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Salt Effects on the Racemization of Biphenyls

III.* The Effect of a 4′-Nitro Group on the Racemization of (−)-6-Nitro-2,2′-dicarboxybiphenyl Dianion in Aqueous Solution

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The determination of activation parameters for the inversion of (−)-6-nitro- and (−)-6,4′-dinitro-2,2′-dicarboxybiphenyl dianions in aqueous solutions from rate constants obtained by extrapolation to infinite dilution on plots of rate constant *vs.* concentration demonstrates that the effect of the 4′-nitro group is entirely on the enthalpy of activation term rather than the entropy term as previously supposed.

Substituent effects on the rate of racemization of biphenyls were extensively investigated by Adams and his students[1] about 35 years ago. As a part of their comprehensive study, a series of optically active biphenyls derived from 2-nitro-6-carboxy-2′-methoxybiphenyl (I) by substitution in the 3′, 4′, or 5′ position was prepared, and racemization half-times were determined at about 25°C in ethanol or acetone solution. It was found that substituents in the 3′ or 5′ position had a retarding effect on the rate of racemization, which was much larger for a 3′ substituent than for the same substituent in the 5′ position. The qualitative explanation of these data—the so-called "buttressing effect"— is based on the simple fact that atoms or groups make spatial demands on their environment, and thus for example the 3′ substituents raise the energy of activation for configurational inversion by inhibiting the bending of the methoxyl group out of the way in the transition state.

The effect of a 4′ substituent may be either to accelerate or retard the reaction,[1] usually by a relatively small amount (a factor of about 4 at the most). A notable exception is the 4′-nitro group, which decreases the rate of racemization by almost a factor of ten. These effects have yet to receive a

* For Part II, see Ref. 7.

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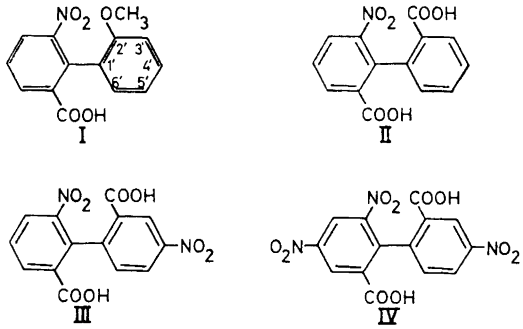
satisfactory rationalization. The influence of the nitro substituent in particular has often been commented upon,[1–4] and has even found its way into at least one introductory organic chemistry textbook.[5]

The present work may be considered an application of conclusions derived from our previous studies of salt effects on the racemization of biphenyls [6,7] to the specific problem of the 4′-nitro group effect, and while we do not claim to have solved the problem, our results unambiguously show that it is a change in *enthalpy* rather than entropy of activation which is responsible for the observed change in rate. We have chosen 6-nitro- and 6,4′-dinitro-2,2′-dicarboxybiphenyl (II and III) for this study in view of our previous work [7] on the former, and the work of Brooks, Harris and Howlett [4] on II and III as well as the corresponding 4,6,4′-trinitro compound (IV).



RESULTS AND DISCUSSION

Rate data for the racemization of II and III were determined at four to ten different concentrations of the corresponding dipotassium salts in aqueous solutions. Plots of the observed rates *vs.* concentration (15 mM or less) at a given temperature gave reasonable straight lines (*cf.* Ref. 7). A least-squares treatment of these data, bearing in mind that the rate of *inversion* is half of the rate of racemization, led to values for k_0, the extrapolated rate constant for configurational inversion in a thermodynamically well-defined system, the infinitely dilute solution. Values of k_0 for II and III at various temperatures are presented in Table 1. The activation parameters for inversion in the same table were obtained from a least-squares treatment of a linear plot of $\ln(k_0/T)$ *vs.* $1/T$ according to the Eyring equation [8] in the form

$$\ln(k_0/T) = -\Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R + \ln(k/h)$$

with the transmission coefficient assumed to be unity.

Also included in Table 1 are $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values for inversion calculated from the data of Brooks, Harris and Howlett,[4] which were obtained in 2 N sodium carbonate solution.

Our interest in determining activation parameters in the absence of salt effects is clearly justified by a comparison of the two sets of parameters for

Table 1. Kinetic data and activation parameters for the inversion of 6-nitro- and 6,4′-dinitro-2,2′-dicarboxybiphenyl dianion in aqueous solution.[a]

Compound	Temp., °K	$10^5 k_0$, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, e.u.
6-Nitro-2,2′-dicarboxybiphenyl (II)	310.1	0.302 ± 0.001		
	323.8	1.44 ± 0.01		
	332.3	3.48 ± 0.04		
	342.0	9.17 ± 0.05	22.1 ± 0.1	−12.7 ± 0.4
	351.9	23.3 ± 0.8	(21.9 ± 0.2)[b]	(−13.8 ± 0.6)[b]
	356.2	35.9 ± 0.2		
	363.2	68.3_5 ± 0.10		
6,4′-Dinitro-2,2′-dicarboxybiphenyl (III)	323.8	0.430 ± 0.005		
	332.3	1.08 ± 0.02		
	342.0	3.00 ± 0.03	22.90 ± 0.06	−12.7 ± 0.2
	351.9	7.79 ± 0.05	(22.0 ± 0.4)[b]	(−15.8 ± 1.3)[b]
	361.9	20.3 ± 0.3		

[a] The limits of error in this table are standard deviations obtained from least-squares treatment of the corresponding data.
[b] The values in parentheses were calculated from the data in Ref. 4, determined in 2 N Na_2CO_3 solution.

