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Selective Reductions. 24. Acyloxyboranes in the Controlled Reaction of Carboxylic Acids with Borane–Tetrahydrofuran. Acyloxyboranes as Intermediates in the Fast Reduction of Carboxylic Acids by Borane–Tetrahydrofuran

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Abstract: The controlled reaction of carboxylic acids with borane–THF at appropriate temperatures makes available mono-, di-, and triacyloxyboranes, RCO_2BH_2, $(RCO_2)_2BH$, and $(RCO_2)_3B$. A number of these have been synthesized and characterized. The first unambiguous examples of triacyloxyboranes have been isolated and characterized. A number of addition compounds of tetrahydrofuran with diacyloxyboranes have been prepared. Finally, a relatively stable monoacyloxyborane has been identified, as well as less stable monoacyloxyboranes, possible intermediates in the reduction of carboxylic acid. Treatment of the carboxylic acids with borane–THF (1:1), the diacyloxyborane with borane–THF, or the triacyloxyborane with borane–THF (1:2) produces at the same rate the corresponding trialkoxyboroxines (readily hydrolyzed to the alcohols). These results establish that the extraordinarily fast reduction of carboxylic acids by borane–THF must proceed through the intermediate formation of monoacyloxyborane, either formed directly from the carboxylic acid and borane, or formed by a redistribution reaction of diacyloxyborane with borane.

We have recently described the remarkable ease with which carboxylic acids, both aliphatic and aromatic, are reduced by borane–tetrahydrofuran.[2,3] However, acyloxyboranes, proposed intermediates in these reductions, have never been carefully characterized or explored. Consequently, the precise mechanism of the reduction is not well understood.

The only system which has been repeatedly explored is triacetoxyborane (**1**), reportedly synthesized by a variety of procedures (eq 1).[4-6]

$$\begin{aligned} &\tfrac{1}{2}B_2O_3 + \tfrac{3}{2}(CH_3CO)_2O \\ &B(OH)_3 + 3(CH_3CO)_2O \xrightarrow[-3HCl]{-3HOAc} (CH_3CO_2)_3B \quad (1) \\ &BCl_3 + 3CH_3CO_2H \end{aligned}$$

1

Other workers using these procedures have reported the product to be not **1**, but rather, oxybis(diacetoxyborane) (**2**), presumably formed in the dismutation of **1** (eq 2, R = CH_3).[7-9]

$$2(RCO_2)_3B \rightarrow (RCO_2)_2BOB(O_2CR)_2 + (RCO)_2O \quad (2)$$

2

The reaction of carboxylic acids with borane–THF is remarkably clean.[2] If the subsequent reduction of the intermediates could be controlled, this reaction offered promise of providing a new, very mild general route to triacyloxyborane, $(RCO_2)_3B$, and possibly to the intermediate derivatives, diacyloxyborane, $(RCO_2)_2BH$, and monoacyloxyborane, RCO_2BH_2. Accordingly, we undertook a study of the reaction of representative carboxylic acids with borane–THF under mild, controlled reaction conditions.

Results and Discussion

Stoichiometry of the Reaction of Carboxylic Acids with Borane–THF. The reduction of carboxylic acids by borane–

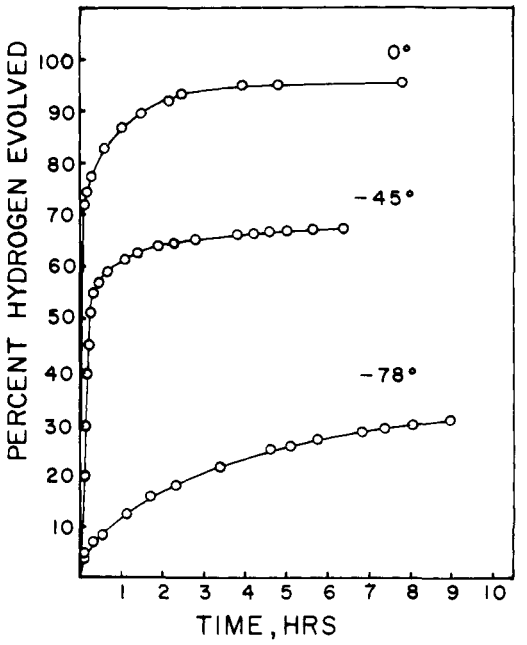


Figure 1. Rate of hydrogen evolution for the reaction of acetic acid (3.0 M) with borane–THF (1.0 M) in THF at various temperatures.

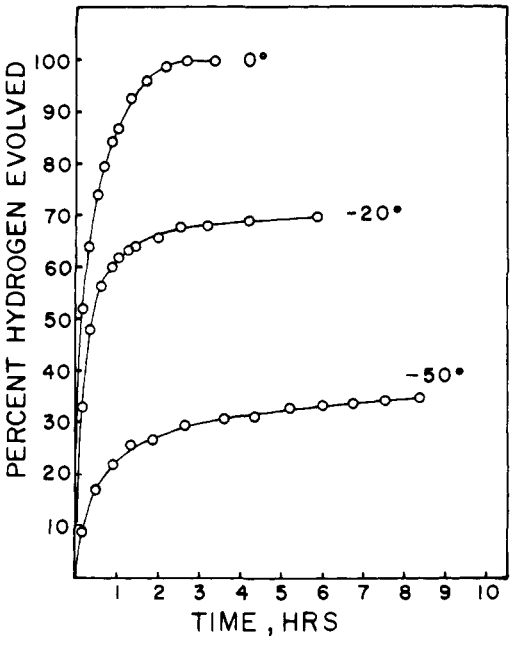


Figure 2. Rate of hydrogen evolution for the reaction of pivalic acid (2.59 M) with borane–THF (0.86 M) in THF at various temperatures.

THF is generally very rapid. In fact, the reaction is difficult to control at temperatures above 0 °C.[10] Hydrogen evolution and reduction appear to proceed almost simultaneously. However, if the reaction temperature is lowered sufficiently, reduction becomes negligible, while hydrogen evolution occurs at a reasonable rate. By a careful selection of the temperature, it proved possible to control the reaction of appropriate carboxylic acids with borane–THF to proceed stepwise to the monoacyloxyborane **3**, the diacyloxyborane **4**, or the triacyloxyborane **5**. The course of the reaction leading to the formation of the desired product can be readily followed by monitoring the amount of hydrogen evolved.

$$RCO_2H + BH_3 \xrightarrow{T_1} RCO_2BH_2 + H_2 \qquad (3)$$

3

$$2RCO_2H + BH_3 \xrightarrow[THF]{T_2} (RCO_2)_2BH + 2H_2 \qquad (4)$$

4

$$3RCO_2H + BH_3 \xrightarrow[THF]{0\ °C} (RCO_2)_3B + 3H_2 \qquad (5)$$

5

Two representative examples are the behavior of acetic acid and pivalic acid.

Addition of a solution of acetic acid in THF to a rapidly stirred solution of borane–THF in THF in the molar ratio of 3 CH_3CO_2H/BH_3 results in the evolution of 1 equiv of hydrogen at −78 °C, 2 equiv at −45 °C, and 3 equiv at 0 °C (Figure 1).

