Effect of 4-t-Butyl and Other 4-Substituents on the Rate Constants for Nucleophilic Displacement with Thiophenate Anion in Diethylene Glycol at the Benzyl Methylene Groups in 1-Benzylpiperidine Benzobromides

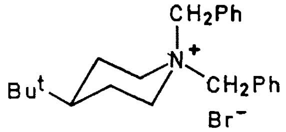
By P. G. Leviston, J. McKenna,* J. M. McKenna, R. A. Melia, and J. C. Pratt

(*Chemistry Department, The University, Sheffield,* S3 7HF)

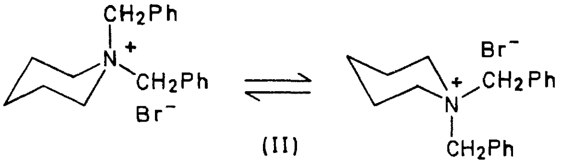
Summary A 4-t-butyl group approximately doubles the overall rate constant for nucleophilic displacement with thiophenate anion at the benzyl methylene groups in 1-benzylpiperidine benzobromides.

In the kinetic method[1] for conformational analysis of monosubstituted cyclohexanes, a 4-t-butyl group is supposed to have no effect on the reactivity of a 1-substituent, so the *cis*- and *trans*-4-t-butyl derivatives are taken as models for the axial and equatorial conformers respectively of the conformationally mobile monosubstituted cyclohexane. There have been criticisms[2] of this method, but rate constants for the individual conformers of the monosubstituted cyclohexane cannot of course be measured separately to permit direct comparison with rate constants for the 4-t-butyl analogues. However, such a direct comparison can be made for cyclohexanes carrying identical geminal 1-substituents, or (as we report here) for the stereochemically analogous but more readily accessible quaternary piperidinium salts.

If the 4-t-butyl group in the salt (I) has no effect on the rate of nucleophilic attack by thiophenate anion at the axial and equatorial benzyl methylene groups, then the overall rate constant for (I) should be the same as that for the 4-unsubstituted salt (II) under the same reaction conditions. The results summarised in the Table indicate just how unsatisfactory is this supposition. Results for the 4-methyl and 4-phenyl salts are given for comparison; it is of interest that both 4-alkyl and 4-phenyl groups increase the rate of reaction, so that in each case the effect may arise mainly from steric rather than from polar factors.



(I)



(II)

Relative rate constants[a] *for decomposition of* ^{14}C-*labelled* N-*benzylpiperidine benzobromides with sodium thiophenate at* 60·5°

4-Substituents in 1-benzylpiperidine benzobromides	Conditions[b] (A)	(B)	(C)
H	1·00[c]	1·00[d]	1·00
Me	1·40	1·30	1·20
Bu^t	2·40	2·15	1·85
Ph	3·15	2·80	3·00

[a] Reaction followed by radioactivity of toluene extracts containing products (*N*-benzyl-base + phenyl benzyl sulphide). Ratios precise to *ca.* ±5%.

[b] (A): Twelve-fold excess of 0·15M-sodium thiophenate in diethylene glycol containing 0·5% water, saturated with toluene (4 ml glycol solution shaken with 10 ml toluene before reaction). ^{14}C-label in benzyl methylene groups; no observed non-linearity in first-order plots from kinetic-isotope effects.

(B): As (A) without saturation of diethylene glycol solution with toluene before reaction.

(C): As (B) except that the diethylene glycol contained 1·0% water, and the 4-H- and 4-Bu^t-salts were labelled with ^{14}C in the benzene rings.

[c] 6·40 relative to reaction under conditions (C).

[d] 2·70 relative to reaction under conditions (C). $k_{\text{uni}} = 1{\cdot}84 \times 10^{-5}$ sec.$^{-1}$.

(*Received, April 6th,* 1970; *Com.* 476.)

---

[1] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, 1965, pp. 47—50.

[2] *e.g.* H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, 1964, **86**, 1161; J. L. Mateos, C. Perez, and H. Kwart, *Chem. Comm.*, 1967, 125; *cf.* ref. 1, p. 188.