II and III in Table 1. From the results of Brooks *et al.*[4] one might be tempted to conclude that the effect of the 4′-nitro group lies in the entropy term and could thus, for example, be interpreted in terms of solvation effects. Our results reveal that the nitro group actually exerts its effect on the rate *via* the enthalpy of activation, and the explanation of the effect is therefore more likely to be found in changes in the internal energy of the molecule due to the electronic nature of the substituent.

Attempts to include 4,6,4′-trinitro-2,2′-dicarboxybiphenyl (IV) in the present work were unsuccessful due to darkening of the test solutions of the dipotassium salt. Under conditions corresponding to those of Brooks *et al.*[4] (0.100 g acid/20 ml 2 N Na_2CO_3 solution in a 20 cm tube at 94°C *), it was possible to follow the reaction for at least 60 min before the darkening of the solution seriously interfered with the polarimetric measurements. After this time, the per cent absorption in the visible region had risen to about 70 % at 546 nm, which was found to be the most suitable wavelength of those available for polarimetry. At higher wavelengths (578, 589 nm) the initial rotation was too low for our purposes in the necessary concentration range. At lower wavelengths (365, 436 nm), the per cent absorption was already of the order of 90 % or greater at "zero time" in the solution of the dipotassium salt of IV. In our solutions (*i.e.* no excess of base) it was impossible to obtain reliable data at 546 nm after only about 15 min. Since the half-life of the reaction is *ca.* 60 min at 94°C in 2 N sodium carbonate solution,[4] we con-

* J. W. Brooks, Ph.D. Thesis, London University, 1959. These data were kindly supplied by Dr. M. M. Harris in a private communication to P.B.

sidered it imperative to be able to accurately follow the change in rotation for at least 30 min, and we were thus forced to abandon our study of this compound.

EXPERIMENTAL

Melting points were determined on a Kofler Hot-Stage Microscope or a Kofler Heizbank.

6-Nitro-2,2'-dicarboxybiphenyl [9] was prepared and its resolution accomplished as previously described.[7,10]

2,5-Dinitrophenanthrenequinone was synthesized from 4-nitrophenanthrenequinone as described by Kato and co-workers [11] except that the mixing of the reactants was performed at about 10°C, and afterwards the temperature was not allowed to rise above room temperature. When all of the 4-nitrophenanthrenequinone had dissolved, the reaction mixture was allowed to stand for 0.5 h before it was poured on to ice. The precipitate was recrystallized from glacial acetic acid to yield 2,5-dinitrophenanthrenequinone with m.p. 228°C; lit.[11] m.p. 228.2–228.7°C.

6,4'-Dinitro-2,2'-dicarboxybiphenyl (III) and its resolution. 2,5-Dinitrophenanthrenequinone was oxidized by the method of Schmidt and Austin [9] and the product was recrystallized from the minimum amount of C_2H_5OH/H_2O 1:1. M.p. 308°C (d); lit.[9] m.p. 303°C (d).

The acid was resolved with quinine in abs. ethanol according to the procedure of Christie *et al.*,[12] but the hydrolysis of the quinine salt was carried out with 2 N K_2CO_3. The quinine was filtered off and the optically active acid was precipitated from the filtrate by acidification with dilute aq. HCl. This was repeated twice to ensure complete separation of quinine and III. The acid obtained in this way had $[\alpha]_{4360}^{50.6} = -736°$ ($c = 0.995$ g/100 ml, $l = 1$ dm, H_2O).

2,4,7-Trinitrophenanthrenequinone was prepared by nitration of 2-nitrophenanthrenequinone. The latter compound (5 g) was dissolved in conc. H_2SO_4 (30 ml), and a mixture of equal amounts (25 g) of fuming HNO_3 and conc. H_2SO_4 was added with stirring and cooling. The yield was considerably decreased if the temperature was not maintained below 5°C during the mixing process. The mixture was then heated at 65°C for 18 h, whereupon it was poured onto ice (150 g) and the resulting precipitate was filtered off, dried and recrystallized from benzene (300 ml). The product (4.5 g) had m.p. 209–210°C; lit.[11] m.p. 212–213°C.

4,6,4'-Trinitro-2,2'-dicarboxybiphenyl (IV) was obtained by oxidation of 2,4,7-trinitrophenanthrenequinone by the method of Schmidt and Austin,[9] and the product was recrystallized from H_2O/C_2H_5OH 6:1. M.p. 292–294°C; lit.[11] m.p. 290–291°C.

Test solutions. All kinetic runs were made on the dipotassium salt of the appropriate acid, obtained by adding two equivalents of a KOH solution per mole of acid. After the acid had dissolved the volume was increased to 5.25 ml with deionized water. The KOH used was *pro analysi* quality, and the water had been deionized by passage through a Zerolit deionizer.

The kinetics of the racemization were determined on a Perkin-Elmer 141 polarimeter (*cf.* Ref. 7). The magnitude of the standard error in the observed racemization rate constant (k_{obs}), obtained by least-squares treatment of the polarimetric data on an Olivetti Programma 101 desk computer, was always less than 0.3 % of the value of k_{obs}. The reproducibility of a given k_{obs} value was of the order of ±1 %. In control runs for each batch of optically active material, in which the racemization was followed to completion, no residual rotation was observed.

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