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DIRECT NUCLEOPHILIC SUBSTITUTION IN HOMOLOGOUS SERIES. TRANSMISSION OF POLAR EFFECTS ALONG A HYDROCARBON CHAIN

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IN direct nucleophilic substitution reactions at the saturated carbon atom in homologous series $[R(CH_2)_{\underline{n}}X + Y^-]$, an alternation of rates has long been noticed with increasing the length of the hydrocarbon chain. For instance, the effect is observed for direct substitutions (chlorine for iodine) in series such as $Ph(CH_2)_{\underline{n}}X$ and $PhCO(CH_2)_{\underline{n}}X$ and others, where the rate is invariably found to be a maximum for $\underline{n} = 1$, to decrease for $\underline{n} = 2$ and again increase for $\underline{n} = 3$. Where available, e.g. in the $Ph(CH_2)_{\underline{n}}X$ series, the data seem to indicate a zigzagging of rates up to the highest members ($\underline{n} = 7$). In discussing such an effect, Eliel[1] refers to a hypothesis[2] according to which the increased rate for the $PhCO(CH_2)_{\underline{n}}X$ series, and the alternation of rates, could be ascribed to a cyclic transition state of

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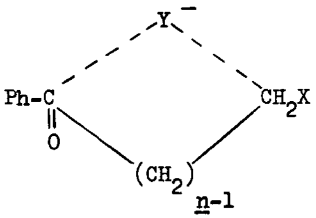
[1] E.L. Eliel, Steric Effects in Organic Chemistry (Edited by M.S. Newman) pp. 138-140. John Wiley, New York (1956); to which the reader should refer for a summary of data.

[2] E.N. Trachtenberg, Thesis; Harvard University (1952).

type



whose stability would depend on n in relation to the size of the ring formed.[3] Eliel suggests also that a similar explanation may apply to the series $Ph(CH_2)_nX$. The hypothesis is equivalent to assuming some kind of electrophilic assistance by the phenyl ring to the entering (and leaving) group. This is analogous formally at least, to the nucleophilic assistance provided by phenyl groups in solvolysis of ω-phenyl-1-alkyl-benzenesulfonates (anchimeric assistance), for which a definite dependence on n has been recently established.[4]

A way to check the validity of this hypothesis is offered by the study of the kinetic substituent effect. Let us consider, for instance, the series $Ph(CH_2)_nX$ and the rate effects consequent to substitution, say in the 4-position of the phenyl ring, as measured by the reaction constant (ρ of the Hammett equation). If in the transition state there is no assistance by the phenyl group, the substituent effect will simply arise from an inductive effect transmitted along the hydrocarbon chain; the outcome would be a steady decrease of ρ with increasing n (without prejudice of the sign

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[3] Actually, convincing evidence has been provided [P.D. Bartlett and E.N. Trachtenberg, J. Amer. Chem. Soc. **80**, 5808 (1958)] that the enhanced S_N2 reactivity of phenacyl compounds (i.e. $n = 1$) can be accounted for by a transition state of this kind.

[4] R. Heck, and S. Winstein, J. Amer. Chem. Soc. **79**, 3105 (1957); E.J. Corey and C.K. Sauers, Ibid. **79**, 248 (1957).

of ρ). If, however, there is phenyl group participation at the transition state, the overall substituent effect would arise from the superimposition, onto the inductive effect transmitted along the chain, of a field effect acting directly at the center of reaction. The latter effect would by-pass the hydrocarbon chain and operate at all n values, its magnitude being determined by the steric requirements of the cyclic transition state. Actually, if this effect were to predominate (i.e. in the case of large phenyl group participation), while ρ should be positive, a parallelism between rate and substituent effect should also be observed.

Data are presented here showing that in the phenylalkyl series the cyclic transition state hypothesis in unlikely. The data concern the rates of substitution (iodine for radioiodine) in the series $Ph(CH_2)_nI$ and its corresponding $4\text{-}NO_2$ substituted series (n 1 to 5). The relevant results are summarized in Table 1.

It is observed that ρ decreases monotonically from n = 1 to n = 5 without showing any tendency to parallel the rate trend. This indicates that the extent of phenyl group participation, if any, must be very small, since it is insufficient to invert the trend imposed by the weakening inductive effect.

A stronger argument[5] against the cyclic transition state hypothesis is offered, however, by the consideration of $\Delta\rho/\Delta_n$ (last column in Table 1): It is observed that, while ρ decreases only slightly from n = 1 to n = 2, the largest drop occurs for n = 3. This is exactly opposite to what should obtain, were the alternation of rate due to a phenyl group participation which is at a minimum for n = 2 and at a maximum for n = 3. The conclusion

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[5] This has been suggested by a referee, whose contribution is gratefully acknowledged.

TABLE 1.

Relative rates of substitution (R-I + $Na^{131}I$) in acetone at 25° [a]

$\underline{n}$	$C_6H_5(CH_2)_{\underline{n}}I$	$\underline{p}$-$NO_2C_6H_4(CH_2)_{\underline{n}}I$	$\underline{k}_{NO_2}/\underline{k}_H$	$\rho^{\underline{b}}$	$\Delta\rho$
	$\underline{k}_{\underline{n}}/\underline{k}_2$	$\underline{k}_{\underline{n}}/\underline{k}_2$			
1	484	658	4.73	0.87	0.17
2	1.00	1.00	3.49	0.70	0.36
3	2.46	1.28	1.82	0.34	0.07
4	1.90	0.89	1.64	0.27	0.10
5	2.06	0.80	1.37	0.17	

[a] Second-order rate coefficient for $Ph(CH_2)_2I$:

$\underline{k} = (2.45 \pm 0.06) \times 10^{-2}\ sec^{-1}\ l.\ mole^{-1}$

[b] $\rho = \dfrac{\log \underline{k}_{NO_2}/\underline{k}_H}{\sigma_{\underline{p}}\text{-}NO_2}$, $\sigma_{\underline{p}}\text{-}NO_2 = 0.778$

is that, in the phenylalkyl series, the hypothesis of a cyclic transition state does not apply.

As to an alternative explanation of the so-called alternation effect, while it is doubtful that such an effect really exists for the higher members of homologous series, the observed rate sequence could arise, for the first members, from a combination of inductive and steric hindrance effects: While the rate-enhancing inductive effect of the ω-phenyl group progressively weakens with increasing $\underline{n}$, steric hindrance goes through a maximum for $\underline{n} = 2$, i.e. when the bulky phenyl group is β to the seat of substitution.[6] For

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[6] P. Beltrame, L. Oleari and M. Simonetta, Gazz.Chim.Ital. **89**, 2039 (1959).

n = 3. steric hindrance might be reduced to the point that, in spite of the diminished inductive effect, an over-all rate increase obtains.