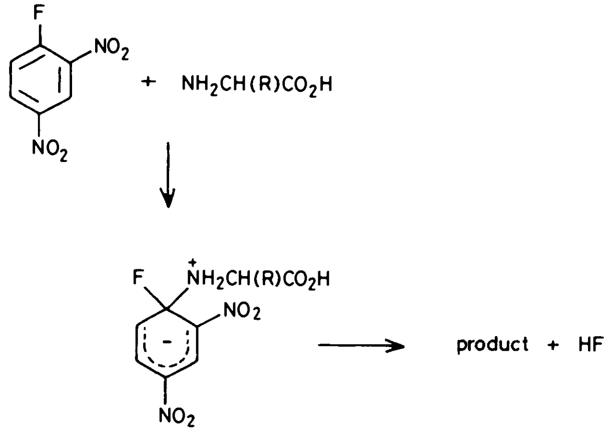
The reaction of 2,4-dinitrofluorobenzene with the ethyl ester of tyrosine was studied in 11 solvents; values of k_{obs} and k_2 (second order) were determined. The k_2 values increase in the order: benzene, 1,2-dichloroethane, ethyl acetate, dioxane, acetonitrile, methanol, propylene carbonate, ethanol, propan-2-ol, *NN*-dimethylformamide, and dimethyl sulphoxide. The k_2 values are strongly dependent on the Lewis basicity of the solvents. A correlation analysis is made, the multiparameter equations of Koppel and Palm, of Krygowski and Fawcett, and of Kamlet and Taft all being examined. The activation parameters in eight solvents were also determined, and a linear correlation between $\Delta S^‡$ and donor number DN is discussed.

In recent years, much attention has been paid to the reactions of 2,4-dinitrofluorobenzene (DNFB) with amines,[1] amino acids, and some peptides (Sanger reaction).[2] This extensive study shows that these are aromatic nucleophilic substitution reactions, $S_N2(Ar)$, and follow the addition–elimination mechanism from two neutral molecules to a polar transition state with charge separation, according to Scheme 1. In some cases the reactions are catalysed by bases and in other cases they are not.[1] In particular, for the reactions of DNFB with amino acids in water and in binary organic solvent–water mixtures, the reactions are not base-catalysed (Scheme 2), in spite of the fact that the rate increases when the pH of the solution increases.[3] It has also been found that the rate increases greatly when the reaction is transferred from water to DMSO–H_2O,[3] but the kinetics of this reaction in a series of organic solvents have not previously been studied.

On account of the solubility, instead of an amino acid we selected an ester of an amino acid, the ethyl ester of tyrosine (I). The solubility of this is large enough for the ester to be studied in a series of solvents, which includes selected protic, dipolar aprotic, and apolar aprotic solvents.



Scheme 1.



Scheme 2.

Results and Discussion

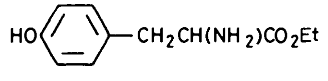
The reaction of the ethyl ester of tyrosine with DNFB was studied in 11 solvents. It is a second-order reaction. In *NN*-dimethylformamide (DMF), dimethyl sulphoxide (DMSO), propan-2-ol (Pr^{i}OH), ethanol (EtOH), propylene carbonate (PC), methanol (MeOH), dioxane, 1,2-dichloroethane (DCE), and benzene, the second-order rate constants k_2 are independent of the concentration of (I) (*ca.* 10^{-2}M). Only in acetonitrile (An) and ethyl acetate (EtOAc) are the k_2 values somewhat dependent on the concentration of (I), from *ca.* 0.07 to 0.002M.

$$\text{In An } k_2 = 0.770 + 14.3[(\text{I})] \quad (r\ 0.998;\ n\ 7)$$

$$\text{In EtOAc } k_2 = 0.208 + 7.80[(\text{I})] \quad (r\ 0.987;\ n\ 14)$$

The reaction rate constant is strongly solvent-dependent: it increases by a factor of 1.7 × 10^4 as the reaction is transferred from benzene to DMSO. The experimental results are given in Table 1 in order of increasing rate constant.

