Notes

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Reactions of Trialkylborane. VI.[1] Reduction of Carbonyl Compounds with Trialkylborane

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The reduction of anhydrides, lactones, esters, carboxylic acids and acyl chlorides with trialkylborane is described. Cyclic anhydrides were reduced with 4 mol eq of trialkylborane at temperatures above 300 °C to give diol derivatives *via* the lactones. Lactones, esters, carboxylic acids and acyl chlorides were reduced under similar conditions to give the corresponding alcohol derivatives.

Keywords——reduction; trialkylborane; anhydride; lactone; ester; carboxylic acid; alcohol; carbonyl compound

In the previous paper,[2] we reported that aromatic aldehydes afforded the corresponding styrene derivatives when heated directly with trialkylborane, whereas the similar reaction (using 2 mol eq of trialkylborane) of carboxylic acids, acyl halides and anhydrides gave the corresponding esters. The present paper deals with the reduction of these acylating agents with trialkylborane under improved conditions using 4 mol eq of trialkylborane at temperatures above 300 °C.

Biphenyl-2,2′-dicarboxylic anhydride (**3**) was directly heated with 2 mol eq of tricyclohexylborane (**1**) at 200 °C to give 2-hydroxymethylbiphenyl-2′-carboxylic acid lactone (**4**), and the similar reaction using 4 mol eq of **1** or trihexylborane (**2**) at 300—320 °C gave 2,2′-dihydroxymethylbiphenyl (**5**). Similarly, as shown in Chart 1, naphthalene-1,8-dicarboxylic anhydride (**6**) and phthalic anhydride (**7**) gave the corresponding reduced products **8**—**10**. It was reported that alkyl benzoate was obtained by the reaction of benzoic anhydride (**11**) with trialkylborane (2 mol eq) at 260—290 °C, but the similar reaction of **11** using 4 mol eq of trialkylborane **2** at 300—320 °C afforded benzyl alcohol (**12**) as a main product.

Since it was presumed that alcohols were obtained *via* the lactones (esters) as above, lactones **4** and **9**, hexyl benzoate (**14**), dihexyl biphenyl-2,2′-dicarboxylate (**15**) and dimethyl biphenyl-2,2′-dicarboxylate (**16**) were treated with 2—4 mol eq of trialkylborane under similar conditions to give the corresponding alcohol derivatives (Chart 2). However, dicyclohexyl phthalate (**17**) was not reduced under similar conditions, presumably because of steric hindrance.

Furthermore, in order to examine the reactivity of carboxylic acids and acyl chlorides with trialkylborane, benzoic acid (**18**), benzoyl chloride (**19**), biphenyl-2,2′-dicarboxylic acid (**20**), phthaloyl chloride (**21**) and 2-*p*-toluoylbenzoic acid (**22**) were treated with 2—4 mol eq of trialkylborane to give the corresponding reduced products as shown in Chart 3. Compounds **21** and **22** bearing a carbonyl group at the *ortho* position were treated with 2 mol eq of trialkylborane to give the corresponding lactones.

In contrast with the previous finding[2] that alkylated esters were formed with 2 mol eq of