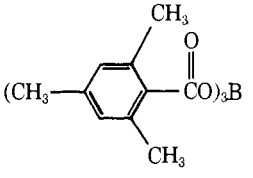
The corresponding reactions of pivalic acid are more sluggish, presumably a consequence of its greater steric requirements. Accordingly, somewhat higher temperatures were required to achieve convenient rates and the transformations shown in eq 3–5. One equivalent of hydrogen was evolved at −50 °C, 2 equiv was evolved at −20 °C, and 3 equiv was evolved at 0 °C (Figure 2).

Analysis of aliquots of the reaction mixtures for residual hydride established that no active hydride had been utilized for reduction.

These results establish that the rate of hydrogen evolution decreases as each successive acid group becomes bound to boron. An interpretation of this phenomenon will be presented in the mechanism section.

Triacyloxyboranes ($3RCO_2H + BH_3$). The reactions of several carboxylic acids with borane–THF in the stoichiometric ratio to produce the triacyloxyborane were investigated. The general procedure was to add 6 mmol of BH_3–THF within 10 min to 18 mmol of acid in sufficient THF to give 18 mL of solution. The mixture was kept at 0 °C and the volume of hydrogen evolved with time was noted.

Two compounds, tris(2,4,6-trimethylbenzoyloxy)borane (**6**) and tripivaloxyborane (**7**), were established to be indefi-



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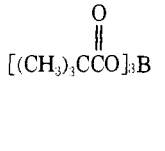

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nitely stable in THF at 20 and 0 °C, respectively. If **7** was warmed to 20 °C, it slowly underwent dismutation into the anhydride and the oxybisborane derivatives (eq 2).

Examination of solutions of **6** and **7** for the presence of the anhydrides by IR revealed their absence. Consequently, **6** and **7** appear to be the first unambiguous examples of triacyloxyboranes.

During our early investigations of diborane as an acid-type reducing agent,[11] we observed that benzoic acid reacted with diborane in THF (or diglyme)[12] in the stoichiometric ratio to liberate the theoretical amount of hydrogen. Hydrolysis of the product produced a quantitative recovery of benzoic acid. We assumed that we had synthesized tribenzoyloxyborane.[11] More recently, Pelter and his co-workers have reported that the tribenzoyloxyborane, if formed momentarily, undergoes a rapid dismutation (eq 2).[13]

In THF the reaction to liberate the third mole of hydrogen is very slow.[13] It proceeds more readily in diglyme. Accordingly, we treated 1 equiv of borane–methyl sulfide (BMS) in diglyme with 3 equiv of benzoic acid. The quantitative amount of hydrogen was evolved, and a white solid precipitated. Infrared examination of the solution revealed the presence of

benzoic anhydride. The solid was identified as oxybis(dibenzoyloxyborane) (**2**, R = Ph).

On the other hand, if the reaction was carried out under much more dilute conditions, 0.1 M in the $(RCO_2)_3B$, no dismutation was observed in the fresh reaction mixture. It would appear that dismutation is a polymolecular reaction which is slow for hindered systems, such as **6** and **7**, and can be slowed down for less hindered systems by dilution.

Dismutation is evidently still more rapid for simple, relatively unhindered aliphatic carboxylic acids. Thus carboxylic acids, such as acetic, propionic, hexanoic, and cyclopropanecarboxylic acid, liberated the theoretical amount of hydrogen with borane-THF in THF to form the corresponding triacyloxyboranes, $(RCO_2)_3B$. However, IR examination of the solutions shortly after the hydrogen had been completely evolved revealed the presence of anhydride corresponding to that predicted for dismutation (eq 2).

Formic acid behaved differently. It failed to liberate the theoretical amount of hydrogen. We achieved a maximum of 47% hydrogen evolved with complete loss of the remaining hydride. Evidently, in this case reduction of the carboxylic group occurs at a rate competitive with the reaction liberating hydrogen.

Upon attempting to react trifluoro- or trichloroacetic acid with BH_3-THF in the usual 3:1 molar ratio, we observed that less than the quantitative amount of hydrogen was evolved and solid polymerized THF formed. This result is comparable to that described by Muetterties using tris(trifluoroacetoxy)borane, $(CF_3CO_2)_3B$,[14] and represents an alternative method for polymerizing THF.

Alternatively, addition of neat borane-methyl sulfide to excess neat trifluoroacetic acid resulted in quantitative hydrogen evolution, and formation of $(CF_3CO_2)_3B$.[15,16] Removal of the excess trifluoroacetic acid under vacuum produced a solid whose weight corresponded to $(CF_3CO_2)_3B{:}SMe_2$.

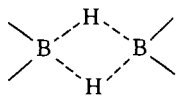
The results are summarized in Table I.

Diacyloxyboranes ($2RCO_2H + BH_3$). Treatment of chloroacetic, benzoic, or *p*-chlorobenzoic acid with borane-THF (3:1) results in the evolution of only 2 equiv of hydrogen (eq 6, R = $ClCH_2$, Ph, *p*-ClPh).

$$3RCO_2H + BH_3 \xrightarrow[THF]{0\ ^\circ C} 2H_2 + (RCO_2)_2BH + RCO_2H \quad (6)$$

Because these results were so dramatic, a detailed investigation was undertaken.

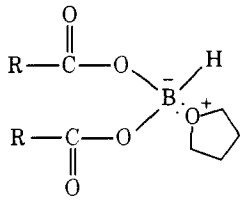
The fact that the reaction of benzoic acid with borane-THF in THF essentially stops at the dibenzoyloxyborane stage had been previously noted.[13] By treating each of the aforementioned carboxylic acids with borane-THF (2:1), we observed that the infrared spectrum of each of the diacyloxyboranes failed to show a strong absorption at ~1600 cm^{-1}, indicating that the carbonyl group is not coordinated to boron[17] (>C=O→B<). Moreover, a strong peak at ~1560 cm^{-1} was missing (indicating the absence of B-H bridging) while a band



at 2470 cm^{-1} was present (indicating the existence of monomeric >BH).[18] The ^{11}B NMR spectrum of $(PhCO_2)_2BH$ and $(ClCH_2CO_2)_2BH$ in THF showed resonances at +4.8 and +3.0 ppm (relative to $BF_3{\cdot}OEt_2$), respectively. Thus, the boron atom must be tetracoordinated.

When a THF solution of each of the diacyloxyboranes was evaporated, a plateau in the time vs. sample weight curve showed the existence of a 1:1 addition compound, $(RCO_2)_2$-BH-THF.

All of these findings led us to the conclusion that acids containing electron-withdrawing groups tend to form diacyloxyboranes, which are stabilized in the form of a molecular addition compound with THF (**8**).



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The stabilities of these diacyloxyborane derivatives are remarkable. Samples maintained in THF at 0 °C showed 0.98 ± 0.02 B-H bonds per boron even after standing for the following times: $(Cl_2CHCO_2)_2BH$, 96 h (gelled after 120 h); $(PhCO_2)_2BH$, 244 h; $(p\text{-}ClC_6H_4CO_2)_2BH$, 277 h.

Monoacyloxyboranes ($RCO_2H + BH_3$). Although monoacyloxyboranes are extremely reactive intermediates, they can be prepared at low temperatures (Figures 1 and 2) and have a considerable life under these conditions. In a typical experiment, acetic acid was mixed with borane-THF (1:1) at −78 °C in THF. Once hydrogen evolution was complete, a 1-mL aliquot was removed and analyzed for residual hydride by hydrolysis. No reduction had taken place. Even after 10 h at −78 °C, no hydride uptake was observed. However, if the mixture were brought to 0 °C, hydride loss was rapid, with formation of the boroxine (vide infra). Pivalic acid also produced a stable monoacyloxyborane, the synthesis proceeding satisfactorily at −45 °C.