Correlation Analysis.—We examine the results with single- and multi-parameter equations. Except where otherwise noted, all correlations involve 11 data points. The first set of equations



(I)

Table 1. Second-order rate constants and activation parameters for the reaction of DNFB with the ethyl ester of tyrosine

Initial concentrations: DNFB 10^{-4}M, ester 10^{-2}M (except for nos. 3 and 5)

	Solvent	k_2/l mol^{-1} min^{-1} 20 °C	25 °C	30 °C	35 °C	$\Delta S^‡$/cal mol^{-1} K^{-1}	$\Delta H^‡$/kcal mol^{-1}
1	Benzene		0.002 25				
2	DCE		0.0808	0.0907	0.104	−50.1	4.01
3	EtOAc		0.208*				
4	Dioxane	0.246	0.285	0.381		−36.9	7.17
5	An		0.770*				
6	MeOH	0.698	0.883	1.30		−23.7	10.4
7	PC		1.24	1.50	1.90	−33.8	7.25
8	EtOH		1.85	2.33	2.85	−32.9	7.28
9	Pr^{i}OH		2.41	3.01	3.38	−37.9	5.63
10	DMF	14.6	17.0	23.7		−26.2	7.90
11	DMSO	24.9	38.7	48.3		−14.11	11.1

* $k_2 = k' + k''[(\mathbf{I})] = k'$ when $[(\mathbf{I})] = 0.00$.

(1)—(4) presented involves Koppel–Palm analysis by stepwise regression.[4] k is the second-order rate constant at 25 °C. Solvent parameters are in Table 2, with leading references in footnotes.

$$\log k = 0.023\,11B - 2.6996 \qquad (1)$$
$$(\pm 0.0043)\quad (\pm 0.5075)$$
r 0.873; s 0.5863

$$\log k = 0.018\,69B + 5.4634\mathrm{f}(\varepsilon) - 4.5038 \qquad (2)$$
$$(\pm 0.002\,00)\quad (\pm 0.8700)\quad (\pm 0.3625)$$
r 0.980; s 0.2554

$$\log k = 0.018\,65B + 5.663\mathrm{f}(\varepsilon) - 0.011\,95E - 4.516 \qquad (3)$$
$$(\pm 0.002\,09)\quad (\pm 0.9764)\quad (\pm 0.0212)\quad (\pm 0.3796)$$
r 0.9806; s 0.2670

$$\log k = 0.018\,82B + 5.523\mathrm{f}(\varepsilon) - 0.019\,40E - 2.783\mathrm{f}(n^2) - 3.8858 \qquad (4)$$
$$(\pm 0.002\,27)\quad (\pm 1.097)\quad (\pm 0.029\,16)\quad (\pm 6.877)\quad (\pm 1.609)$$
r 0.9812; s 0.2845

If we use B' as an alternative measure of solvent Lewis basicity, equations (5)—(8) are obtained (the quantities b' are 'weighted' regression coefficients[5]).

$$\log k = 0.010\,47B' - 2.1709 \qquad (5)$$
$$(\pm 0.001\,98)\quad (\pm 0.4223)$$
r 0.870; s 0.593

$$\log k = 0.008\,43B' + 5.4292\mathrm{f}(\varepsilon) - 4.055 \qquad (6)$$
$$(\pm 0.001\,01)\quad (\pm 0.9618)\quad (\pm 0.3895)$$
r 0.9753; s 0.2815

$$\log k = 0.008\,61B' + 5.9822\mathrm{f}(\varepsilon) - 0.0378E - 4.1086 \qquad (7)$$
$$(\pm 0.000\,87)\quad (\pm 0.8748)\quad (\pm 0.0193)\quad (\pm 0.3363)$$
$$(b_1' = 0.7158)\ (b_2' = 0.5198)\ (b_3' = 0.1423)$$
$$\bar{\alpha} = b_1'/\Sigma b' = 0.5195;\ \bar{\beta} = b_2'/\Sigma b' = 0.3772$$
$$\bar{\gamma} = b_3'/\Sigma b' = 0.1033$$
r 0.9841; s 0.2422