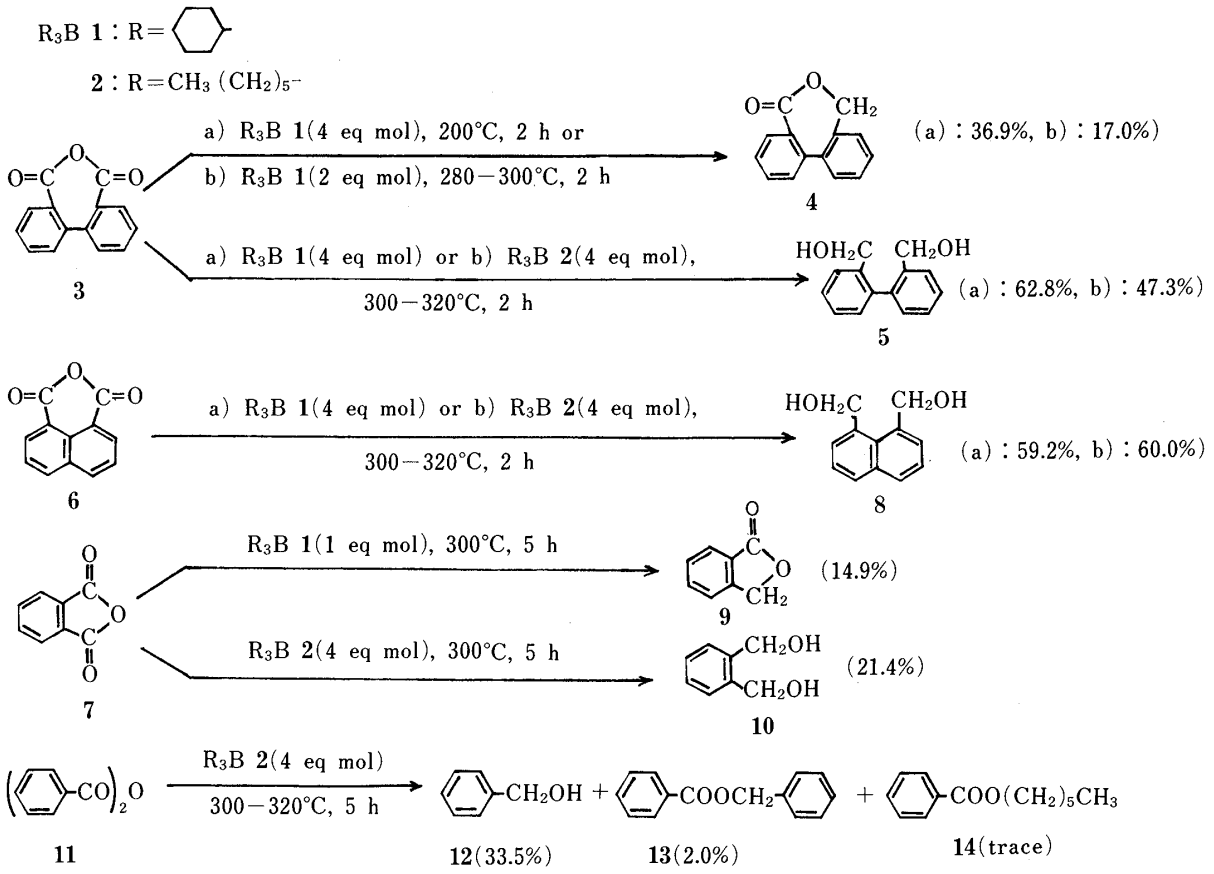

Chart 1

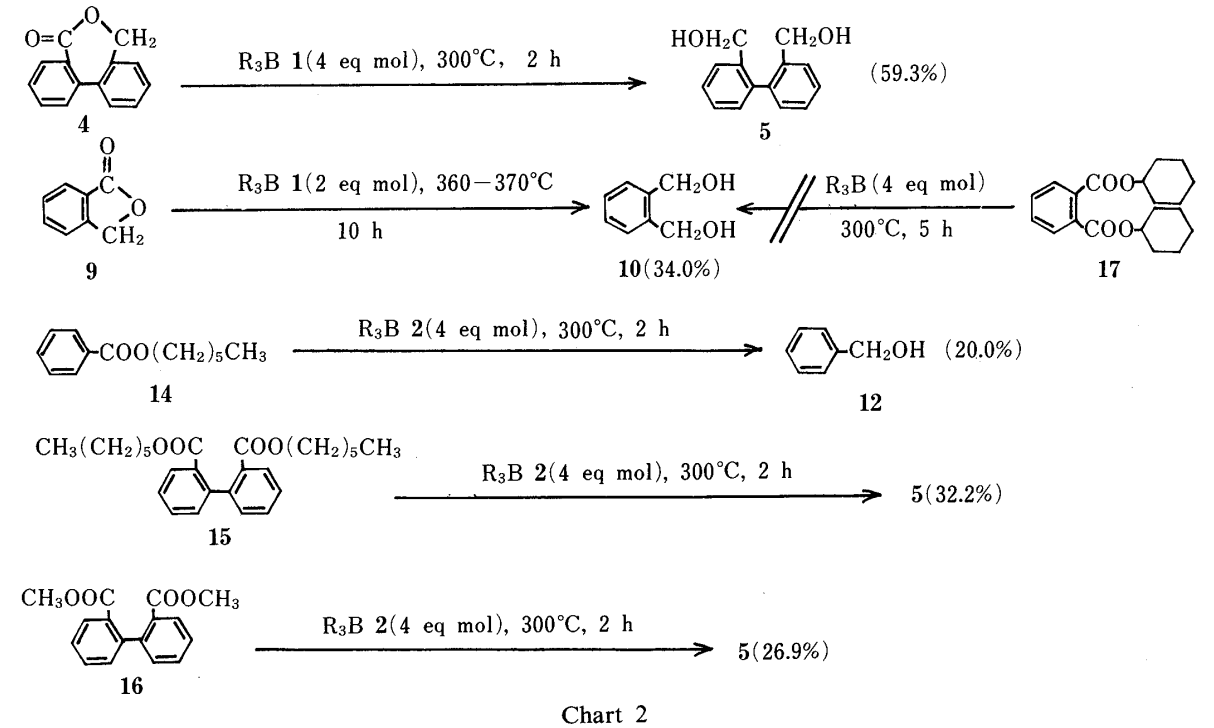

Chart 2

trialkylborane at 260—290 °C, as described above, carboxylic acids, acyl chlorides and anhydrides were reduced with 4 mol eq of trialkylborane at temperatures above 300 °C to give alcohols (*via* the lactones or esters).