In light of the fact that $(PhCO_2)_2BH$-THF, $(Cl_2CHCO_2)_2BH$-THF, and $(ClCH_2CO_2)_2BH$-THF proved to be remarkably stable in THF, the possibility that a much stronger acid, such as trifluoroacetic, would form a stable monoacyloxyborane at the relatively high temperature of 0 °C was explored. Although THF solutions of $(CF_3CO_2)_3B$ and $(CF_3CO_2)_2BH$ rapidly polymerize THF, monotrifluoroacetoxyborane failed to promote such polymerization. Furthermore, the compound proved to be fairly stable in THF, losing no hydride in 24 h at 0 °C, and maintaining 93% of its original hydride activity after 72 h. An infrared spectrum of the compound in THF revealed that it too is a monomer without either bridged hydrogen or boron-carbonyl complexation. Consequently, it also must be stabilized by coordination with THF.

This appears to be the first monoacyloxyborane, stable at 0 °C, a new member of the general class of monofunctional boranes.

In carbon tetrachloride, $CF_3CO_2BH_2$ is less stable than in THF, slowly losing hydride. Presumably, its stability in THF is the result of weak THF complexation stabilized by the excess THF.

Reduction of Acyloxyboranes with Borane-THF. Mono-, di-, and triacyloxyboranes can now be made from the reaction of carboxylic acids with borane-THF. In order to explore their possible roles in the fast reduction of carboxylic acids by borane, we decided to investigate the rates and products formed from the reaction of individual acyloxyboranes with borane-THF.

Monoacetoxyborane, $CH_3CO_2BH_2$, was prepared by the 1:1 addition of acetic acid to borane-THF at −60 °C. The compound was maintained at −60 °C until hydrogen evolution was complete. It was then brought to 0 °C. The reduction was complete in 4 h. An infrared spectrum of the compound corresponded precisely with that of triethoxyboroxine (vide infra). This indicated that the reduction had proceeded as indicated by eq 7 (R = CH_3).

Table I. Reaction of Representative Carboxylic Acids with Borane-THF (3:1) at 0 °C

Acid[a]	Solvent	Time, h	Hydrogen[b] evolved	Anhydride[b,c] present	Hydride[b,d] present
2,4,6-Trimethyl-benzoic	THF	1.9	0.80		
		7.0	0.91	0.0	0.0
		24.0	0.91	0.0	0.0
Pivalic	THF	2.2	0.90		
		6.7	0.97	0.0	0.0
		24.0	0.97	0.0	0.0
Benzoic[e]	DG	1.0	0.25		
		3.5	0.75		
		8.0	1.00	0.0	0.0
		16.0	1.00	0.0	0.0
Benzoic	THF	2.5	0.70		
		7.0	0.76	0.0	0.33
		24.0	0.76	0.0	0.33
p-Chlorobenzoic	THF	2.0	0.67	0.0	0.28
		8.0	0.67	0.0	0.26
		24.0	0.67	0.0	0.22
Chloroacetic	THF	0.8	0.66	0.0	0.33
		4.2	0.66	0.0	0.33
		24.0	0.66	0.0	0.32
Acetic	THF	4.2	0.90		
		11.0	0.95	0.14 (84%)	0.0
		24.0	0.95	0.17 (100%)	0.0
Propanoic	THF	2.8	0.90		
		11.0	0.97	0.14 (84%)	0.0
		24.0	0.97	0.17 (100%)	0.0
n-Hexanoic	THF	2.2	0.90		
		4 9	0.96	0.13 (78%)	0.0
		24.0	0.96	0.17 (100%)	0.0
Cyclopropane-carboxylic	THF	0.90	0.80		
		7.0	0.92	0.14 (84%)	0.0
		24.0	0.92	0.16 (90%)	0.0
Formic	THF	0.3	0.40		
		1.0	0.47	0.0	0.32
		2.7	0.47	0.0	0.08
		6.3	0.47	0.0	0.01
		8.0	0.47	0.0	0.00
Trifluoroacetic	THF	1.1	0.63		
		4.5	0.73		
		7.2	0.73	Solution had gelled	
		24.0	0.73	Solid polymer had formed	
Trifluoroacetic[f]	CF_3CO_2H	1.0	1.00	0.0	0.0
		10.0	1.00	0.0	0.0
Trichloroacetic	THF	1.0	0.51		
		3.9	0.64		
		6.3	0.67		
		7.8	0.67		
		23.0	0.67	Solution had gelled	

[a] 6 mmol of BH_3 (18 mmol of hydride) added to 18 mmol of acid in 18 mL of solution; 1.0 M in acid and 1.0 M in hydride. [b] mmol/mmol of compound. [c] Analyzed by IR. 100% corresponds to 0.167 M. [d] Analyzed by injection of 1-mL aliquots of the reaction mixture into water-glycerine-THF and measuring the amount of hydrogen evolved with a 50-mL gas buret. [e] 3 mmol of BMS (9 mmol of hydride) added to 9 mmol of acid in 30 mL of solution; 0.3 M in acid and 0.3 M in hydride. [f] 10 mmol of BMS added to 10 mL of CF_3CO_2H.

$$RCO_2H + BH_3 \xrightarrow[THF]{-60\ ^\circ C} H_2 + RCO_2BH_2 \xrightarrow[THF]{0\ ^\circ C} {}^1/_3(RCH_2OBO)_3 \quad (7)$$

It was then decided to treat a diacyloxyborane at 0 °C with 1 equiv of BH_3-THF, and to compare the rate of hydride uptake and product formed with that of the reaction of the corresponding acid with 1 equiv of BH_3-THF at 0 °C. Dibenzoyloxyborane was chosen. Indeed, the rate of reduction and the product formed proved to be identical with those for the reduction of benzoic acid under the same conditions (eq 8).

$$(PhCO_2)_2BH + BH_3 \xrightarrow{0\ ^\circ C,\ THF} {}^2/_3(PhCH_2OBO)_3 \quad (8)$$
$$2PhCO_2H + 2BH_3 \xrightarrow[-2H_2]{0\ ^\circ C,\ THF}$$

Finally, the reduction of a triacyloxyborane was compared to that of the corresponding acid. The reduction of tripivaloxyborane (**7**) was compared with that of pivalic acid under identical conditions. Again, the rate of hydride uptake and the product formed were identical (eq 9).

$$(Me_3CCO_2)_3B + 2BH_3 \xrightarrow{0\ ^\circ C,\ THF} (Me_3CCH_2OBO)_3 \quad (9)$$
$$3Me_3CCO_2H + 3BH_3 \xrightarrow[-3H_2]{0\ ^\circ C,\ THF}$$

The results are summarized in Figures 3 and 4

Characterization of the Product: Trialkylboroxine. The reactions of benzoic or acetic acids with borane-THF in the ratio 1:1 were carried out at 0 °C. After quantitative hydrogen had evolved, the concentration of residual hydride was followed