$$\log k = 0.008\,59B' + 6.053\mathrm{f}(\varepsilon) - 0.0335E - 1.551\mathrm{f}(n^2) - 4.463 \qquad (8)$$
$$(\pm 0.000\,94)\quad (\pm 0.982)\quad (\pm 0.0269)\quad (\pm 6.224)\quad (\pm 1.467)$$
r 0.9843; s 0.2603

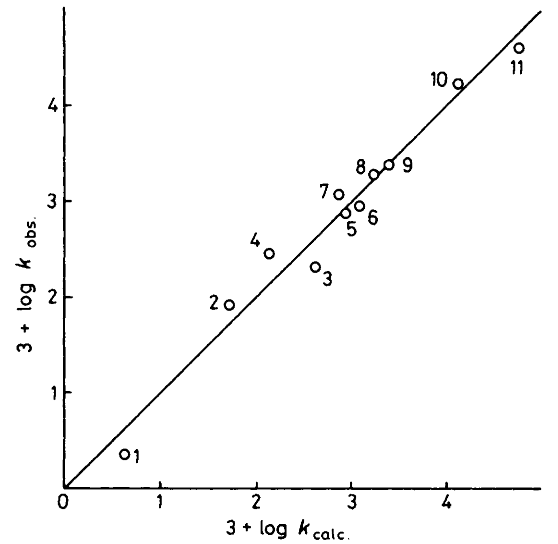


Figure. log k_{obs} for the reaction of DNFB with the ethyl ester of tyrosine *versus* log k_{calc} from equation (7) involving B', f(ε), and E (the numbering of the solvents is the same as in Table 1)

The solvent Lewis basicity parameters B or B' enter the stepwise regression first. The one-parameter correlations are rather poor but are greatly improved by the introduction of the Kirkwood dielectric function f(ε) (polarisation); compare equation (2) with (1), and (6) with (5). There is no significance in the stepwise regressions beyond the equation involving B and f(ε), because the standard errors of the regression coefficients for E (solvent Lewis acidity) and f(n^2) (Kirkwood refractive index function, polarisability) in equations (3) and (4) are greater than the coefficients themselves.

When B' is used instead of B, however, the introduction of the term in E is just about worthwhile [equation (7)] and of course improves the log k (calc.) pattern for the alcohols, the solvents of highest E values. The fact that the highly collinear B and B' values behave differently in this respect may perhaps be connected with B' being, in principle, a purer measure of solvent basicity, uncomplicated by any possibility of non-specific polarisation–polarisability effects. As indicated by the negative coefficient of E in equation (7), solvent Lewis acidity retards this reaction, opposing the acceleratory effect of solvent basicity and polarisation. The further introduction of f(n^2), in equation (8), is not significant.

Table 2. Solvent parameters for correlation analysis

	Solvent	$3 + \log k$[a]	B[b]	B'[c]	E[d]	f(ε)[e]	f(n^2)[f]
1	Benzene	0.352	52	48	2.1	0.231	0.228
2	DCE	1.907	49	40	3.0	0.432	0.210
3	EtOAc	2.318	89	172	1.6	0.385	0.185
4	Dioxane	2.455	128	237	4.2	0.226	0.203
5	An	2.886	103	160	5.2	0.480	0.174
6	MeOH	2.946	114[j]	219	14.9	0.477	0.169
7	PC	3.093	85[k]	144	4.9	0.489	0.202
8	EtOH	3.267	117[j]	229	11.6	0.470	0.181
9	Pr^{i}OH	3.382	122[j]	240	8.7	0.462	0.187
10	DMF	4.230	166	284	2.6	0.480	0.204
11	DMSO	4.588	192	358	3.2	0.484	0.221

