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FACILE ALKYLATION OF *o*-HYDROXYARYLALDEHYDES AND α-FORMYLKETONES WITH TRIALKYLBORANES

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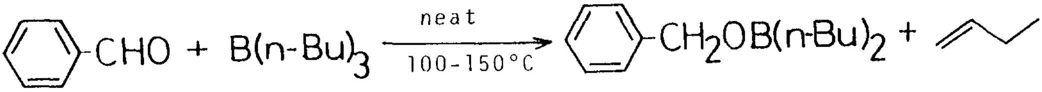
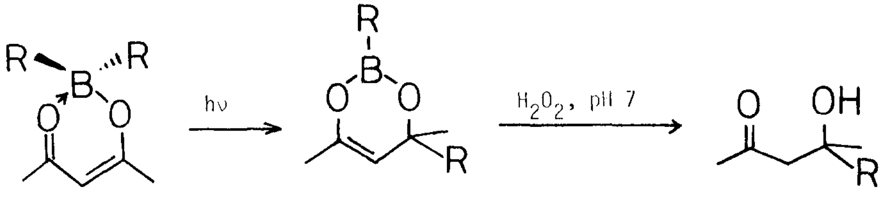
Summary: Trialkylboranes readily undergo alkylation reactions with *o*-hydroxyarylaldehydes and α-formylketones via the dialkylboryl complexes.

Although the conjugate addition of trialkylboranes to α,β-unsaturated carbonyl compounds is well known, 1,2-addition to simple carbonyl groups has seldom been observed.[1] Monomeric formaldehyde undergoes exceptionally fast alkylation with trialkylboranes in the presence of oxygen.[2] The reaction is diverted to the reduction of formaldehyde under inert atmosphere.[2] Reactions of nonenolizable aldehydes or ketones with trialkylboranes generally require forced conditions,[3] giving reduced alcohols and alkenes.[4,5] For example, the reaction of benzaldehyde with tri-n-butylborane gives the reduced dibutylbenzyloxyborane and butene at 100-150°C (eq 1).

During photochemical studies of dialkylborylacetylacetonate chelate-complex (eq 2),[6] we have found that some chelates derived from *o*-hydroxyarylaldehyde or α-formylketones are unstable and thermally undergo alkylation reactions.

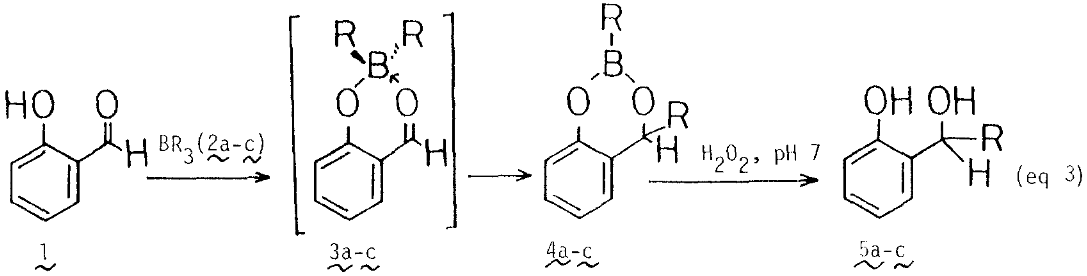


(eq 1)



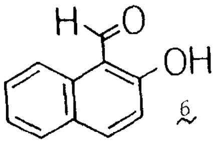
(eq 2)

When tricyclohexylborane (2a: 1.1~1.5 equivalent) is mixed with salicylaldehyde (1) in benzene at room temperature, red color due to the dialkylboryl complex (3a) is developed and fades away upon heating. After evaporation of the solvent and distillation of the residual oil, the borane compound (4a) was obtained in high yield as colorless oil [4a M^+ (m/e) 298; ^{1}H NMR δ (ppm) in $CDCl_3$, 0.8-2.1 (m, 22H), 4.89 (d, 1H, J=2.0 Hz), 6.8-7.3 (m, 4H)]. Oxidative hydrolysis of 4a gave 5a in 83% yield.[7] Table 1 summarizes the results of alkylation reaction