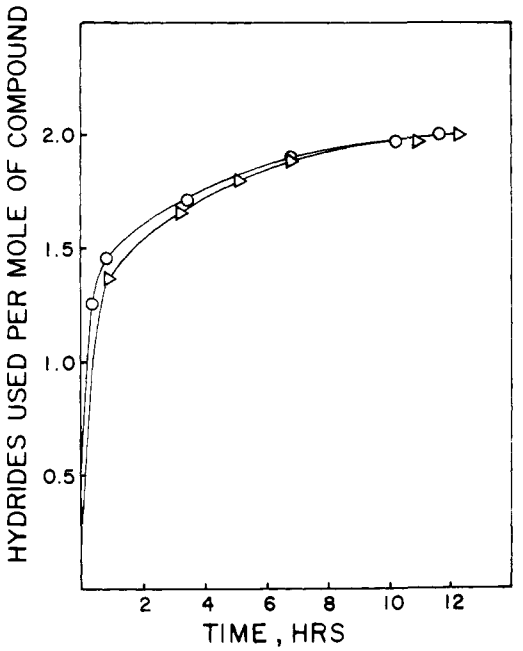


Figure 3. Comparison of the rate of hydride utilization at 0 °C for $(PhCO_2)_2BH + BH_3$, 0.667 M each in THF (△); and for $PhCO_2H + BH_3$, 1.33 M each in THF (○).

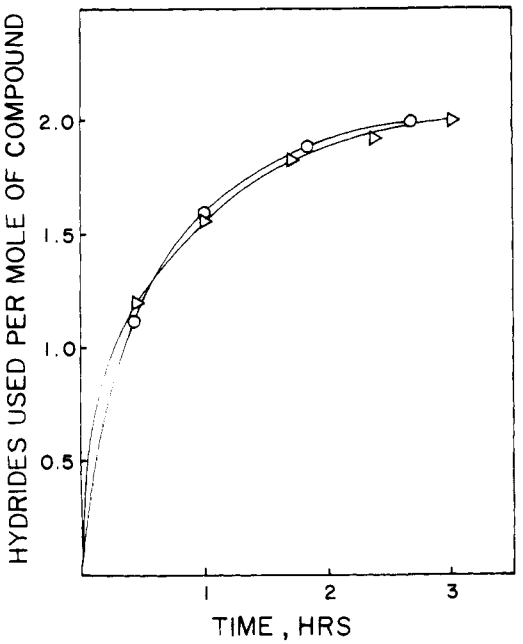


Figure 4. Comparison of the rate of hydride utilization at 0 °C for $(Me_3CCO_2)_3B$, 0.56 M, + 2 BH_3, 1.11 M, in THF (△); and for $Me_3CCO_2H + BH_3$, 1.67 M each in THF (○).

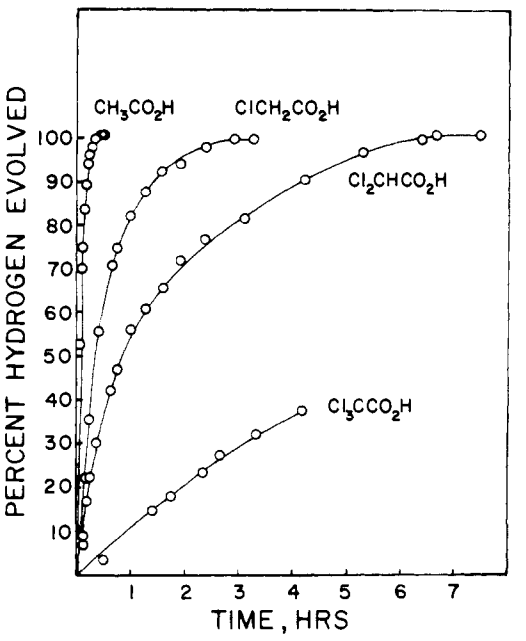


Figure 5. Rate of hydrogen evolution at −20 °C for the reaction of carboxylic acids with borane–THF, 0.05 M each in THF.

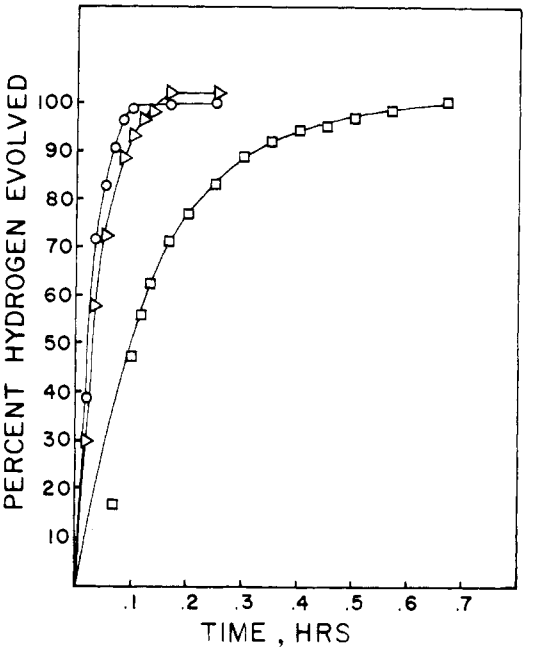


Figure 6. Rate of hydrogen evolution at 0 °C for the reaction of carboxylic acids with borane–THF, 0.05 M each in THF: ○, *p*-$MeOPhCO_2H$; △, $PhCO_2H$; □, *p*-O_2NPhCO_2H.

with time. The time for complete reduction for acetic acid was 3.5 h; for benzoic acid, 14 h. The products were isolated and examined by infrared[19] and ^1H NMR spectroscopy. The results indicate that the boroxines were indeed produced in high yield.

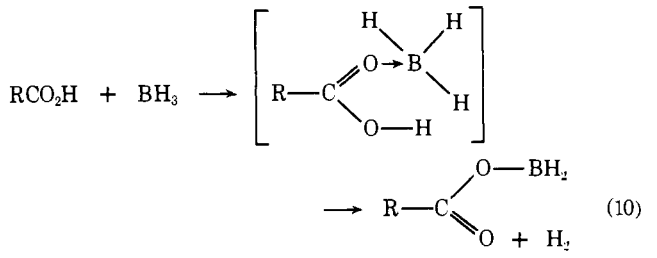
Mechanism of the Reduction of Carboxylic Acids with Borane–THF

Because many diverse acyloxy species can be produced in the simple reaction of 3 carboxylic acids with 1 BH_3–THF, it was decided to explore the question as to whether a general theory could be developed regarding the reduction pathway.

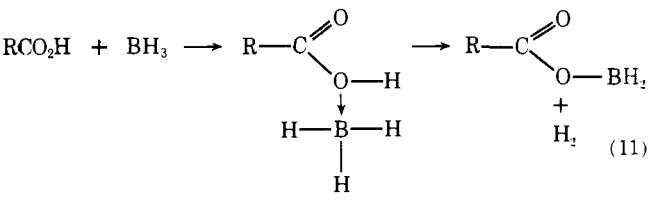
Initial Complex Formed. The first question to be considered was whether boron complexes with oxygen prior to hydrogen evolution. The idea of such coordination is not new. Prior coordination of borane with the carbonyl group had been proposed to explain the rates of reduction of ketones, esters, and aldehydes with borane.[20] Similar coordination with the hydroxyl group has also been proposed to explain the rates of alcoholysis of boranes.[21]

Accordingly, we treated various aliphatic and aromatic acids with borane–THF (1:1), and measured the rate of hydrogen evolution. The reactions are quite fast. Consequently, the reactions were run under relatively dilute conditions, 0.05 M, to ensure accurate rate measurements. The results are shown in Figures 5 and 6.