	Solvent	E_T[g]	DN[h]	β[i]	π*[i]	α[i]
1	Benzene	34.5	0.1	0.04	0.56	0.00
2	DCE	41.9	0.0	0.00	0.76	0.14
3	EtOAc	38.1	17.1	0.47	0.50	0.00
4	Dioxane	36.0	14.8	0.42	0.55	−0.17
5	An	46.0	14.1	0.36	0.73	0.31
6	MeOH	55.5	19 (25.7)[l]	0.73	0.54	1.00
7	PC	46.6	15.1			
8	EtOH	51.9	20[m] (31.5)[l]	0.75	0.53	0.79
9	Pr^{i}OH	48.6		0.77	0.49	0.52
10	DMF	43.8	26.6	0.70	0.87	0.00
11	DMSO	45.0	29.8	0.74	1.00	0.00

[a] Second-order rate constant for reaction of DNFB with ethyl ester of tyrosine at 25 °C, from Table 1. [b] Koppel–Palm solvent Lewis basicity; values mainly from M. H. Aslam, G. Collier, and J. Shorter, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1572, and earlier papers. [c] Koppel–Paju solvent Lewis basicity; values mainly from I. A. Koppel and A. I. Paju, *Org. React., Tartu*, 1974, **11**, 121, or by personal communication from G. Collier, I. A. Pickering, and J. Shorter. [d] Koppel–Palm solvent Lewis acidity; values mainly from I. A. Koppel and A. I. Paju, *Org. React., Tartu*, 1974, **11**, 137, from note *b* and earlier papers, or by personal communication from G. Collier, I. A. Pickering, and J. Shorter. [e] Kirkwood dielectric function, $(\varepsilon - 1)/(2\varepsilon + 1)$; see note *b*. [f] Kirkwood refractive index function, $(n^2 - 1)/(2n^2 + 1)$; see note *b*. [g] Dimroth–Reichardt solvent parameter; values mainly from Chr. Reichardt, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 98. [h] Gutmann donor number; values mainly from V. Gutmann, *Coord. Chem. Rev.*, 1976, **18**, 225 and references therein. [i] These are the Kamlet–Taft solvent parameters: β, solvent hydrogen-bond acceptor basicity; π*, solvent dipolarity–polarisability; α, solvent hydrogen-bond donor acidity. M. J. Kamlet, J. L. M. Abboud, and R. W. Taft, *Prog. Phys. Org. Chem.*, 1981, **13**, 485. Values slightly revised and amplified by I. A. Pickering, personal communication. [j] *B* values determined *via* *B'*; see reference in note *b*. [k] *B* value determined *via* *B'* by I. A. Pickering, personal communication. [l] 'Bulk donicity' values. See reference in note *h*. [m] Value estimated from values for related solvents.

Since equation (7) seems to be the most satisfactory, we show the correlation graphically (Figure). Also, below equation (7) we display the quantities $\bar{\alpha}$, $\bar{\beta}$, and $\bar{\gamma}$, which indicate respectively the relative contributions of solvent basicity, polarisation, and solvent acidity in the 11 solvents. The collinearity of B' with f(ε) is fairly low, r *ca.* 0.35, which is typical for a reasonably wide selection of solvents. The collinearities of E with B' and f(ε) are also satisfactorily low, r *ca.* 0.22 and 0.35, respectively. The failure of f(n^2) to enter the regression significantly may be ascribed to a high collinearity with E (r *ca.* 0.69).