(eq 3)

R= a;cyclohexyl, b;n-butyl, c;norbornyl



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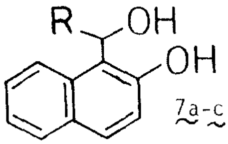

7a-c

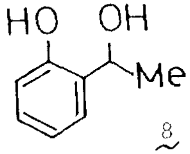

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Table 1. Yields of the reactions of salicylaldehyde or 1-formyl-2-naphthol with trialkylboranes (2a-c)

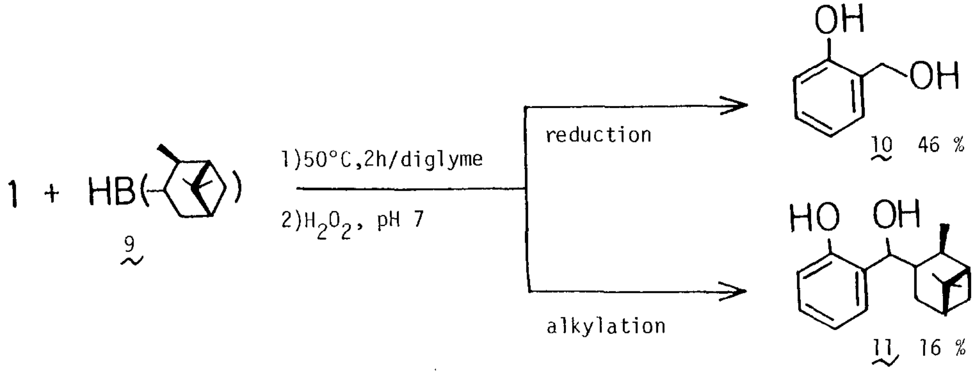
Starting material	trialkylborane	product	yield[a]
1	2a	5a	83%
1	2b	5b	57%
1	2c	5c	52%
6	2a	7a	69%
6	2b	7b	53%
6	2c	7c	47%
o-methoxy-benzaldehyde	2a	recovery	0%
o-hydroxy-acetophenone	2a	8	28%[b]

a; refluxed in benzene under N_2 for 3 h b; refluxed in toluene under N_2 for 10 h

of salicylaldehyde and 1-formyl-2-naphthol with several trialkylboranes (2a-c). Relatively bulky norbornyl group can be introduced by this procedure.[8] *o*-Hydroxyacetophenone is inert for the alkylation and gives only the reduced product (8), suggesting that formyl group is essential for the alkyl migration. Phenolic hydroxyl group is also necessary for the alkylation as shown in the complete recovery of *o*-methoxybenzaldehyde. The initial participation of the borane complex is evidenced by the visible absorption (449 nm in benzene). The value is close to that of stable diphenyl analogue[9] (3; R=Ph 424 nm in Bz).

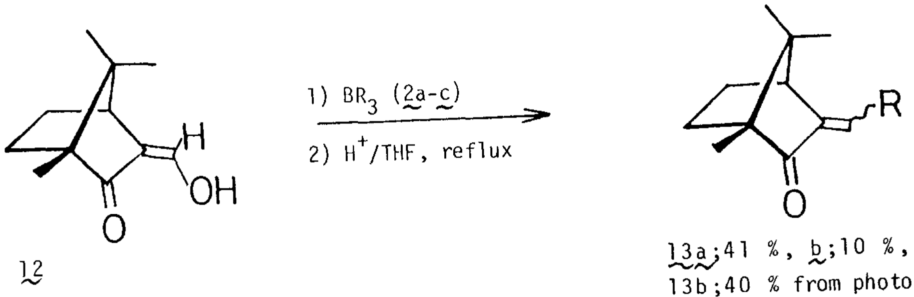
Although the reaction proceeds under nitrogen atmosphere, addition of a small amount of galvinoxyl radical (5 mol%) depressed the yield to 46% and 22% for tricyclohexyl- and tri-n-butylboranes, respectively.[1c,10] This result suggests participation of radical species either in the initial complexation or the subsequent alkylation processes (see eq 3). The alkyl migration may occur via a radical pair mechanism as proposed in our previous study of photochemical alkylation of the related systems.[6]

