THE DIRECT PRODUCTION OF MONOISOPINOCAMPHEYLBORANE BY THE REDISTRIBUTION OF DIISOPINOCAMPHEYLBORANE WITH BORANE

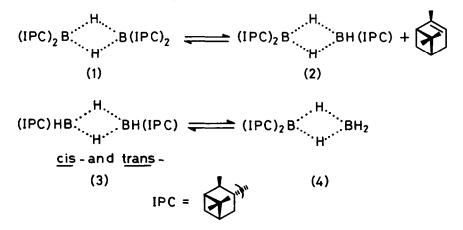
By A. Pelter,<sup>a</sup> D.J. Ryder,<sup>a</sup> J.H. Sheppard,<sup>a</sup> C. Subrahmanyam,<sup>a</sup> H.C. Brown<sup>b</sup> and A.K. Mandal.<sup>b</sup>

- a. Department of Chemistry, University College of Swansea, W. Glamorgan, U.K.
- b. Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, U.S.A.

Two simple and direct methods are outlined for the production of monoisopinocampheylphenylborane, a valuable chiral hydroborating agent.

The introduction of generally applicable chiral reagents is a matter of the greatest importance for the future of organic synthesis. The chiral hydroborating agent, tetraiso-pinocampheyldiborane (1)<sup>\*</sup> is readily available from the reaction of  $BH_3$ .THF and optically active  $\alpha$ -pinene.<sup>1</sup> It reacts with <u>cis</u>-disubstituted alkenes with excellent chiral induction but with even moderately hindered alkenes it reacts in a complex fashion involving the displacement of  $\alpha$ -pinene, to give species such as (2). As a result, the degree of chiral induction is dramatically lowered.<sup>2</sup>

It has therefore been a matter of high interest to synthesis sym-diisopinocampheyldiborane (3), or its monomer stabilised as a complex, to test whether or not it would react rapidly and with chiral induction with alkenes that react with (1) with difficulty. Moreover as a bifunctional hydroborating agent it may be used to hydroborate dienes to yield boracyclic compounds which can be converted to carbocycles. As with other dialkylboranes,<sup>3</sup> it is to be expected that (3) will exist in equilibrium with (4), and also that (4) will be a relatively poor chiral hydroborating agent.



The reaction of  $\alpha$ -pinene with BH<sub>2</sub>. THF in equimolar proportions (the "1:1 reagent")

For convenience, in the text monomeric structures such as (IPC)<sub>2</sub>BH will be used where applicable.

at 0°C was stated to give mainly (4) which is in equilibrium with a small amount of (1) and BH<sub>3</sub>.THF.<sup>4</sup> A claim<sup>5</sup> to have produced (3) by direct hydroboration in THF has been disproved.<sup>6</sup> The course of the reaction of benzonorbornadiene and <u>cis</u>-3-hexene with the "1:1 reagent" varies with the age of the reagent.<sup>7,8</sup> The explanation proposed was that (4) was the reagent mainly present in the fresh solution and that on standing a slow equilibration occurred to produce (3).<sup>\*</sup> A similar explanation was put forward to explain the anomalous results obtained in the partial resolution of racemic allenes by the 1:1 reagent.<sup>9</sup>

Recently much work has been expended on the production of  $(IPC)BH_2$ .<sup>10,11,12</sup>. The best method currently available is illustrated in the Scheme. It leads to the TMEDA complex of  $(IPC)BH_2$  and from this the borane can be regenerated to yield the active hydroborating agent.

$$2Me_2S.BH_3 + \alpha$$
-pinene  $\xrightarrow{i}$  2(1)  $\xrightarrow{ii}$  TMEDA.2(IPC)BH<sub>2</sub> + 2- $\alpha$ -pinene  
 $iii \downarrow$   
2(IPC)BH<sub>2</sub> + TMEDA.2BF<sub>3</sub> $\downarrow$ 

i. Et<sub>2</sub>0, 34<sup>o</sup>C, 0.5h; ii. TMEDA, Et<sub>2</sub>0, 34<sup>o</sup>C, 0.5h. iii. BF<sub>3</sub>.Et<sub>2</sub>0, THF, 25<sup>o</sup>C, 1h.

Scheme.

