Investigations of Boranediylation and Exchange Reactions of Some 1,2-Dihydroxy Compounds and their O-Organylboranediyl Derivatives Using ¹⁸O and ¹⁰B Isotopically Labelled Triethylboroxines

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The boranediylation of dihydroxy compounds and exchange reactions involving R—B—O groups of a number of their O-boranediyl derivatives with ¹⁸O and ¹⁰B labelled triethylboroxines has been investigated. It has been found that in simple 1,2-dihydroxy compounds only the RB group is substituted or exchanged. In hydroxy compounds such as ninhydrin and octahydroxycyclobutane both RB and RBO groups are involved. The mechanisms of these exchange reactions are discussed.

Introduction

In a previous paper [1] we reported that in the boron heterocycle 1a with an RBO₂ grouping the substituent R can in some cases readily be exchanged by heating with a tri-organylboroxine (R’BO₃).

There are three possible modes for this exchange to take place: (a) The complete replacement of an RBO₂ grouping, (b) exchange of RB, or (c) substitution of R by R’. One or more of these modes could be operative in the above reaction.

A number of reactions involving substituent exchanges on boron are known and some have been extensively studied. Thus in the metathesis reaction with triorganylboranes [2] the substituent exchanges observed clearly involve the rupture of the B—C bonds. Another similar exchange takes place when a trialkoxyborane (RO)₃B is reacted with a trialkylborane (R’₃B) to give a mixture of (RO)₂BR’ and RROB’ [3]. The direct rupture of the bond between the boron and the substituent is also indicated in the reaction of a boroxine (RBO), with a trialkylborane (R’₃B) to give a mixture of boroxines and boroxanes with mixed substituents [4]. In the recently described substituent exchange reaction on 1,3,2-dithiaborolanes and 1,2,3-trimethyl-1,3,2-diazaborolidine [5], however, it has been shown that both (b) and (c) type exchanges take place. Ruptures of the type (a) involving the exchange of an RBO group is probable in the reaction of one triorganylboroxine (RBO₃) with another with substituents R’ to give mixed boroxines of the type (RBO₂)₂R’BO and (R’BO₂)₂RBO. In the exchange reaction of the boranediyl groupings in 1 and also the boranediylation of hydroxy compounds it is a priori not clear where the bond rupture takes place. In this report we describe our results on the boranediylation of a number of hydroxy compounds and the exchange reactions between their O-boranediyl derivatives and ¹⁸O and ¹⁰B labelled triethylboroxine.

Results and Discussions

In the reaction of 1a (R = i-Pr) with ¹⁸O-triethylboroxine to give 1b (R = Et) no inclusion of the label could be detected. ¹⁸O was also not transferred to 1b when dihydroxyfumaric acid 2 was reacted with labelled boroxine.

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Reaction of 1a with excess $^{10}$B-boroxine, however, produced 1c which had retained the same isotope content as in the enriched boroxine used ($^{10}$B/$^{11}$B = 1/1) and in 1c formed from the reaction of the boroxine with dihydroxyfumaric acid. Thus in this reaction both of the exchange modes (a) and (c) did either not take place at all, or their contributions were within the experimental error of measurements (<2%).

Another compound with an RBO$_2$ grouping, the 1,2-diol derivative 3a reacted with the $^{18}$O labelled reagent to give, as in 1c, compound 3b without incorporation of the label. The result was the same when 3b was obtained from the reaction of dimethyl-tartrate 4 and the labelled boroxine.

Also, like in the reaction of 1a and 2, compounds 3a and 4 gave on reaction with $^{18}$O enriched boroxine 3b with the same isotope distribution as in the boroxine used.

The exchange reaction on 5a, a tetrakis-O-phenyl-boranediyl derivative of the hydrated oxo-carbon 6, however, led to $^{18}$O incorporation in the products 5b and 5c. Likewise, the boranediylation of 6 gave 5c with a similar isotope distribution.

