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A METHOD FOR EXPLORING THE DIPOLAR CHARACTER OF TRANSITION STATES. A GENERAL DIRECTING EFFECT OF POLAR SUBSTITUENTS IN OLEFIN ADDITION REACTIONS

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THE study of the direction of addition of reagents to unsymmetrically substituted open chain olefins has a long history, but until recently,[1] very much less information has been available concerning the effects of substituents on the direction of addition of reagents to cyclic olefinic bonds in a plane perpendicular to the initial double bond. Cyclopentenes, substituted at C_4 (*cf.* I), provide some of the simplest compounds for the evaluation of such perpendicular directing effects,[1] addition occurring either *cis* or *trans* to the potentially directing substituent. 4-Cyanocyclopentenes (I; R = H and Me) have been prepared; their reactions with peracid and with acetyl hypobromite show that the substituent at C_4 can strongly influence the direction of addition to the olefinic bond. In order to find out if a nitrile group would exert an effect across two or more saturated rings, related tricyclic (III) and bicyclic (II; R = H and Me) compounds

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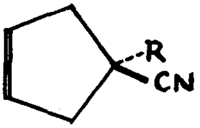
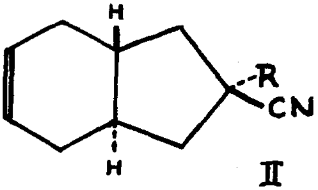
[1] Summary of recent work given by H.B. Henbest, B. Nicholls, W.R. Jackson, R.A.L. Wilson, N.S. Crossley, M.B. Meyers and R.S. McElhinney, *Bull.Soc.Chim.Fr.* 1365 (1960).

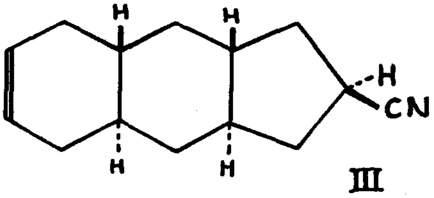
have been synthesized. These molecules are flat in general shape due to the trans fusion of rings and, as with the monocyclic compounds (I), differences from a 50:50 cis:trans ratio of products provide a measure of the directing effect of the polar substituent.



I



II



III

The olefin-peracid reaction is a simple addition in that the simultaneous or subsequent attack of a nucleophilic species upon the reacting carbon-carbon bond is not involved. The reaction can be carried out in a wide variety of solvents and, kinetically, is first order in olefin and in peracid. A spiro, chelated structure has been plausibly proposed[2] for the transition state, but for the moment, the simplified expression, $(\delta+)$ olefin -- $O \cdot O(H)COR$ $(\delta-)$, will be used; substituent effects show that the reacting carbon-carbon bond becomes electron deficient during the reaction.[2]

Good yields (85-95%) of epoxide mixtures were obtained from reactions of the olefinic nitriles (I, II, III) with pure perlauric acid in cyclo-

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[2] Lynch and Pausacker, J.Chem.Soc. 1525 (1955); references to earlier work are given in this paper.

pentane and in acetonitrile (chosen to represent non-polar and polar solvents respectively). Analysis (gas chromatography for the mono- and bicyclic compounds, adsorption chromatography for the tricyclic compound) of each of the total reaction products gave the following *cis*:*trans* ratios of epoxy-nitriles.* Possible percentage errors in the ratios are ± 1-2% for the mono- and bi-cyclic compounds, and ± 2-3% for the tricyclic compound. The ratios were not altered by moderate changes in concentrations of reactants, and separate experiments showed that the epoxides were not isomerised under the reaction conditions. The *cis*:*trans* ratios represent therefore the relative rates of reaction of the peracid at each face of the molecule.

cis : trans *Ratios of Epoxy-nitriles from Reactions of Unsaturated Nitriles with Perlauric Acid at 20°*

	Reaction in cyclopentane	Reaction in acetonitrile
	cis:*trans* ratio	*cis*:*trans* ratio
Hydrogen series (R = H		
I	5:95	24:76
II	31:69	46:54
III	43:57	53:47
Methyl series (R = Me)		
I	13:87	48:52
II	28:72	45:55

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* The individual *cis*- and *trans*-epoxy-nitriles have been isolated, each being a crystalline compound with the exception of (±)-4β-cyano-1α, 2α-epoxy-4α-methylcyclopentane. Configurations are assigned from dipole moment values and other evidence. [The product from the bicyclic nitrile (II; R = H), previously thought (H.B. Henbest and B.Nicholls, *Proc.Chem.Soc.* 225 (1958)) to be the *cis*-compound, has been shown to be a mixture of both isomers, the dipole moments of the pure *cis*- and *trans*- compounds being 4.78 D. and 2.49 D. respectively. We thank Dr. L.E. Sutton and Mr. G.M. Glover (Oxford) for these measurements.]

