

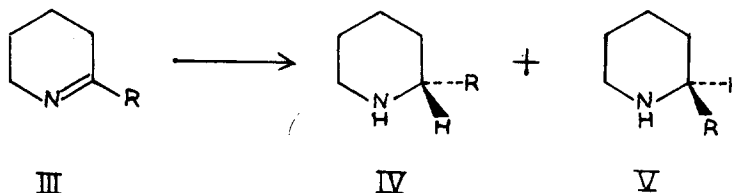
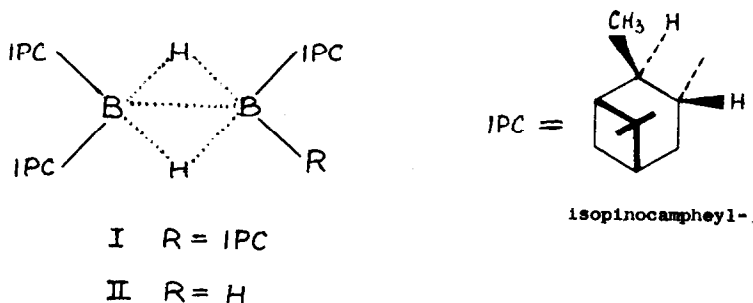
LITHIUM HYDRO-(1-BUTYL)-BIS-ISOPINOCAMPHEYLBORATE: A REAGENT FOR ASYMMETRIC
REDUCTION OF IMINES

D. R. Boyd, M. F. Grundon and W. R. Jackson

Department of Chemistry, The Queen's University of Belfast, N. Ireland

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Brown and his collaborators showed that addition of diisopinocampheylborane (DIPCB) (I) to unhindered cis-olefins followed by oxidation of the resultant borane with alkaline hydrogen peroxide gave alcohols of very high optical purity, whose absolute configurations could be related to a sterically preferred transition state (1). Other olefins afforded alcohols in much lower optical yields. In these cases the transition state model devised for cis-olefins



cannot be used to predict absolute configurations, and it was suggested that the effective reagent was triisopinocampheylborane (TIPCB) (II) formed from the requisite proportions of α -pinene and diborane or by liberation of α -pinene from DIPCB (2). Alcohols of 10-30% optical purity were obtained from ketones by similar procedures (3).

We now report the asymmetric reduction of imines by optically-active organoboron derivatives; preliminary results are summarised in the Table. 2-Methyl- and 2-propyl- Δ^1 -piperidine (III) were chosen for the initial study, since the absolute configurations of the corresponding piperidines have been established (4). In reactions 1-3 (Table) the Δ^1 -piperidines were treated with DIPCIB or TIPCB produced from diborane generated externally. Oxidation of the intermediate boranes was unnecessary, and the mixtures of piperidines and Δ^1 -piperidines were isolated via the hydrochlorides and analysed by gas chromatography. Optical purity was determined as specific rotations of the neat liquids, allowing for unreacted imine; optically-active crystalline sulphonamides were formed in each experiment. Optical induction was low, but the predominant enantiomer consistently had the S-configuration (IV). Results for the two reagents were indistinguishable, suggesting that trisopinocampheylidiborane was the effective species even when DIPCIB was available.

TABLE
Reduction of 2-Alkyl- Δ^1 -piperidines (III)

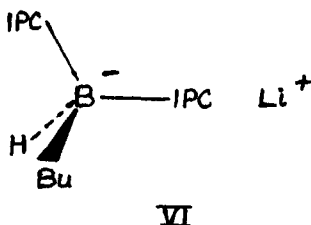
Reaction no.*	Reactant	Reagent	Recovery (%) of total bases	Reduction (%) calculated on recovered bases	Configuration	Optical purity (%) †
1	III R=Me	DIPCIB	48-53	28-33	S	2.0-3.3
2	III R=Me	TIPCB	47-52	33-36	S	2.2-3.2
3	III R=Pr	TIPCB	54-66	24-40	S	2.9-10.7
4	III R=Me	LHBIB	31-37	100	R	19.5-24
5	III R=Pr	LHBIB	75-78	28-54	R	4.0-4.3

* Each entry refers to at least two runs.

† These are not optimum values, since commercially-available Δ^1 -piperidine of only 74% optical purity was employed.

Trisopinocampheylidiborane (II) has disadvantages as a reagent for asymmetric reduction; optical yields are low and the presence of non-bridging and bridging hydrogens makes the interpretations of the reactions ambiguous. We have sought to overcome these difficulties by investigating the preparation and reactions of optically-active hydroborates containing only

one B-H bond. Trigonal boron derivatives are readily attacked by nucleophiles, and in a first attempt to obtain hydroborates by the reaction $R_2BH + R'Li \longrightarrow R_2R'BH^- Li^+$ diisopinocampheylborane was treated with n-butyl-lithium. Addition of 2-methyl- or 2-propyl- Δ^1 -piperidine and work-up by the method described above gave the results recorded in the Table (reactions 4 and 5). Compared with the reactions of DIPCB and TIPCB a much higher degree of induction was obtained with 2-methyl- Δ^1 -piperidine, and reduction of both imines led to a preference for the amine of opposite (R) configuration (V). The results are best explained by assuming that lithium hydro-(1-butyl)-bis-isopinocampheylborate (LHBIB) (VI) is the effective reducing species. In one run the reagent was treated with ethylene prior to the addition of



2-methyl- Δ^1 -piperidine, but the optical purity of the product was unaffected. This is a further indication that DIPCB and TIPCB, which would have reacted with the olefin, were not involved.

We are at present investigating the isolation of hydroalkyl-bis-isopinocampheylborates and exploring the scope of their reactions.

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