In Fig. 1a the ions M$^+$−Et of 5c [6] with natural isotope abundance are shown and compared to those of 5c after reaction with $^{18}$O-boroxine (Fig. 1b). A calculation of the composition of this group of ions based on the known abundance of the involved $^{18}$O-enriched oxygen results in 35% of the unlabelled, 39% of the mono-labelled, 23% of the di-labelled, and a trace (<3%) of the tri-labelled product. Fig. 1c shows the theoretical distribution calculated for the given percentages of the differently labelled 5c. Whereas the formation of unlabelled 5c is in accordance with the results obtained from the simple 1,2-diol 4 and its O-boranediyl derivative 3a, the introduction of $^{18}$O label in 5c indicates that there are also other mechanisms in operation. One such mechanism could be the scrambling of the oxygen isotopes subsequent to the initial formation of 5c. However, various attempts at incorporating $^{18}$O from boroxine into unlabelled 5c by refluxing it for as long as 24 h with a large excess of the $^{18}$O boroxine in the absence or presence of a $^{3}$BH catalyst, failed to give measurable amounts of $^{18}$O in 5c. In contrast the reaction of 5c with excess of $^{10}$B triethylboroxine in the absence of a BH catalyst led to the incorporation of $^{10}$B into 5.

To gain an insight into the mechanism involved, a simpler model substrate was required. Ninhydrin 7 with it’s two vicinal hydroxyl groups had previously been found to react with triethylboroxine to give its bis-boranediyl derivative 8 [7]. The reaction of 7 with $^{18}$O labelled ethylboroxine gave 8 which had the mass spectrum shown in Fig. 2 [8]. It has the molecular ion peaks at m/e 272 and 274 in the ratio of 1:4, approximately corresponding to the isotope ratio in the boroxine used. It is thus evident that in the formation of 8 one each of an RBO and an RB moieties are involved. These can be introduced into ninhydrin by either of the two mechanisms shown in Scheme 1.

From this scheme it can be seen that pathway I would place the $^{18}$O at C3 while pathway II leads to C2 carrying the labelled oxygen. An analysis of the fragmentation pattern of 8 is shown in Fig. 2 and reveals that except in the step involving the loss of CO from the indantrione ion [m/e 160(162) → 132(134)], in each of the other fragmentation steps...
Fig. 1. Segment of the mass spectrum showing the M–Et fragment of 5c obtained from (a) unlabelled, (b) $^{18}$O-labelled triethylboroxine, and (c) the theoretical distribution based on the composition of the products (see text).
involving the loss of oxygen atoms, there is a progressive loss of about 20% of the $^{18}$O label. The ratio of the peaks at m/e 104 and 106 show the retention of about 20% of the label in this last fragment containing oxygen.

If one assumes that the principal fragmentation of the indantrione ion [peak m/e 160/162]) leads to the loss of CO from C2 and give the ions at m/e 132 and 134 without the loss of the label, as observed, then pathway I would be probable. Alternatively, it is also possible that the indantrione ion carries the $^{18}$O at C2, as required by pathway II, and fragments with the loss of a CO from C1, or C3.

To distinguish between the two pathways in Scheme I a daughter ion analysis of the m/e 162 (indantrione ion), generated by M-18 fragmentation of C2 mono-$^{18}$O labelled ninhydrin (obtained from careful hydration of indantrione with $^{18}$O water), was performed and compared with that from a similarly treated labelled 8. These are shown in Fig. 3. The appearance of only the peak at m/e 132 in (a) correlates with the loss of C$^{18}$O from C2. Labelled 8 on the other hand, shows mainly, although possibly not exclusively, the peak at m/e 134 as the daughter ion of the indantrione fragment ion peak at m/e 162. It follows that in the formation of 8, the major route for introducing the boranediyl groups is pathway I. However, the presence of a peak at m/e 132 in the daughter ion spectrum of 8 indicates that pathway II can not conclusively be ruled out.

![Fig. 2. Mass spectrum and fragmentation pattern of $^{18}$O labelled 8.](image)

![Scheme 1.](image)
In Contrast to the formation of 8 from 7 the boranediyl exchange reaction performed on the bis-O-ethyl- or O-phenylboranediyl-3-oxo-indane 8, or 9, respectively, with $^{18}$O-triethylboroxine resulted in the formation of 8 with an $^{18}$O enrichment of only about 20% and 24%, respectively, based on the molecular ion at m/e 272/274. This shows that in the main the exchange mode (b) has been utilized. Moreover, the relatively small amount of $^{18}$O incorporated into 8 seems to be random as the fragment ions at m/e 216/218, 160/162, and 132/134 all show a nearly constant 4:1 ratio of $^{16}$O/$^{18}$O. The exchange reaction leading to the random $^{18}$O incorporation is probably catalyzed by traces of moisture and can be thought to be the result of a series of deborylations (loss of RBO) and reborylations (introduction of R'B$^{18}$O). The reaction of unlabelled 8 with excess $^{10}$B-triethylboroxine which gave 8 in which both of the boron atoms had exchanged with those of the reagent is also in agreement with the above interpretation.

