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Ambident Neighbouring Groups. III. The Stereochemistry of Anchimerism by Urethane Functions

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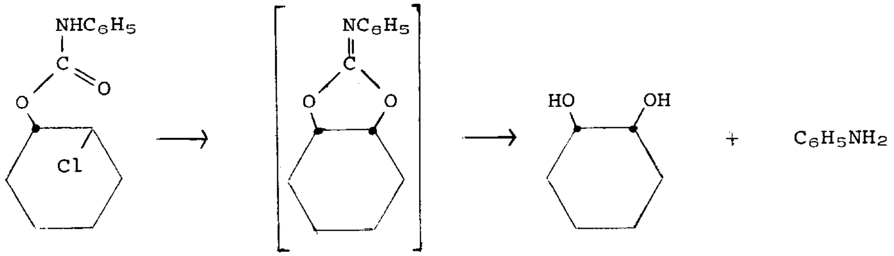
Ambident neighbouring groups have found considerable use in the introduction of adjacent functional groups stereospecifically related (2) . In the case of one such group namely the urethano group we have previously demonstrated both its anchimeric effectiveness and the conditions under which it displays its ambident character via O-5 and N^--5 reactions. We now report our results on its stereochemical control of appropriate reactions, a control which makes it an extremely efficient group for stereospecific transformations.

We examined first the stereochemistry of its O-5 closures using as substrate trans-2-N-phenylurethanocyclohexyl chloride (I). Compound (I), m.p. 94-96°, was prepared by heating a mixture of trans-2-hydroxycyclohexyl chloride and excess phenyl isocyanate (neat) at 100° for 10 minutes. Compound (I) was heated in 80% aqueous ethanol for 70 hours (10 half-lives) at 100° in a sealed ampoule and it formed cis-1,2-cyclohexane diol (II), m.p. 92-94°, in 95% yield and aniline (III), isolated as its picryl chloride derivative, m.p. 176-178°, in 88% yield (Scheme 1.). Compound (II) was unequivocally identified by mixture m.p. (and identity of i.r. spectra) with an authentic sample. That the cis-diol isolated did not contain any

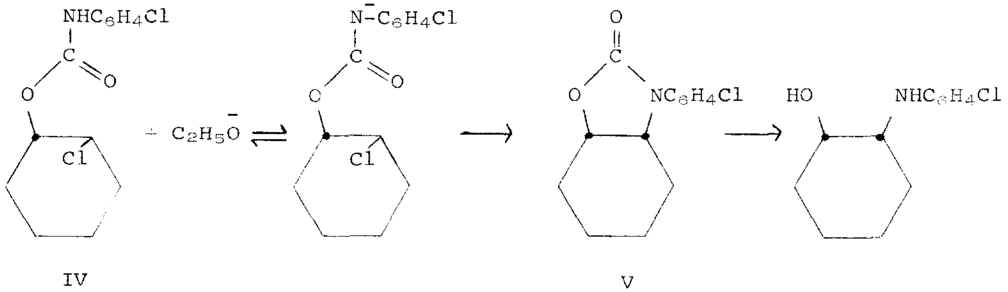


I II III

Scheme 1

appreciable quantity of *trans*-isomer we first established using the eutectic technique devised by Winstein (3) . An additional check on this was performed using v.p.c. (4). A product run was performed, 10 ml. of the mother liquor therefrom was evaporated to dryness and the residue, dissolved in a little benzene was analysed using a Pye Series 104 chromatograph (flame ionisation detector) and the support system described by Eisenbraun (4). The *cis*-diol (II) was detected in 98% yield. However some *trans* might still have been present as we were unable to detect quantities smaller than 3% of *trans*- 1,2-cyclohexane diol in an artificial mixture of the *cis*- and *trans*-diols. Within the limits obtained however the O-5 urethano closure was extremely efficient stereochemically. Inasmuch as the O-5 cyclisation of compound (I) (k, 75° = 2.7×10^{-7} $\mathrm{sec.}^{-1}$) was substantially slower than that for the corresponding open-chain compound, $C_6H_5NH\text{-}COOCH_2CH_2Cl$ (k, 75° = 1.38×10^{-5} $\mathrm{sec.}^{-1}$) , yet the O-5 reaction for (I) was so stereospecific that the O-5 reactions of open-chain urethano halides will also be highly stereospecific.

To examine the N^--5 process we choose, for work-up convenience, *trans*-2-N-*p*-chlorophenylurethanocyclohexyl chloride (IV), m.p. 75-77°, as substrate. When this compound was refluxed in ethanol with one equivalent of ethoxide ion for 1 hour, it yielded the oxazolidone (V) , m.p. 87-89° in 96% yield (Scheme 2). To indicate the efficiency of this N^--5 process even in the presence of water, an equally high yield of compound (V) was obtained when the chloride (IV) was refluxed for 1 hour in 80% aqueous ethanol containing 1.5 equivalents of sodium hydroxide. When compound (V) was refluxed with four equivalents of sodium ethoxide in ethanol it formed the *cis*- 2-N-*p*-chloroanilinocyclohexanol (VI), m.p. 110-113°, in 98% yield.



Scheme 2

For identification purposes the corresponding trans-isomer (of VI), m.p. 102-104° was made (in 46% yield) by heating p-chloroaniline with excess cyclohexene oxide (in a ratio of 1 : 16) at 100° in a sealed ampoule for seven days. The infra-red spectra of both isomers were different and they depressed (m.p. 74-81°) on mixture melting-point. An additional confirmation of the cis-nature of compound (VI) was obtained when it was reconverted to the oxazolidone (V). This was achieved (in ca. 30% yield) when compound (VI) was refluxed at 126° for 30 minutes in an excess of dibutyl carbonate in the presence of some sodium carbonate as catalyst. The cis-nature of compounds (V) and (VI) demonstrates the highly stereoselective nature of the N^{-}-5 cyclisation.

The reactions described above when compared to the studies of Baker on other thionourethane (5) and urethane systems (6) indicate a similar pattern between their systems and ours but also confirm the more efficient stereochemistry that our model systems displayed.

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REFERENCES

(1) Part II of this series, F. L. Scott and D. F. Fenton, Tetrahedron Letters 25, 1681 (1964).

(2) See, for examples, B. Capon, Quart. Revs., 18, 106 (1954) and amongst many other papers the series by B. R. Baker et al., J. Org. Chem., 30, 4038-4053 (1965).

(3) S. Winstein, J. Am. Chem. Soc., 64, 2785 (1942).

(4) E. J. Eisenbraun, A. R. Bader, J. W. Polacheck and E. Reif, J. Org. Chem. 28, 2057 (1963).

(5) L. Goodman, A. Benitez, C. D. Anderson and B. R. Baker,. J. Am. Chem. Soc., 80, 6582 (1958).

(6) B. R. Baker and H. S. Sachder, J. Org. Chem., 28, 2135 (1963).