The next two correlations use B or B' and the Dimroth–Reichardt E_T value [equations (9) and (10)]. These correlations using E_T are rather less successful than the Koppel–Palm-type correlations. This can be explained by the fact that E_T is not a pure measure of Lewis acidity but involves also some contribution from polarisation–polarisability interactions. Since solvent Lewis acidity and polarisation appear to act in opposition in this reaction [*cf.* equation (7)], the use of E_T rather than the separate E and f(ε) is inevitably rather ineffective.

$$\begin{array}{l} \log k = 0.020\,59B + 0.0582E_T - 5.002 \\ \quad (\pm 0.003\,62) \quad (\pm 0.0241) \\ \quad r\ 0.929;\ s\ 0.473 \end{array} \tag{9}$$

$$\begin{array}{l} \log k = 0.009\,27B' + 0.0486E_T - 4.096 \\ \quad (\pm 0.001\,92) \quad (\pm 0.0280) \\ \quad r\ 0.908;\ s\ 0.536 \end{array} \tag{10}$$

The next set of equations involves the donor number DN. A value is not available for Pr^{i}OH, so these correlations are for 10 data points only. Also, there is some uncertainty as to the correct values to use for MeOH and EtOH. Equations (11)—(13) involve the values 25.7 and 31.5, respectively.

$$\begin{array}{l} \log k = 0.089\,37\text{DN} - 1.7577 \\ \quad (\pm 0.020\,17) \\ \quad r\ 0.843;\ s\ 0.678 \end{array} \tag{11}$$

$$\begin{array}{l} \log k = 0.068\,19\text{DN} + 4.1679\text{f}(\varepsilon) - 3.1190 \\ \quad (\pm 0.021\,35) \quad (\pm 2.3137) \\ \quad r\ 0.896;\ s\ 0.599 \end{array} \tag{12}$$

$$\begin{array}{l} \log k = 0.088\,94\text{DN} + 0.001\,12E_T - 1.7994 \\ \quad (\pm 0.028\,00) \quad (\pm 0.0470) \\ \quad r\ 0.843;\ s = 0.725 \end{array} \tag{13}$$

Equations (14)—(16) involve DN values of 19.0 and 20.0 for MeOH and EtOH, respectively. Here again the use of E_T is rather unfruitful. The results demonstrate that for this reaction the Krygowski–Fawcett[5] equations (13) and (16) are inferior to the Koppel–Palm treatment but that when the DN values of MeOH and EtOH are taken as 19 and 20, the results are better than those for the corresponding 'bulk donicities' of 25.7 and 31.5. The collinearity of DN with f(ε) or E_T is a little high (r 0.45—0.64, no matter which values are used for the alcohols), which probably accounts also for the inability of these to improve the DN regression very much.

$$\log k = 0.112\,5\mathrm{DN} - 1.9579 \tag{14}$$
(± 0.0174)
r 0.916; s 0.506

$$\log k = 0.091\,5\mathrm{DN} + 3.765\,9\mathrm{f}(\varepsilon) - 3.1929 \tag{15}$$
(± 0.0157) (± 1.465)
r 0.958; s 0.388

$$\log k = 0.1035\mathrm{DN} + 0.0293E_{\mathrm{T}} - 3.1038 \tag{16}$$
(± 0.0194) (± 0.0281)
r 0.928; s 0.503

The next set of equations involves Kamlet–Taft parameters β, π^*, and α. Values are not available for PC, so the stepwise regressions involve 10 data points only. Here β by itself is very unsuccessful, but the introduction of π^* produces a marked improvement, so that the two-parameter equation (18) in β and π^* is comparable in performance with equations (2) and (6) involving B (or B') and f(ε). There is absolutely no justification for going on to introduce α [equation (19)]. On the whole the Kamlet–Taft treatment seems inferior to the Koppel–Palm treatment for this reaction. β and π^* show a very low collinearity (r 0.037) but α shows significant collinearity with both β and π^* (r 0.46 and 0.38, respectively), which probably accounts for the inability of α to enter the regression significantly once β and π^* are there.

$$\log k = 3.3906\beta - 1.8553 \tag{17}$$
(± 0.809) (± 0.4615)
r 0.8289; s 0.712

$$\log k = 3.3153\beta + 3.378\pi^* - 4.024 \tag{18}$$
(± 0.3939) (± 0.653) (± 0.475)
r 0.9671; s 0.346

$$\log k = 3.3674\beta + 3.305\pi^* - 0.0825\alpha - 3.981 \tag{19}$$
(± 0.4941) (± 0.788) (± 0.402) (± 0.553)
r 0.9673; s 0.373

