Asymmetric Induction in the Rearrangement of Monocyclic Endoperoxides into γ-Hydroxy-αβ-unsaturated Aldehydes

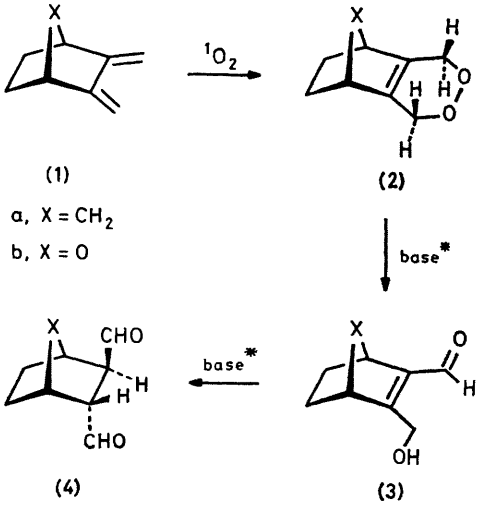
By JEAN-PIERRE HAGENBUCH and PIERRE VOGEL*

(*Institut de chimie organique de l'Université, 2 rue de la Barre, CH-1005 Lausanne, Switzerland*)

Summary The endoperoxide obtained by addition of singlet oxygen to 2,3-bis(methylene)-7-oxanorbornane is isomerised to the chiral γ-hydroxy-αβ-unsaturated aldehyde by catalytic amounts of various natural bases with an enantiomeric excess ranging up to 46%

EXAMPLES of chiral bases showing selectivity between enantiotopic protons in prochiral molecules are rare [1] Recently, Whitesell and Felman[2] reported a 31% optical yield for the isomerization of cyclohexene oxide into cyclohex-2-enol promoted by a chiral lithium amide We report on the asymmetric induction in the Kornblum-DeLaMare[3,4] rearrangement of monocyclic endoperoxides into γ-hydroxy-αβ-unsaturated aldehydes by optically active natural bases

The endoperoxides (**2a**)[5] and (**2b**) (m p 57—59 °C) were obtained by singlet-oxygen addition to 2,3-bis(methylene) norbornane (**1a**) and 2,3-bis(methylene)-7-oxanorbornane (**1b**),[6] respectively In the presence of a catalytic amount of $Rh_2(CO)_4Cl_2$, (**2a**) and (**2b**) were isomerized into (**3a**) and (**3b**) [^{1}H n m r δ ($CDCl_3$) 9·98 (s, 1 H), 5·25 and 5·01 (2d, *J* 3·5 Hz, 2 H), 4·61 (s, 2 H), 2·0—1·7 (m, 2 H), and 1·25 (m, 2 H)], respectively The *s-trans*-configuration of (**3a**) and (**3b**) was indicated by the i r spectra {ν_{OH} 3630 (narrow) and 3400—3500 cm^{-1} (broad), decreases upon dilution (more important in CCl_4 than in CH_2Cl_2), $\nu_{HC=O}$ 1665 cm^{-1} [1660—1665 cm^{-1} in the corresponding α-methoxy-α-trifluoromethyl-α-phenylacetate (MTPA)[7] derivatives]} In the presence of 0·0045 M (+)-quinidine, a 10% solution of



(**2a**) in MeCN was rearranged slowly into (−)-(**3a**) at 20 °C ($\tau_{\frac{1}{2}}$ *ca* 60 h) with an enantiomeric excess (e e) of 9%, as determined by the ^{1}H and ^{19}F n m r spectra of the MTPA derivative[7] Other natural bases such as (−)-cinchonidine and (−)-ephedrine catalysed the conversion (**2a**) → (+)-(**3a**) with a lower optical yield While (−)-noradrenaline and (−)-proline were poor catalysts, brucine induced a relatively fast isomerization (**2a**) → (+)-(**3a**) ($\tau_{\frac{1}{2}}$ *ca.* 4 h,

20 °C, 0·0045M in MeCN) with relatively good optical yields (12—29%), but poor chemical yields. This was because brucine catalysed the isomerization (**3a**) → (**4a**)[8] competitively and enantioselectively. Using (±)-(**3a**), we found, after 50% transformation, an e.e. of 16% in the remaining (+)-(**3a**) (for 100% e.e., an $[\alpha]_D^{23}$ *ca.* 135° was calculated).

In the rearrangement of (**2b**), it was envisaged that the OH group in a base such as cinchonine, cinchonidine, quinidine, or quinine could lead to better asymmetric induction because of the possibility of hydrogen bonding between the oxygen bridge of the 7-oxanorbornane and the catalyst. Indeed, while brucine (no OH group) catalysed (**2b**) → (**3b**) and (**3b**) → (**4b**) with low optical yields (< 5%), (+)-quinidine [0·0045M, 10% (**2b**) in MeCN, 20 °C, $\tau_{\frac{1}{2}}$ *ca.* 17 h] induced the rearrangement (**2b**) → (**3b**) with an e.e. of 46—47% (by ^{1}H-n.m.r. of the MTPA derivative, see the Figure) and an n.m.r. chemical yield > 95% [(**3b**) was stable in solution only; attempts to isolate it led to decomposition]. (+)-Cinchonine (0·017 M, MeCN, 20 °C, $\tau_{\frac{1}{2}}$ *ca.* 5 h) and (−)-cinchonidine (0·017 M, MeCN, 20 °C, $\tau_{\frac{1}{2}}$ *ca.* 1·5 h) gave (**3b**) with opposite optical rotations and an e.e. of 19 and 23%, respectively.

Although the absolute configurations of (+)-(**3a**) and (+)-(**3b**) are not established yet, these optically active compounds are potential synthetic intermediates. A different combination of base and solvent might lead to even higher optical yields. It is striking that a relatively weak base such as quinidine can distinguish between enantiotopic protons[2] that are three carbons away from the chiral centres C(1,4) of the norbornane derivatives (**2a**) and (**2b**).

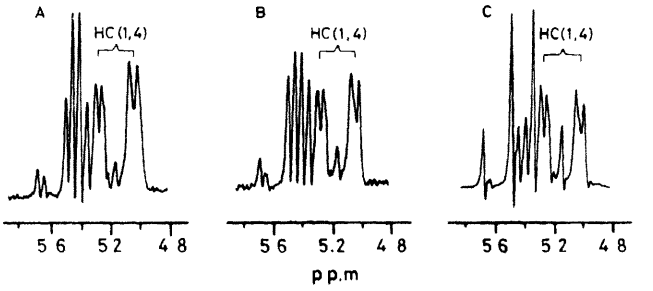


FIGURE. ^{1}H N.m.r. spectra (80 MHz, CD_3CN) of the MTPA of (**3b**) obtained by the catalysed isomerization of (**2b**) by: (A) (−)-cinchonidine; (B) $Rh_2(CO)_4Cl_2$; and (C) (+)-quinidine [-CH_2-O-MTPA and H-C(1,4) are shown].

We thank Hoffmann-La Roche, Basel, the Swiss National Science Foundation, and Fonds Herbette, Lausanne, for generous support.

(*Received, 7th July* 1980; *Com.* 730.)

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