These results reveal that the stronger the carboxylic acid, the slower the evolution of hydrogen. Hence, a simple protonation of borane is not involved. The reaction can be envisioned as proceeding either according to eq 10 or eq 11.



(10)



(11)

It appears quite clear from the data that coordination of borane with the proton source is a necessary condition for reaction. The stronger the coordination, the faster the evolution of hydrogen.

As was pointed out earlier, in the reaction of carboxylic acids with borane (Figures 1 and 2) the rate of hydrogen evolution decreases as each successive carboxylic acid group becomes bound to boron (eq 3, 4, 5). This is fortunate, since it makes it possible to control the reaction so as to proceed to each successive stage. Can this behavior also be accounted for in terms of prior complexation?

The replacement of a hydrogen atom on boron by an acyloxy group would be expected to increase the Lewis acid acidity of the borane. Indeed, the isolation of stable THF complexes of dibenzoyloxyborane reveals that this substituted borane is a stronger acceptor than borane itself.[22] Why then do we observe decreasing rates of hydrogen evolution with increasing number of acyloxy groups? One reason may be that THF competes successfully with the carboxylic acid for the borane intermediate. Another possibility is that the hydridic character of the >BH bond is greatest in borane and diminishes with acyloxy substituents. Thus, we can rationalize the observations, but are not now in position to provide a definitive explanation for the observed decreasing rates with increasing acyloxy substitution.

The actual reduction step had been considered by us originally to occur through the triacyloxyborane[2,11] (eq 12)

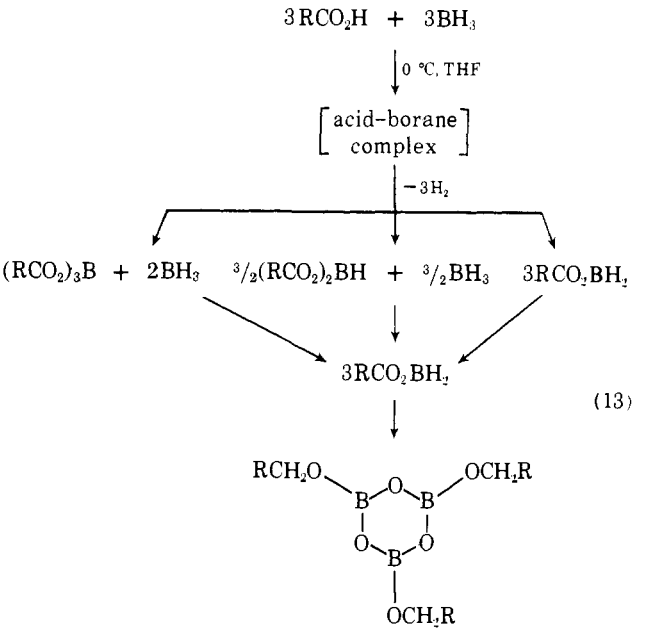
$$3RCO_2H + BH_3 \xrightarrow[THF]{0\ ^\circ C} 3H_2 + (RCO_2)_3B \xrightarrow[THF]{2BH_3} (RCH_2OBO)_3 \quad (12)$$

in cases where the diborane is added to the carboxylic acid. However, others have pointed out that such triacyloxyboranes often undergo dismutation to the anhydride and oxybis(diacyloxyborane) (eq 2) so that these may be the actual species undergoing reduction.[13]

Although we agree that triacyloxyboranes can undergo relatively rapid dismutation, we have always considered the reduction of carboxylic acids by borane-THF to be more rapid than that of the corresponding anhydride.[21] Consequently, it appeared questionable to postulate the formation of the anhydride as an intermediate in the reduction. We therefore undertook to compare carefully the rates of reduction of carboxylic acids and the corresponding anhydrides.

Reactivity toward Borane-THF. Carboxylic Acids vs. Anhydrides. Four representative carboxylic acids and their anhydrides were investigated at 0 °C in THF (Table II). In all cases the carboxylic acid was reduced at an appreciably faster rate than its anhydride. Consequently, it appears that the dismuted products (eq 2) are not intermediates in the reduction of carboxylic acids. In view of the data presented here, it is also clear that the triacyloxyborane cannot be an important intermediate.

Monoacyloxyborane as the Intermediate. We are faced with an interesting alternative. We have shown above that in THF some acids do not form triacyloxyboranes (i.e., $ClCH_2CO_2H$, Cl_2CHCO_2H, *p*-$ClPhCO_2H$, $PhCO_2H$), while others do not easily form diacyloxyboranes (CF_3CO_2H, CCl_3CO_2H). However, in all cases the monoacyloxyborane is easily formed. In all cases, the same product, a trialkoxyboroxine, appears to be formed (eq 7). Furthermore, since the rate of reduction is the same, regardless of whether we start with the acid, the monoacyloxyborane, the diacyloxyborane, or the triacyloxyborane (eq 7, 8, 9), we are left with the conclusion that the same reduction intermediate may be involved in all cases. Thus, no matter which acyloxyborane is initially formed, we propose that the reduction proceeds through the same intermediate, formed by exchange with free BH_3-THF in solution (eq 13).



(13)

Conclusion

Although the remarkably rapid, highly selective reduction of carboxylic acids with borane-THF has been an exceptionally useful synthetic procedure for years, only now have we gained some insight into the mechanism of the reaction. It appears clear that the essential intermediate is the monoacyloxyborane. The study has had other important consequences. It has provided the first unambiguous examples of triacyloxyborane sufficiently stable to permit isolation and characterization. It has opened up a convenient synthetic route to a wide variety of diacyloxyborane-THF complexes. Finally, it has established conditions for preparing and studying monoacyloxyboranes in solution, as well as one example of a relatively stable monoacyloxyborane.

Experimental Section

Infrared spectra were recorded on Perkin-Elmer IR-137 or -700 spectrometers. Solutions were run using a sample cell containing the reaction mixture, compensated by a matched reference cell containing solvent. ^1H NMR spectra were recorded on a Varian T-60 (60 MHz) spectrometer. All ^1H chemical shifts are relative to tetramethylsilane (δ 0 ppm). ^{11}B NMR spectra were recorded on a Varian XL-100

Table II. Reaction of Borane-THF with Representative Carboxylic Acids and Their Anhydrides in THF at 0 °C

Carboxylic acid				Acid anhydride		
Acid[a]	Hydrogen[b] evolved	Hydride used[b,c] for redn	Time, h	Anhydride[d]	Hydrogen[b] evolved	Hydride used[b,c] for redn
Acetic	0.98		0.1	Acetic	0.00	
		0.86 (43%)	0.2			1.36 (34%)
		1.40 (70%)	0.5			1.88 (47%)
		1.67 (83%)	1.0			2.40 (60%)
		1.84 (92%)	2.0			2.92 (73%)
		2.00 (100%)	5.0			3.52 (88%)
			10.0			4.00 (100%)
Propanoic	1.00		0.1	Propanoic	0.00	
		1.28 (64%)	0.2			2.60 (65%)
		1.55 (77%)	0.5			3.04 (76%)
		1.76 (88%)	1.0			3.28 (82%)
		2.00 (100%)	2.5			3.64 (91%)
			4.0			3.84 (96%)
			5.5			4.00 (100%)
Hexanoic	0.99		0.1	Hexanoic	0.00	
		1.07 (54%)	0.2			1.80 (45%)
		1.34 (67%)	0.5			2.60 (65%)
		1.61 (80%)	1.0			3.00 (75%)
		2.00 (100%)	2.2			3.48 (87%)
			5.0			3.92 (98%)
			6.0			4.00 (100%)
Benzoic	1.02		0.3	Benzoic	0.00	
		0.68 (34%)	1.0			0.72 (18%)
		1.37 (68%)	5.0			1.48 (37%)
		1.70 (85%)	10.0			2.04 (51%)
		1.85 (93%)	15.0			2.48 (62%)
		2.00 (100%)	22.5			2.88 (72%)
			50.0			3.68 (92%)
			75.0			4.00 (100%)