Activation Parameters.—In this reaction, the reactants pass from two neutral molecules to a dipolar activated complex with charge separation. The orientation of the reactants in the activated complex causes a great loss of entropy; the $\Delta S^{\ddagger}$ values are thus negative. Experiment shows that the $\Delta S^{\ddagger}$ values become more negative in the same sequence as $\log k_2$ increases; $\delta\Delta S^{\ddagger}$ -36 cal mol^{-1} K^{-1}, $\delta\Delta H^{\ddagger}$ 7.1 kcal mol^{-1}. This implies that entropy changes dominate the free-energy expression $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$ and that $\Delta S^{\ddagger}$ should also be Lewis basicity-dependent. We obtained equations (20)—(22) (seven data points, *i.e.* omitting Pr^{i}OH).

$$\Delta S^{\ddagger} = 1.096\mathrm{DN} - 50.725 \tag{20}$$
r 0.934; s 4.44 (confidence level 0.99)

$$\Delta H^{\ddagger} = 0.2019\mathrm{DN} + 4.259 \tag{21}$$
r 0.833; s 1.42 (confidence level 0.95)

$$\log k = 0.0911\,0\mathrm{DN} - 1.4186 \tag{22}$$
r 0.938; s 0.821 (confidence level 0.99)

From the relative correlation coefficients it can be seen that the Lewis basicity as measured by DN plays a more important role in $\Delta S^{\ddagger}$ than in $\Delta H^{\ddagger}$.

This situation can also be examined in earlier papers. For example, Francesco *et al.*[6] studied the reaction of aniline with benzyl chloride in several solvents. In the sequence MeOH, EtOH, Pr^{i}OH, and An the k_2 values decrease. The activation parameters were also determined and we find equations (23)—(25) (four data points). The $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ both depend on E_{T} values, *i.e.* mainly on the Lewis acidity of the solvents. (Here we can see that with rather few data points it is insufficient only to apply r to measure the linear correlation; the number of the data points and the confidence level should also be considered.)

$$\Delta S^{\ddagger} = -151 + 2.20E_{\mathrm{T}} \tag{23}$$
r 0.948; s 3.37 (confidence level 0.90)

$$\Delta H^{\ddagger} = -18.4 + 0.600E_{\mathrm{T}} \tag{24}$$
r 0.943; s 1.07 (confidence level 0.90)

$$\log k_2 = -7.746 + 0.075\,03E_{\mathrm{T}} \tag{25}$$
r 0.953; s 0.278 (confidence level 0.95)

Rogne *et al.*[7] studied the reaction of imidazole with benzenesulphonyl chloride in several solvents. In the sequence An, MeNO$_2$, water, benzonitrile, MeOH, EtOH, Pr^{n}OH, the k_2 values decrease. It is roughly a $\Delta H^{\ddagger}$-controlled reaction, $\delta\Delta H^{\ddagger}$ 7.4 kcal mol^{-1}, $\delta\Delta S^{\ddagger} = 16$ cal mol^{-1} K^{-1}. In correlations with the Koppel–Palm Lewis acidity parameter E (seven data points) we find equations (26) and (27). The correlation for $\Delta H^{\ddagger}$ is rather poor, but when f(ε) is introduced a marked improvement occurs. Surprisingly the correlation of $\log k_2$ with E is very poor (r 0.313), far below the corresponding values for $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$. Thus the two-parameter equation (29) applies. Here the $\Delta S^{\ddagger}$ values depend mainly on the E parameter, and $\Delta H^{\ddagger}$ values depend both on the E and on the f(ε) parameters. To obtain a good linear correlation for $\Delta H^{\ddagger}$ (and thus for $\log k_2$) the f(ε) term cannot be neglected.