The facility of the alkylation reaction can be demonstrated by the competition with the reduction by use of dialkylhydroborane, typical reducing agent of the carbonyl groups. Thus, the reaction of salicylaldehyde with diisopinocampheylborane (9; 0.5 equivalent) at 50°C gave the expected reduced salicyl alcohol (10) and the alkylation product (11) in 46% and 16% yields based on 9, respectively (eq 4). NMR and HPLC analysis of 11 showed that the alkylation was nondiastereoselective and 11 was obtained as an essentially equimolar diastereomeric mixture.[11]



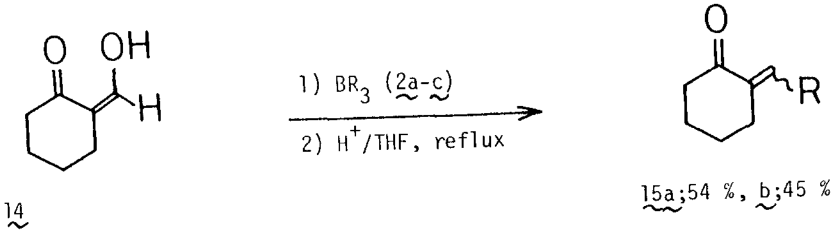
(eq 4)

We have also found that similar alkylation proceeds in the reaction of trialkylboranes with α-formylketones. Since the reaction of β-diketones with trialkylboranes has been extensively studied and is already known to give the stable dialkylboryl complexes,[12] it is rather surprising that the reaction of α-formylketones gives alkylation-product. As shown in eq (5) and (6), the reactions of α-formylcamphore (**12**) or α-formylcyclohexanone (**14**) readily afford the alkylation products after acidic hydrolysis.[13]



(eq 5)

13a;41 %, **b**;10 %, **c**;76 %
13b;40 % from photolysis



(eq 6)

15a;54 %, **b**;45 %, **c**;50 %

The reaction is highly regiospecific and the alkylation occurs only on the aldehyde carbon (eq 5 and 6). This selectivity is probably due to steric effect in the alkylmigration step in the radical pair intermediate.[6] Initial coloring after mixing α-formylketones with trialkylboranes suggests the intermediacy of the chelate-complexes (370 and 375 nm in benzene, for **12** and **14**, respectively). Assignment of the absorption can be supported by the analogy with the thermally stable dicyclohexylborylacetylacetonate complex[6,12a,b] (348 nm in benzene).

In eq (5), low reactivity of α-formylcamphore toward tri-n-butylborane can be noticed (**13b**, 10% with recovery of 71% of **12**). It is expected from our previous study[6] that the alkylation may be performed by photochemical processes. Thus, selective excitation (> 330 nm) of the chelated intermediate (λ_{max} 370 nm), produced *in situ* from **12** and **2b**, in benzene at room temperature under nitrogen atmosphere gave **13b** in the improved yield of 40%.[14] Obviously the reaction is accelerated by irradiation. In other cases, however, the role of photo-acceleration is not clear because of the relatively facile thermal alkylation process even at room temperature. Further investigations in this and related systems are in progress in this laboratory.

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13 Trans isomers are overwhelmingly formed.

14 Externally irradiated for 50 min with a 500-W Xenon lamp through a Toshiba UV-33 filter ([**12**]=$7.1x10^{-2}$M, [**2b**]=$1.1x10^{-1}$M). No recovery of the starting material was observed.

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