The above results with boranediylation of ninhydrin can now be applied to the elucidation of the mechanism of the boranediylation of 6. The latter has in many of its reactions persistently resisted dehydration to the keto form [1, 9]. However, after an initial mono-boranediylation by the same mechanism as found for the simple 1,2-diols, it may be more amenable to dehydration and therefore can react, at least in part, by the mechanism observed for the $\alpha,\alpha$-dihydroxyketone system of ninhydrin. As can be seen in the mechanistic Scheme 2 the conversion of 6 into 5c is started by the introduction of an RB group. This is followed by the incorporation of an RB$^{18}$O moiety into that portion of the resulting mono-boranediylated 6 that exists in the mono-keto form. In the similar following steps first an RB$^{18}$O and finally an RB group is used to form mono-, or di-$^{18}$O-labelled 5c. The presence of the small amount (<3%) of the tri-$^{18}$O labelled product, if significant, can be rationalized by deboranediylation-reboranediylation by way of the equilibria shown in Scheme 2 (dashed lines). This scheme thus rationalizes the formation of unlabelled 5b by a series of RB incorporations and the formation of mono, di and tri $^{18}$O labelled product by RBO additions.
Conclusion

We have thus shown that the α-hydroxy acid 2, 1,2-diols such as 4, or their boranediylated derivatives 1 and 3 exclusively react, or exchange substituents with triethylboroxine by way of path (b). Per-hydrated α-polyketones of the type 6, or its per-boranediylated derivative 5a, however, utilize two pathways. In one they act like simple 1,2-diols and therefore follow path (b). In the other depending on the stability and thus concentration of a dehydrated keto form present, utilize an RB\(^{18}\text{O}\) group in accordance with path (a). In the stable α,α-dihydroxyketone system of 7 the latter pathway is the sole route for the introduction of the first boron group. In the second boranediylation step the resulting species then behaves like a simple 1,2-diol and utilizes pathway (b).

Experimental

The \(^{18}\text{O}\) enriched water was purchased from Vencon and the \(^{10}\text{B}-\text{boron trioxide from Oak-Ridge Tennessee Co. Mass-spectra: Varian MAT CH 5 and daughter ion analysis using B/E = const scans on a Finnigan MAT MS 8200.}

Preparation of \(^{18}\text{O}-\text{triethylboroxine} [9]: To 1.5 g (75.0 mmol) of H\(_2\)\(^{18}\text{O}\) (isotope content 90.0% \(^{18}\text{O}\), 3.5% \(^{17}\text{O}\), and 5.6% \(^{16}\text{O}\)) and 10 mg of pivalic acid are slowly added about 16 ml of a total of 20.7 g (211.2 mmol) of triethylborane. An initially rapid gas evolution continued for about 1 h. The mixture was heated to 60–65 °C and the remaining borane added. The total gas volume evolved was 3.5 l (calcld. 3.6 l). On cooling to r.t., 0.8 ml of diethylborane was added and the excess triethylborane removed by distillation at atmospheric pressure. Most of the residual triethylborane was subsequently removed by water pump vacuum at r.t. The residue distilled b.p. 143–6 °C to give 3.9 g of a colourless liquid, g.l.c. (15 m Dexil capillary column) 87% triethylboroxine, 9.1% tetrathylidiboroxane, and 2.4% triethylborane. MS: M\(^+\), m/e 168–174 (isotope ratio 90.8% \(^{18}\text{O}\); 3.5% \(^{17}\text{O}\), and 6.5% \(^{16}\text{O}\)).