$$\Delta S^{\ddagger} = 1.613E - 44.14 \tag{26}$$
r 0.968; s 3.22 (confidence level 0.999)

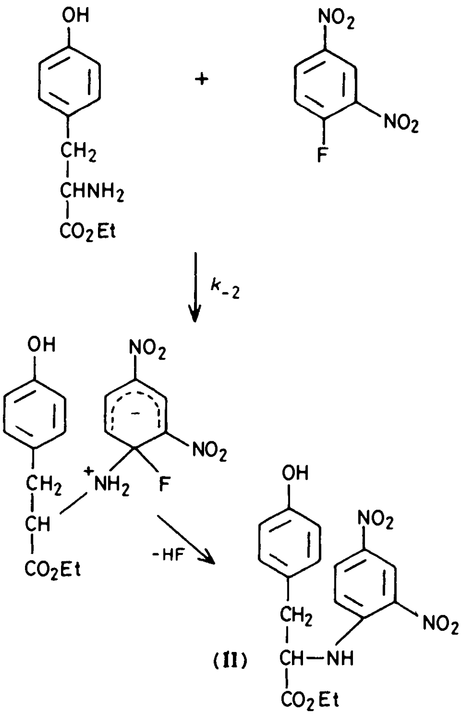
$$\Delta H^{\ddagger} = 0.5357E + 4.080 \tag{27}$$
r 0.906; s 4.16 (confidence level 0.99)

$$\Delta H^{\ddagger} = 0.6481E - 207.5\mathrm{f}(\varepsilon) + 101.7 \tag{28}$$
r = 0.989; s 0.763 (confidence level 0.999)

$$\log k_2 = 94.37\mathrm{f}(\varepsilon) - 0.0902\,8E - 44.33 \tag{29}$$
r 0.956 (details in ref. 8)

Thus in some cases the correlation of a reaction rate with an empirical solvent parameter can be extended to the correlation of the governing activation parameters ($\Delta S^{\ddagger}$ or $\Delta H^{\ddagger}$) with the corresponding emperical solvent parameters.

Mechanism.—The reaction in DMSO, DMF, dioxane, MeOH, PC, Pr^{i}OH, EtOH, DCE, and benzene shows second-order kinetics, first order in DNFB and first order in (**I**). So the mechanism (Scheme 3) in most solvents is the same. Only in An and EtOAc do the k_2 values depend somewhat on the concentration of (**I**), and the mechanism shows some complexity. In EtOAc it may be base-catalysed (Scheme 1). But in An, as the ratio k''/k' is low (see relevant equations earlier and in Table 1), according to the views of Ayediran and Bunnett[9] it cannot be simply ascribed to a true base-catalysed mechanism. The formation of the activated complex may still be the rate-determining step. According to Scheme 3, there is charge separation in the transition state; the negative charge is delocalized over the dinitropentadienide system and shielded by the two nitro groups. On the other hand the positive charge is localized on the nitrogen atom and is exposed to solvent molecules. Therefore the solvation depends strongly on the nucleophilic solvation capability of the solvents, *i.e.* on the



Scheme 3.

HBA, EPD ability (Lewis basicity), for which the parameters B, B', or DN are the preferred measures. {The marginal significance of E with a negative coefficient [equation (7)] may indicate that electrophilic solvation stabilises the reactant amine relative to the transition state.} The orientation of reactant and solvent molecules in the transition state causes a great decrease in both entropy and energy. In the solvents of high Lewis basicity, owing to the 'freezing' of solvent molecules in the initial state, the loss of entropy decreases, and the rate increases.

Experimental

Materials.—Solvents. All solvents, originally CA or CP grade, were treated according to the procedures described by Riddick and Bunger.[10] The fractions with refractive index value identical with those in the literature were collected and stored.