[a] 10 mmol of acid added to 10 mmol of BH_3-THF (30 mmol of hydride) in 50 mL of solution: 0.2 M in acid and 0.6 M in hydride. [b] mmol/mmol compound. [c] See Table I, note *d*. [d] 10 mmol of anhydride added to 13.33 mmol of BH_3-THF (40 mmol of hydride) in 50 mL of solution; 0.2 M in anhydride and 0.8 M in hydride.

spectrometer (32.1 MHz). All ^{11}B chemical shifts are relative to boron trifluoride etherate (δ 0 ppm). Glassware was oven dried and cooled under a dry nitrogen atmosphere. All liquids were handled with syringes.[23] All manipulations were done under nitrogen.

Materials. THF was dried and distilled over lithium aluminum hydride and stored under nitrogen. Borane-THF was prepared from sodium borohydride and boron trifluoride etherate. Borane-methyl sulfide (BMS) was the commercial product, diluted in the appropriate solvent. The BH_3-THF and BMS were standardized by hydrolyzing a 1-mL aliquot of the solution with glycerine-water-THF mixture and measuring the hydrogen evolved. Carboxylic acids were the commercial products of the highest purity. They were further purified by distillation or recrystallization as necessary. In all cases, physical constants agreed satisfactorily with constants in the literature.

Stoichiometry of the Reaction of Carboxylic Acids with Borane-THF. Acetic acid is representative. To a 50-mL round-bottom flask equipped with side arm, stirring bar, and connecting tube attached to a gas buret apparatus were added 4.58 mL of acetic acid (80.0 mmol) and 10.7 mL of THF. The mixture was cooled to −78 °C using a dry ice-acetone bath. Then 11.4 mL of 2.34 M BH_3-THF (26.7 mmol) was slowly added. The rate of hydrogen evolved was followed with time. This procedure was repeated at −45 and 0 °C (Figure 1).

Triacyloxyboranes ($3RCO_2H + BH_3$). Acetic acid is representative. The experimental setup was the same as described above. To a 200-mL round-bottom flask immersed in an ice bath was added 5.41 g of acetic acid (90.0 mmol) followed by 69.5 mL of THF. After the mixture had cooled, 15.6 mL of 1.92 M BH_3-THF (30.0 mmol) was added within 10 min. Hydrogen evolution, 2140 mL (85.5 mmol), ceased within 10 h, corresponding to 0.95 mmol of H_2 per mmol of acid. The 1828-cm^{-1} anhydride carbonyl stretching frequency was monitored by IR. The concentration of acetic anhydride was found to be 0.14 M (84%) within 11 h, rising to a maximum of 0.167 M (100%) within 24 h. GLC analysis also revealed a concentration of 0.167 M (5% DOW-710 on Chromosorb W, 6 ft × 0.125 in. column). The solvent was removed under vacuum, leaving a white solid, crude weight 3.90 g [14.24 mmol, 95% based on **2** (R = CH_3)]. After recrystallization from $CHCl_3$-benzene, 3.15 g (77%) was isolated, mp 146-147 °C. Its ^1H NMR and IR spectra were identical with those of an authentic sample of **2** (R = CH_3), described below.

Preparation of Tris(trifluoroacetoxy)borane (5, R = CH_3). The same apparatus as described above was used. To 10 mL of trifluoroacetic acid at 0 °C was added 1 mL of 10.0 M BMS (10.0 mmol). After 0.5 h, hydrogen evolution, 713 mL (28.5 mmol), ceased. An IR spectrum of the mixture did not reveal any acid anhydride. The excess acid was stripped at 20 °C (20 mm), leaving 4.10 g of a viscous liquid, corresponding to a 99.5% yield of $(CF_3CO_2)_3B$-SMe_2. Pumping overnight at 0 °C brought the weight to 3.42 g, corresponding to a 97.8% yield of tris(trifluoroacetoxy)borane: mp 95 °C dec (lit.[14] 99 °C dec); IR (Nujol mull) 1780 (vs), 1660 (w), 1560 (sh), 1400 (vs), 1340 (sh), 1290 (s), 1190 (br, vs), 1050 (sh), 1020 (vs), 940 (sh), 875 (m), 850 (sh), 820 (s), 780 (s), 725 cm^{-1} (s), where vs = very strong; s = strong; m = moderate; w = weak; br = broad; and sh = shoulder.

Preparation of Oxybis(diacetoxyborane) (2, R = CH_3). To an oven-dried, nitrogen-flushed, 300-mL round-bottom flask with side arm and stirring bar, reflux condenser, connecting tube, and mercury bubbler was added 30.9 g (0.50 mol) of boric acid, followed by 165 mL of acetic anhydride (1.75 mol). While stirring, this slurry was brought slowly to 72 °C by means of an oil bath. At this temperature, a vigorous exotherm took place,[24] and the slurry became a clear, pale yellow solution within 10 s. Upon cooling, the product precipitated out as a white solid. The acetic acid was removed via a 15-gauge double-ended needle. The precipitate was recrystallized from 200 mL of chloroform-benzene and washed with 30 mL of this mixture: yield 54.5 g (79.7%); mp[25] 147-148 °C (lit.[9] 147-148 °C; IR (THF) 1746 (vs), 1605 (s), 1489 (s), 1420 (m), 1375 (s), 1330 (w), 1273 (s), 1250 (m), 1191 (vs), 1100 (m), 1000 (w), 805 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 2.27 (s, CH_3).

Tripivaloxyborane (7). IR (THF) 1728 (vs), 1595 (m), 1500 (m), 1482 (m), 1400 (m), 1370 (s), 1330 (sh), 1300 (s), 1236 (w), 1210 (sh), 1160 (s), 1100 (m), 1060 (sh), 840 (w), 760 cm^{-1} (w); ^1H NMR (THF) δ 1.15 (s, Me_3C); ^{11}B NMR (THF) +1.5 ppm.

Tris(2,4,6-trimethylbenzoyloxy)borane (6). Mp 180–181 °C; IR (THF) 1725 (vs), 1612 (s), 1590 (s), 1560 (m), 1520 (sh), 1510 (sh), 1500 (sh), 1480 (sh), 1445 (s), 1410 (m), 1385 (m), 1350 (w), 1335 (sh), 1282 (vs), 1270 (sh), 1187 (sh), 1165 (vs), 1100 (s), 850 (m), 828 (m), 810 (m), 770 (m), 750 cm^{-1} (m); ^1H NMR (CCl_4) δ 2.24 (s, 3 H, CH_3), 2.47 (s, 6 H, CH_3), 6.90 (s, 2 H, aromatic); ^{11}B NMR (THF) +1.7 ppm.

