Relative Rates of Ethoxy Exchange in 4-Substituted Diethylcyclohexane-1,1-dicarboxylates. Validation of the Use of 4-t-Butyl Derivatives as Reactivity Models in the Kinetic Method of Conformational Analysis of Cyclohexanes

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Summary A 4-t-butyl group has no effect on the observed rate of ethoxy exchange in diethylcyclohexane-1,1-dicarboxylates, a significant result in relation to the validity of the usual kinetic method for conformational analysis of cyclohexanes.

THE *cis-* and *trans*-4-t-butyl derivatives (I) have been employed as reactivity models for the conformers (II) in the standard kinetic method of conformational analysis of cyclohexanes, although objections[1] have sometimes been raised to the underlying assumptions. Since one cannot directly measure rate constants for both individual conformers (IIa; IIb) under normal experimental conditions, for comparison with rate constants for the 4-t-butyl analogues (Ia; Ib) we compared the reactivities of some 4-substituted cyclohexane 1,1-dicarboxylic esters (III; R = H, Me, Bu^t, Ph) in the alkoxy exchange process. The esters were uniformly labelled with ^{14}C in both ethoxy groups and the initial rates of loss of ^{14}C from each ester were measured at 9° in excess of 0·091M ethanolic sodium ethoxide; this procedure avoided difficulties associated with the competitive and consecutive nature of the reactions at *eq-* and *ax*-CO_2Et when R $\neq$ H resulting in the impossibility of accurately measuring rate-constants.

Within the attainable precision limits ($\sigma \sim 5\%$) it was not possible to distinguish the initial rates for the 4-H, 4-Me, and 4-Bu^t esters, but that for the 4-Ph ester was 1·6 times greater, presumably as a result of polar influences. These results provide the most direct evidence so far available on the validity of the kinetic method, and confirm the conclusion previously reached indirectly by other workers.[2] We cannot exclude the possibility that a 4-Bu^t (or 4-Me) group affects exchange rates at *ax-* and *eq*-1-CO_2Et

groups to the same extent but in opposite directions, but this seems remote.

Bonding at the 1-carbon atom is not disturbed during the exchange; our earlier work[3] on displacement reactions with 4-substituted 1-benzylpiperidine benzobromides (IV; R = H, Me, Bu^t, Ph) and sodium thiophenate indicates that here a 4-t-butyl group does seriously (2-fold) influence reactivity, and in this case bonding to the ring (nitrogen) atom is disturbed during the reaction. The kinetic method of conformational analysis of cyclohexanes has been recognised[1b,2b] to be of more questionable applicability when bonding to the 1-position of the ring is altered, and our results bear out this prediction.

(Ia)   (Ib)

(IIa) ⇌ (IIb)

(III)   (IV)
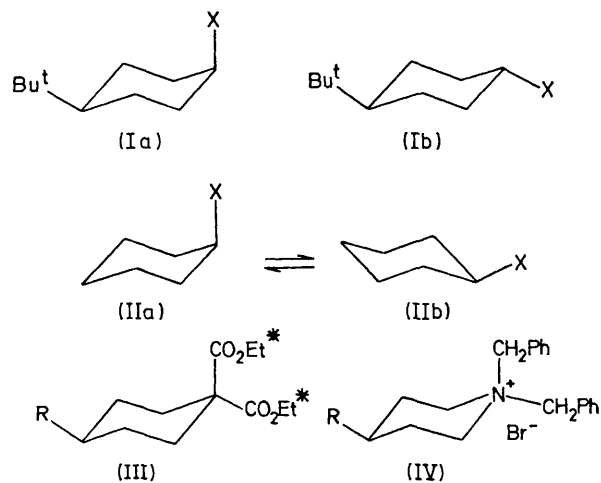
It could be suggested that the use of geminal substitution to check for kinetically significant perturbations of the reaction surface associated with introduction of a 4-Bu^t group, itself introduces an additional perturbation. However, this additional perturbation is applied equally to the conformationally mobile system and the 4-Bu^t models, whereas the initial perturbation is applied only to the models.

[1] *E.g.* (a) H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, 1964, **86**, 1161; (b) J. L. Mateos, C. Perez, and H. Kwart, *Chem. Comm.*, 1967, 125.

[2] *Cf.* (a) E. L. Eliel and F. J. Biros, *J. Amer. Chem. Soc.*, 1966, **88**, 3334; (b) E. L. Eliel, *Pure Appl. Chem.*, 1971, *Special Supplement* **7**, 219.

[3] P. G. Leviston, J. McKenna, J. M. McKenna, R. A. Melia, and J. C. Pratt, *Chem. Comm.*, 1970, 587.