Preparation of \(^{10}\text{B}-\text{triethylboroxine} [10]: 7.42 g (106.6 mmol) of \(^{10}\text{B}-\text{boron trioxide} and 22.7 ml (159.9 mmol) of triethylborane were heated for 4 h at 235 °C in an autoclave. The light yellow viscous liquid formed was distilled over a spinning band column. The fraction collected at 144–6 °C (11.5 ml) showed molecular ions at m/e 165–168 (\(^{10}\text{B};^{11}\text{B} isotope ratio of 1:1).}

Reaction of 1 (R = n-Pr) with \(^{18}\text{O}\)-, or \(^{10}\text{B}-\text{triethylboroxine}: A mixture of 0.03 g (0.12 mmol) of 1
(R = n-Pr) and 0.1 ml (1.55 mmol) of $^{18}$O-triethylboroxine in 3 ml of benzene were refluxed for 7 h. The volatiles were removed in high vacuum. The residue, a solid, colourless at r.t. and yellow below $-5 ^\circ\text{C}$ showed a molecular ion at $m/e$ 224 for the reaction with $^{18}$O-triethylboroxine and $m/e$ 222–224 ($^{10}$B : $^{11}$B ratio of 49:51) for 1b from $^{10}$B-ethylboroxine.

Reaction of dihydroxyfumaric acid 2 with $^{18}$O-, or $^{10}$B-triethylboroxine: 1.14 g (7.7 mmol) of 2 and 0.9 g (5.2 mmol) of $^{18}$O-triethylboroxine in 50 ml of benzene were brought to reflux and about 30 ml of the benzene distilled at atmospheric pressure and the remainder together with other volatiles at reduced pressure. The solid residue was washed with pentane to give 1.6 g of a colourless solid. MS: $M^+$ at $m/e$ 222–224 for product from $^{10}$B-ethylboroxine.

Reaction of O-phenylboranediyldimethyltartrate 3a with $^{18}$O- and $^{10}$B-triethylboroxine: 0.24 g (0.9 mmol) of 3a and 0.11 g (0.6 mmol) of $^{18}$O-triethylboroxine in 5 ml of benzene were heated for 3.5 h at reflux. The solvent and volatiles were evaporated at reduced pressure. The residue showed molecular ion at $m/e$ 216.

Reaction of octahydroxycyclobutane 6 with $^{18}$O-triethylboroxine: A suspension of 0.05 g (0.27 mmol) of 6 and 0.15 g (0.88 mmol) of $^{18}$O-triethylboroxine in 10 ml of toluene was heated to boiling and about 5 ml of the solvent distilled at atmospheric pressure. The remaining volatiles were removed at reduced pressure. The residue was analyzed by GC–MS. The peak corresponding to 5b showed characteristic fragment ions at $m/e$ 305–312.

Reaction of 5a with $^{18}$O-triethylboroxine: 0.1 g (0.19 mmol) of 5a, 0.09 g (0.52 mmol) of $^{18}$O-triethylboroxine, and 1 drop of diethylborane in 5 ml of toluene were heated to about $100 ^\circ\text{C}$ for 7 h. The solvent and volatiles were removed at reduced pressure. To the residue pentane was added and the insoluble triphenylboroxine removed. The filtrate was analyzed by GC–MS. The fragment ion peaks at $m/e$ 305–312 were nearly identical to product 5b above.

Reaction of ninhydrin 7 with $^{18}$O triethylboroxine: 0.11 g (0.6 mmol) of 7 and 0.11 g (0.62 mmol) of $^{18}$O-triethylboroxine in 8 ml of toluene was heated to boiling and about 5 ml of the solvent distilled at atmospheric pressure. The remaining volatiles were removed at reduced pressure. The colourless solid residue showed molecular ions at $m/e$ 272 and 274 ($^{18}$O : $^{18}$O isotope ratio 1:4).

Reaction of 9 with $^{18}$O-triethylboroxine: 0.058 g (0.13 mmol) of 9 and 0.065 g (0.32 mmol) of $^{18}$O-triethylboroxine in 5 ml of toluene were refluxed for 5 h. The solvent and volatiles were removed in vacuum. The residue a colourless solid showed molecular ions at $m/e$ 272/274 (peak ratio 4:1).

Preparation of 2-$^{18}$O-ninhydrin: 0.016 g (0.1 mmol) of solid ninhydrin was treated with 1 drop of H$_2^{18}$O. After the red-violet colour of the indantrion had vanished the excess water was removed at reduced pressure. MS: $M^+$ at $m/e$ 180.

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[6] Compound 5c shows only a very small (1%) molecular ion peak at $m/e$ 336.
[8] For obtaining 8 labeled with $^{18}$O as shown in Fig. 2 the ratio of ninhydrin to $^{18}$O enriched reagent was about 1:1. With an excess of the reagent, the labelled 8 formed contained up to three $^{18}$O’s.