Preparation of Poly-THF. To an oven-dried, nitrogen-flushed, 100-mL round-bottom flask with side arm, stirring bar, and connecting tube attached to a gas buret setup was added 1.34 mL of trifluoroacetic acid (18.0 mmol), followed by 13.6 mL of THF. The mixture was cooled to 0 °C, and then 3.03 mL of 1.98 M BH_3–THF (6.0 mmol) was slowly added. Stirring at 0 °C, the solution gelled within 7 h, evolving 334 mL of hydrogen (13.4 mmol, 74%). Within 10 h a solid polymer had formed.

Diacyloxyboranes ($2RCO_2H + BH_3$). Benzoic acid is representative. The apparatus is the same as that described previously. In a 100-mL round-bottom flask was placed 4.37 g of benzoic acid (35.8 mmol), followed by 7 mL of THF. The mixture was cooled to 0 °C and then 7.64 mL of 2.34 M BH_3–THF (17.9 mmol) was slowly added. Hydrogen evolution, 914 mL (36.5 mmol), was over in 13 min. A small piece of vacuum tubing was attached to the connecting tube. To the other side of the tubing was inserted a male ball joint. The apparatus was weighed. It was then immersed into an ice bath and connected to a vacuum setup, which employed a 1-mm bore capillary stopcock. The flask was then opened to the vacuum, and the weight change was noted with time (Figure 3). A white, crystalline solid, whose weight corresponded to $(PhCO_2)_2BH$–THF, 5.84 g, mp 166–168 °C, resulted: IR (THF) 2525 (w), 1709 (sh), 1692 (s), 1602 (m), 1586 (m), 1450 (w), 1418 (w), 1335 (s), 1319 (vs), 1298 (vs), 1260 (sh), 1120 (s), 1065 (sh), 1016 (m), 951 (m), 840 (m), 822 (sh), 811 (m), 718 (s), 695 cm^{-1} (sh); ^1H NMR (CCl_4) δ 1.80 (m, 4 H, β THF protons), 3.72 (m, 4 H, α THF protons), 7.33 (m, 6 H, aromatic), 8.00 (m, 4 H, aromatic); ^{11}B NMR (THF) +4.8 ppm.

Bis(chloroacetoxy)borane–THF (8, R = $ClCH_2$). IR (THF) 2540 (w), 1720 (s), 1417 (m), 1378 (w), 1340 (sh), 1319 (vs), 1260 (w), 1206 (s), 1120 (vs), 1060 (sh), 1000 (sh), 978 (m), 865 (sh), 831 (m), 785 (w), 720 cm^{-1} (w); ^1H NMR (CCl_4) δ 1.88 (m, 4 H, β THF protons), 3.80 (m, 4 H, α THF protons), 4.08 (s, 4 H, $(ClCH_2CO_2)_2$); ^{11}B NMR (THF) +3.0 ppm.

Bis(*p*-chlorobenzoyloxy)borane–THF (8, R = *p*-ClPh). IR (THF) 2440 (w), 1724 (sh), 1710 (s), 1600 (m), 1440 (w), 1401 (m), 1350 (sh), 1335 (sh), 1305 (s), 1285 (m), 1135 (s), 1018 (w), 822 (w), 770 (m), 730 cm^{-1} (sh).

Monoacyloxyboranes ($RCO_2H + BH_3$). Acetic acid is representative. The same apparatus as described above was used. To a 50-mL round-bottom flask were added 1.34 mL of acetic acid (23.4 mmol) and 2 mL of THF. The solution was cooled to −60 °C, and very slowly 10.0 mL of 2.34 M BH_3–THF (23.4 mmol) was added, Hydrogen evolution, 588 mL (23.4 mmol), ceased after 4.1 h. A 1-mL aliquot of the mixture evolved 85 mL of hydrogen (3.40 mmol, 97% theoretical). The solution was warmed to 0 °C and the hydride uptake was followed with time. The following data is given in hydride concentration, time (h): 3.40, 0; 1.40, 0.5; 0.79; 1.0; 0.18; 2.0; 0.09; 3.0; 0.00, 4.0. IR and ^1H NMR data agreed exactly with those of triethoxyboroxine (below).

Formation of Trifluoroacetoxyborane–THF (3, R = CF_3). The same apparatus as described above was used. To a 50-mL round-bottom flask were added 4.3 mL of 2.34 M BH_3–THF (10 mmol) and 20 mL of THF. The mixture was cooled to −15 °C and 0.77 mL of trifluoroacetic acid (10 mmol) was slowly added. Hydrogen evolution, 247 mL (9.88 mmol), ceased after 2.6 h. A 1-mL aliquot evolved 20.0 mL of hydrogen (0.80 mmol, 100% theoretical). After 1 day, no hydride loss was observed. After 3 days, a 1-mL aliquot evolved 18.5 mL of hydrogen (0.74 mmol, 93% theoretical): IR (THF) 2450 (m), 1757 (s), 1198 (vs), 1180 (vs), 1150 (vs), 1010 (m), 840 (br, m), 797 (w), 784 cm^{-1} (w).

Reduction of Acyloxyboranes with Borane–THF. Reduction of tripivaloxyborane (7) is representative. The same apparatus as described above was used. To a 100-mL round-bottom flask was added 3.02 g of pivalic acid (29.6 mmol) followed by 4 mL of THF. The solution was cooled to 0 °C, and then 4.2 mL of 2.34 M BH_3–THF (9.86 mmol) was added. Hydrogen evolution, 728 mL (29.1 mmol), ceased within 3.0 h. To this reaction mixture was added dropwise at 0 °C 8.4 mL of 2.34 M BH_3–THF (19.7 mmol). Hydride uptake was then followed with time (Figure 4).

Reaction of Pivalic Acid with Borane–THF. The same apparatus as described above was used. To a 20-mL round-bottom flask were added 1.63 g of pivalic acid (16.0 mmol) and 1.1 mL of THF. The flask was then cooled to 0 °C, then 6.82 mL of 2.34 M BH_3–THF (16.0 mmol) was slowly added. Within 0.3 h the hydrogen evolution, 399 mL (16.0 mmol), stopped. The mixture was kept at 0 °C and the hydride concentration was followed with time (Figure 4).

The IR and ^1H NMR spectra of both reaction mixtures were identical with those of trineopentoxyboroxine (see below).

Isolation of the Final Product: a Trialkoxyboroxine. Acetic acid is representative. The same apparatus as described above was used. To a 100-mL round-bottom flask were added 1.81 g of acetic acid (30.1 mmol) and 13 mL of THF. The flask was cooled to 0 °C, and then 16.0 mL of 1.98 M BH_3–THF (31.6 mmol) was added over 13 min. Hydrogen evolution ceased within 15 min (772 mL, 30.9 mmol). The mixture was stirred for 4.5 h at 0 °C. Analysis of a 1-mL aliquot demonstrated complete uptake of hydride. The THF was removed using a water aspirator, yielding a colorless liquid, 1.83 g (94%): n^{20}_D 1.4069 (lit.[19] 1.4069); IR (salt plates) 1522 (w), 1488 (s), 1424 (s), 1378 (s), 1338 (s), 1288 (sh), 1208 (w), 1166 (w), 1108 (m), 1080 (m), 1050 (sh), 968 (w), 828 (w), 805 (w), 738 (sh), 721 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 1.25 (t, 3 H, CH_3), 4.02 (q, 2 H, CH_2).