In all but one case, the tricyclic nitrile in acetonitrile, the reactions gave predominantly _trans_-epoxy-nitriles. Two main trends can be seen in the results from the hydrogen series of compounds (I, II, III; R = H): the proportion of _trans_-epoxy-nitrile decreases (a) as the distance between the substituent and the reaction centre is made greater, and (b) when the solvent is changed from cyclopentane to acetonitrile. These facts are consistent with an intramolecular polar directing effect of the nitrile group, the relative sizes of the dipole-dipole interactions between the polar substituent and the polar transition states for _cis_- and _trans_-attack favouring the latter reaction (cf. IV). Such an electrostatic effect would diminish with distance and be diminished by the presence of surrounding polar acetonitrile solvent molecules. These arguments are supported by results from the reaction of perlauric acid with the bicyclic chloride (II; R = H; CN replaced by Cl). The experimental ratios, 33:67 in cyclopentane and 50:50 in acetonitrile, show that the chloride has a weaker directing effect than cyanide, in accord with the relative magnitudes of the dipole moments of these groups (C-Cl, 2.04 D.; C-CN, 3.61 D., when attached to secondary carbon).

An alternative reason for the prevalent _trans_-attack might be steric hindrance imposed by the substituent on the _cis_-reactions; but on this basis the solvent effect would be difficult to explain. However, replacement of hydrogen by methyl in the bicyclic series (II; R = Me) led to an _increase_ in the amount of reaction _trans_ to the nitrile (_cis_ therefore to the methyl group). This result can hardly be explained on steric grounds, but it does fit the dipole-dipole interaction theory, as the methyl group, by its inductive effect, increases the effective dipole of the directing group;*

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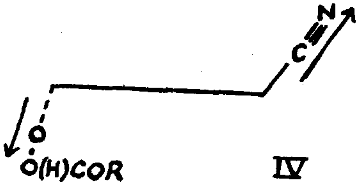
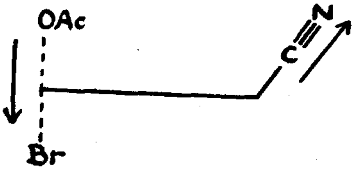
* The dipole moments of acetonitrile, propionitrile and isobutyronitrile are, for solutions in benzene, 3.48, 3.57 and 3.61 D.

significantly also, the increase in the proportion of *trans*-product caused by the methyl group is greater in cyclopentane than in acetonitrile.



IV

Preferred transition state for olefin-peracid reaction



V

Preferred transition state for olefin-acetyl hypobromite reaction

In contrast, introduction of a 4-methyl group into 4-cyanocyclopentene causes a *decrease* in the proportion of attack *trans* to the nitrile group, showing that the alkyl group does exert a steric effect when it is closer to the reaction centre. Nevertheless, the polar directing effect of the 4-cyano-group (augmented by the electron donating effect of the methyl group) outweighs the steric effect of the methyl group in the epoxidation of compound (I; R = Me), especially in the non-polar solvent, cyclopentane. With the exception of these results with 4-cyano-4-methyl-cyclopentene, where the steric factor intrudes, the general *trans* directing effect of the nitrile (or chloride) group can be correlated with calculated potential energy interactions between the polar substituent and the polar transition states for *cis* and *trans* attack. The correlation will be discussed in the detailed papers on this subject.

A method thus becomes available for examining the dipolar nature of transition states of addition reactions in general. Its use in studying additions to carbonyl bonds is discussed in the following communication, but an extension to the work on the olefin-peracid reaction was provided by the addition of acyl hypohalites to the carbon-carbon double bond. Consideration of possible transition states for these additions suggested that the main products from the unsaturated nitriles should be those, that on hydrolysis and ring closure under alkaline conditions, would lead to the production of cis-epoxy-nitriles. The nitriles (I and II; R = H) were treated successively with acetyl hypobromite in carbon tetrachloride and alkali to give epoxy-nitriles of cis:trans-composition 86:14 and 64:36 respectively. If partial bonding of both acetate and bromine groups to the original olefinic centre is postulated for the transition state for the addition step, it may be concluded that the preferred transition state (V) has its dipole in the direction indicated. This is in agreement with the polar character suggested[3] for the transition state of the diaxial to diequatorial rearrangement of steroid 2,3-bromo-acetates, which as a readdition reaction, is related to the initial diaxial addition of halogen and acyloxy groups.

The directing effects encountered in additions to carbonyl bonds (following paper), and in the addition of hydroperoxide anion to 3-oxo-Δ^4-steroids,[1] can also be explained in terms of intramolecular dipole-dipole interactions during the reactions.

Other electron attracting substituents also promote trans-attack of peracid at endocyclic and exocyclic double bonds. These results, together with further discussion of solvent effects, will be presented later.

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[3] D.H.R. Barton and J.F. King, J.Chem.Soc. 4398 (1958).