Reactants. DNFB supplied by the Shanghai Biochemical Institute was biologically pure; it was pure enough for use directly without further treatment. The ethyl ester of tyrosine (**I**) was prepared from tyrosine (CP grade) and $SOCl_2$ and K_2CO_3 according to the methods described by Boissonas *et al.*[11] and Fisch,[12] m.p. 105—106 °C (lit.,[12] 108—109 °C). Its i.r. spectrum was identical with the corresponding one in SADTLER.[13]

N-(2,4-*Dinitrophenyl)tyrosine ethyl ester* (**II**) was prepared from DNFB and (**I**) in ethyl acetate in the mole ratio of 1 : 2. The mixture was finally washed with dilute acid, then with dilute aqueous sodium carbonate, and then with water. The product was repeatedly recrystallized in ether and light petroleum. Yellow-orange needle crystals were finally obtained. The product was tested with ninhydrin; the negative result proved that the primary amine had reacted completely, m.p. 124—125 °C (Found: C, 54.0; H, 4.5; N, 10.9. $C_{17}H_{17}N_3O_7$ requires C, 54.4; H, 4.6; N, 11.2%).

The Beer-Lambert Law.—The u.v.-visible spectra of reactants DNFB and (**I**), and product (**II**), were taken with Pye–Unicam 1700 and Shimadzu UV-300 instruments. The $\lambda_{max.}$ values were somewhat solvent-dependent. For DNFB and (**I**) $\lambda_{max.}$ was 250—290 nm. For (**II**) $\lambda_{max.}$ was 354 nm in DMSO, DMF, and PC and 346 nm in the remaining solvents. The Beer's law behaviour was also studied in these solvents. The optical density obeys Beer's law with values of the molar extinction coefficient ε between 1.4×10^4 and 1.7×10^4.

Kinetic Measurements.—Kinetic determinations were carried out with a Pye–Unicam 1700 or a 751-G spectrophotometer, both equipped with a thermostatted cell holder.

The 10 mm quartz cell was placed in the thermostatted cell compartment. Pure solvents were used as the reference solvents. The temperature was controlled at 20.0 ± 0.1, 25.0 ± 0.1, 30.0 ± 0.1, or 35.0 ± 0.1 °C.

The initial concentration of (**I**) was *ca.* 10^{-2} mol l^{-1} and that of DNFB was *ca.* 10^{-4}—10^{-5} mol l^{-1}. In most of the solvents more than three different initial concentrations of (**I**) were used. In EtOH and DCE the reaction was carried out with two greatly different initial concentrations of (**I**). In all cases a large excess of (**I**) over DNFB was used.

The optical density E was determined at recorded times after mixing, usually at 1 min intervals. For the moderately rapid reactions in DMSO and DMF, the intervals were 20—30 s. For the lower rate in DCE the intervals were *ca.* 8 min or more, and in benzene about one day. The determination for each run commonly continued for more than 12 min, and for several hours or days in DCE and benzene respectively. The reaction solution was preserved and after at least ten half-lives, the E_∞ was determined. The E_∞ value usually agreed with the theoretical value.

The reaction showed first-order behaviour in DNFB and the apparent first-order rate constant k_{obs} was calculated by the least-squares method using the equation $k_{obs}t = -\ln(E_\infty - E_t) + \ln E_\infty$ where E_∞ and E_t are the extinctions measured at times t and ∞, respectively. Excellent first-order plots were obtained. The k_{obs} values are linearly correlated with the concentrations of (**I**); this indicates that the reaction is second-order overall. The values of k_2 were obtained according to the simple rate law $k_{obs} = k_2$ [(**I**)].

In An and EtOAc the k_2 values are somewhat dependent on the initial concentrations of (**I**), as already mentioned above in Results and Discussion and in Table 1.

For all the k_{obs} values determined, the correlation coefficient r is: $0.996 \leqslant r \leqslant 1.000$. For each initial concentration of (**I**), the kinetic runs were performed twice; the reproducibility of k_2 is within 2.5%. The average values k_{obs} and k_2 were taken respectively.

The activation parameters were calculated with correlation coefficient r: $0.983 \leqslant r \leqslant 1.000$.

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