Trineopentoxyboroxine. Mp 79–80.5 °C; IR (Nujol mull) 1520 (s), 1480 (s), 1462 (s), 1420 (s), 1395 (m), 1365 (s), 1340 (s), 1290 (vs), 1260 (vs), 1218 (s), 1118 (sh), 1080 (vs), 1055 (s), 1022 (m), 982 (m), 940 (sh), 918 (m), 880 (sh), 830 (w), 737 (sh), 720 (s), 670 cm^{-1} (w); ^1H NMR (CCl_4) δ 0.93 (s, 9 H, Me_3C), 3.57 (s, 2 H, CH_2); ^{11}B NMR (THF) +18.4 ppm.

Tribenzyloxyboroxine. n^{20}_D 1.5345; IR (thin film) 1600 (w), 1583 (w), 1515 (sh), 1498 (m), 1473 (vs), 1452 (vs), 1415 (vs), 1340 (vs), 1253 (m), 1215 (m), 1178 (w), 1160 (w), 1190 (s), 1070 (s), 1028 (s), 970 (w), 890 (w), 822 (w), 734 (s), 720 (sh), 698 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 5.03 (s, 2 H, CH_2), 7.33 (s, 5 H, aromatic).

Rates of Reaction of Boranes with Carboxylic Acid. Acetic acid is representative. The same apparatus as previously described was used. To a 200-mL round-bottom flask was added 97.6 mL of THF. The flask was immersed into an ice–salt bath (−20 °C), and 2.14 mL of 2.34 M BH_3–THF (5.0 mmol) was added. After the solution had cooled, 0.287 mL of acetic acid (5.0 mmol) was added all at once. The volume of hydrogen was followed with time (Figure 5).

Reactivity toward Borane–THF. Carboxylic Acids vs. Anhydrides. Acetic acid is representative. The same apparatus as described above was used. A 100-mL round-bottom flask was immersed in an ice bath. Then either 10.0 mmol of BH_3–THF was added for the reaction with carboxylic acids, or 13.33 mmol of BH_3–THF was added for the reaction with the anhydrides. A measured amount of THF was then added such that the total volume would be 50.0 mL once all of the reagents had been added, assuming additivity of volumes. A needle-type pyrometer was inserted through the septum of the side arm into the solution. After the mixture had reached 0 °C, either 0.57 mL of acetic acid or 0.94 mL of acetic anhydride (10 mmol) was added over a period of 10 min (it was found that if the addition was faster than this, the reaction temperature rose significantly). Thus the reaction mixtures were 0.2 M in acid and 0.2 M in borane, or 0.2 M in anhydride and 0.267 M in borane. The reaction temperature was maintained within a degree of 0 °C.

At appropriate intervals, 2-mL aliquots of the reaction mixture were analyzed for residual hydride. The percent reduction was based on 20 mmol of anhydride available for reduction of the acid, and 40 mmol of hydride available for reduction of the anhydride. The results are summarized in Table II.

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(17) It is known that a strong absorption at ~1600 cm^{-1} is indicative of a boron-coordinated carbonyl. See B. M. Mikhailov, P. P. Shorygin, B. V. Lopatin, O. G. Boldyreva, V. S. Bogdanov, and V. A. Dorokhov, *J. Gen. Chem. USSR* (*Engl. Transl.*), 2731 (1971), and references cited therein.
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(23) See H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes", Wiley-Interscience, New York, N.Y., 1975, Chapter 9.
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The Oxidation of Amines with Sulfonyl Peroxides. 3. Regioselectivities and Substituent Effects in the Oxidation of Benzylamines, and Kinetic Evidence for a Two-Electron Pathway[1]

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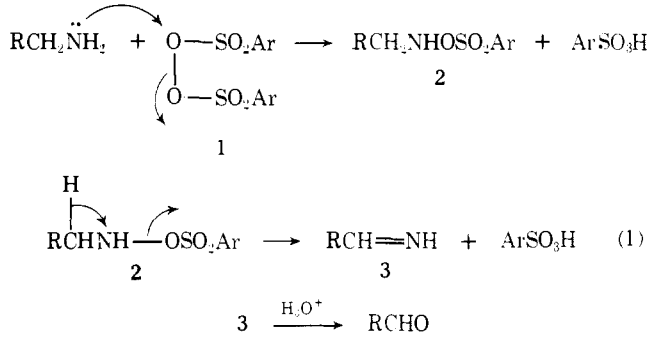
Abstract: A series of substituted primary benzylamines was oxidized with *p*-nitrobenzenesulfonyl peroxide (**1a**), and the results from substituent effects and kinetic studies favor a two-step, two-electron mechanism for this oxidation. The first step is nucleophilic attack by the amine on the peroxide bond which yields a hydroxylamine-*O*-*p*-nitrobenzenesulfonate adduct, **2**. Substituent effects for this step (k_1) were determined by the competitive method and from a Hammett plot, $\rho = -0.53$. Conductometric methods were used to study the rate constants for the second step (k_2), which is base-catalyzed elimination of **2** to the imine. For this, the slower step, Hammett treatment of the rate data gives $\rho = 0.24$ and $k_H/k_D = 4.2$. The regioselectivities for the oxidative deamination of *N*-alkylbenzylamines, **8**, were determined and are also consistent with the preferred two-electron oxidative pathway. The kinetics and substituent effects of imine-forming eliminations are available from this study, and the results are compared to analogous olefin-forming eliminations.

Amine oxidations display a rich diversity of mechanisms which depend on the oxidant, the amine type, the pH, and/or metal additives.[3] The reaction of amines with oxidants can occur at the nitrogen lone pair by one-electron or two-electron oxidation or reaction can occur at the α carbon atom by hydrogen abstraction. In fact a given oxidant may follow different pathways with different amines or competing pathways with the same amine.

It has been reported that arylsulfonyl peroxides $(ArSO_2O)_2$, **1**, react with a variety of primary and secondary amines to give oxidative deamination.[1b,4] This reaction is characterized by a general insensitivity of the reaction to amine structure, and aryl rearrangement to nitrogen where α hydrogens are lacking or where good migrating groups are present.[1a] Based on these observations, the process can be described mechanistically as a two-step, two-electron oxidation (eq 1). The first step is nucleophilic attack by the amine on the peroxide bond to give a hydroxylamine-*O*-arylsulfonate adduct **2**. The second step, which may be base catalyzed, is elimination of arylsulfonic acid from **2** to give the product imine **3** which can be isolated. Hydrolysis to the carbonyl compound completes oxidative deamination of the amine.

Amines are well known to react nucleophilically with peroxides, particularly acyl peroxides, yielding *O*-acylhydroxylamines.[5] These can be isolated[5e] in certain cases, but in solution



(1)

they decompose to other products. Furthermore, sulfonyl peroxides react electrophilically with π donors by two-electron donation to the peroxide bond.[6] The second step of eq 1 is elimination of arylsulfonic acid to give the imine product. Eliminations to give carbon–nitrogen π bonds have been discussed for nitrile-forming eliminations from imines[7] and for imine formation from *N*-halo amines.[8] The good leaving ability of the arylsulfonate group in **2** would promote such a polar elimination.

While there exist good and precedented arguments for the mechanism depicted in eq 1, several alternate pathways can account for the observed products. These involve free-radical