Very recently the equilibrium between (3) and (4) has been reinvestigated<sup>6</sup> and, in THF shown to give 70% of (3) and 30% of (4) after 48h. at  $25^{\circ}$ C. We now report our investigations of the hydroboration of (+)- $\alpha$ -pinone with BH<sub>3</sub>/THF which leads to the simple and direct production of the valuable reagent (3) as in Eq. 1.

The equilibration between  $(IPC)_2BH$  and  $(IPC)BH_2$  was studied by low temperature methanolysis of aliquots followed by <sup>1</sup>H and <sup>11</sup>B n.m.r. determination of the ratio of  $(IPC)_2BOMe$  and  $(IPC)B(OMe)_2$  arising from (4) [or(1)] and (2) respectively.<sup>13</sup>

\* At -25<sup>o</sup>C we find that (4) is the main borane species present and that chiral induction in the hydroboration of 2-methylcyclopentene is only about ca 5%. No. 49

From this work two convenient procedures for the preparation of  $(IPC)_2BH$  have emerged, together with two alternative methods for its utilisation for hydroboration. In each procedure equimolar proportions of  $BH_3$ . THF and  $(+)-\alpha$ -pinene (<u>ca</u> 93% optical purity) are mixed together in THF so that the solution is 0.7M in both reagents. In the first procedure the reagents are mixed at 25° and the solution set aside for a period. The result of one such study is shown in Table 1.

## Table 1.

Ratios of BH<sub>3</sub>, (IPC)BH<sub>2</sub> and (IPC)<sub>2</sub>BH obtained by equilibration at 25<sup>o</sup>C of

equimolar proportions of borane and $\alpha$ -pinene in THF.				
Time (h)	BH <sub>3</sub>	(IPC)BH <sub>2</sub>	(IPC) <sub>2</sub> BH	
24	13.80	72.40	13.80	
48	8.25	83.50	8,25	
76	5.65	88.70	5.65	
96	4.75	90.50	4.75	
120	4.50	91.00	4.50	

About 96h. would seem to be a convenient optimum time. Alternatively the solution may be heated to  $50^{\circ}$ C for  $3\frac{1}{2}$  - 4h, after which time the mixture contains <u>ca</u> 86% (IPC)BH<sub>2</sub> (average of six runs.)

The THF is removed at the pump and replaced by pentane. Addition of the appropriate amount of tetramethylethylenediamine (TMEDA) equivalent to the  $BH_3$ .THF present leads to precipitation of TMEDA.2BH<sub>3</sub>. This complex is not an active hydroborating agent and if direct hydroboration is envisaged it need not be removed from the supernatant, which contains >95% (IPC)BH<sub>2</sub> for the room temperature equilibration and 92.5% (IPC)BH<sub>2</sub> for the 50°C equilibration. Moreover, at the temperature used for hydroboration, (IPC)<sub>2</sub>BH reacts extremely slowly with trisubstituted alkenes so that the alkene reacts essentially only with the (IPC)BH<sub>2</sub> present. Hydroboration of 1-methylcyclopentene with a mixture produced by equilibration at 50° gave, after oxidation, trans-2-methylcyclopentanol of 74.9% optical purity (corresponding to 80.5% optical purity if optically pure  $\alpha$ -pinene had been used.)

A different procedure is to filter off the TMEDA.2BH<sub>3</sub> and then add sufficient TMEDA to bring out TMEDA.2(IPC)BH<sub>2</sub> as a white solid m.p. 139 - 40° (ex. Et<sub>2</sub>0).<sup>12</sup> For hydroboration the solid complex may be dissolved in THF and sufficient quantity of BF<sub>3</sub>.Et<sub>2</sub>0 added to completely generate (IPC)BH<sub>2</sub>. The hydroboration of 1-methylcyclohexene for 2.5h at 0°C with the resultant mixture, followed by oxidation, gave 71.5% optically pure trans-2-methylcyclohexanol (equivalent to 76.8% optical purity using pure (+)- $\alpha$ -pinene.)

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Monoisopinocampheylborane is now a readily available chiral hydroborating agent. It should find wide synthetic application for the hydroboration of those alkenes that react slowly, or not at all, with (1). Other applications of the reagent for asymmetric reductions are under investigation.

<u>Acknowledgements</u>. Three of us (Dr. Ryder, Mrs. J.H. Sheppard and Dr. Subrahmanyam) thank ICI and one of us (Dr. A.K. Mandal) thanks the N.I.H., Maryland for maintenance grants during the course of this work.

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(Received in UK 17 september 1979)