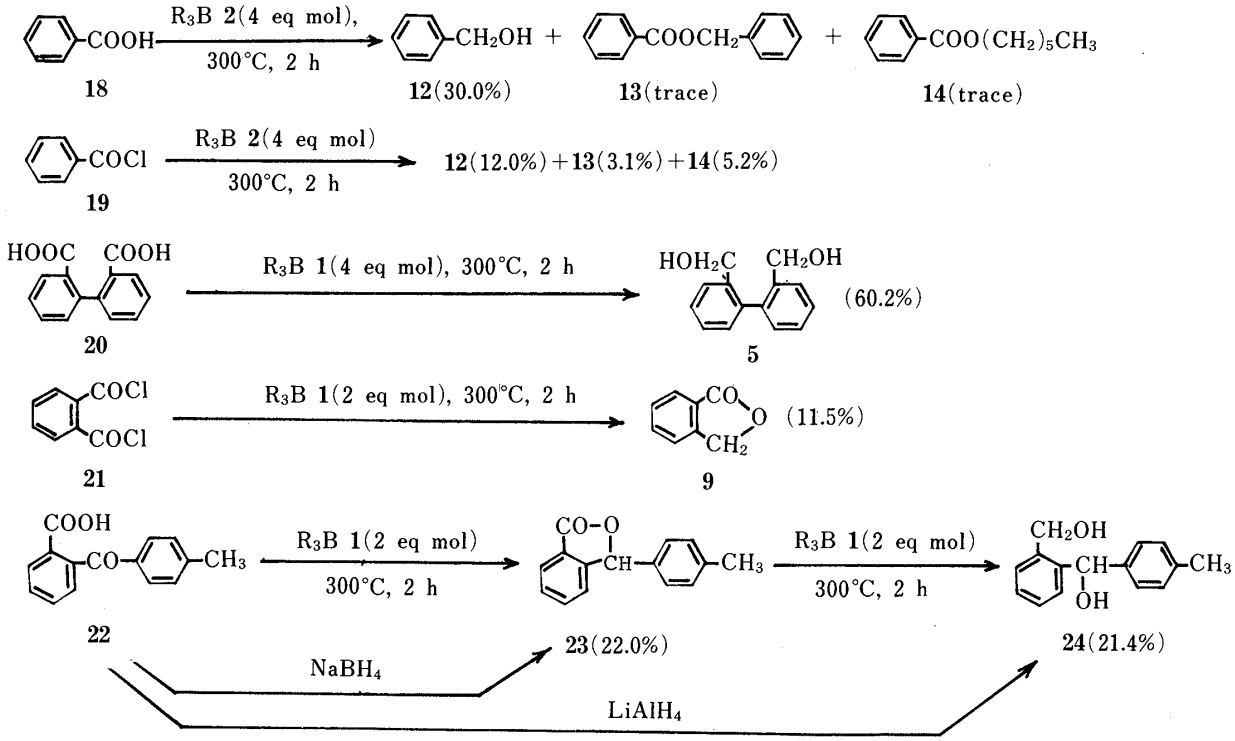

Chart 3

TABLE I. Reaction of the Cyclic Anhydride **3** with Trialkylborane **2** in the Presence of a Radical Scavenger (Galvinoxyl)

Anhydride (mmol)	R_3B (mmol)	Galvinoxyl mol%[a]	Temperature (°C)[b]	Time (min)	Product	Yield (%)
3 (5)	**2** (20)	5	300—320	10	**5**	39.2
3 (5)	**2** (20)	5	300—320	30	**5**	29.9
3 (5)	**2** (20)	5	300—320	60	**5**	58.5
3 (5)	**2** (20)	5	300—320	120	**5**	53.9
3 (5)	**2** (20)	0	300—320	10	**5**	58.1
3 (5)	**2** (20)	0	300—320	30	**5**	52.6
3 (5)	**2** (20)	0	300—320	60	**5**	53.5
3 (5)	**2** (20)	0	300—320	120	**5**	60.0

a) mol% against trialkylborane. *b*) Temperature of the metal bath.

It has been reported that the reaction of trialkylborane proceeds by a free radical mechanism,[3a-f] and trialkylborane reacts readily with oxygen to give organoperoxyborane.[4] In the previous report,[2] it was shown that phenothiazine (a radical scavenger) inhibited the reaction of carboxylic acids with trialkylborane. Since it was presumed that the reductions described above proceeded by a radical mechanism, the similar reaction of the anhydride **3** was examined in the presence of galvinoxyl (a radical scavenger). However, these experiments did not reveal a clear inhibitory effect of the radical scavenger (Table I).

It has been reported that the radical reaction of trialkylborane is not always suppressed by radical scavengers.[5] On thermal treatment, trialkylboranes liberate olefin and hydrogen with the formation of cyclic species.[6] Trialkylboranes also afford alkyl radicals through a radical chain reaction in the presence of oxygen.[3d,e] Taking into account the formation of alkene from alkyl radical, these reports suggest that trialkylboranes act as reducing agents in the presence of oxygen at high temperature, and it can be assumed that the reductions

described above proceed by a radical mechanism.

Further studies on the reaction mechanisms are in progress.

Experimental

Commercially available cyclic anhydrides, acids, acyl chlorides and sodium borohydride were used throughout this work. Diglyme was distilled from $LiAlH_4$ (a small excess over that required to react with active hydrogen impurities) under reduced pressure, and tetrahydrofuran (THF) was distilled from $LiAlH_4$. Melting points were determined on a Yanagimoto micro-melting point apparatus, model MP-S3, and are uncorrected. Infrared (IR) spectra were measured in Nujol mulls or as liquid films with a Nihonbunko IRA-1 infrared spectrometer, and ultraviolet (UV) spectra were recorded on a JASCO Uvidec-505 ultraviolet spectrometer. Mass spectra (MS) were recorded with a JEOL-D100 mass spectrometer, and gas chromatography was done on a JEOL JGC-20K gas chromatograph. Chromatography columns of alumina were prepared with Aluminiumoxid 90 (70—230 mesh ASTM; Merck). Nuclear magnetic resonance (NMR) spectra were recorded on a Hitachi R20-A spectrometer; chemical shifts are expressed in δ value (ppm) with tetramethylsilane as an internal standard (s=singlet, d=doublet, m=multiplet).

Reaction of Cyclic Carboxylic Anhydrides 3 and 6 with Trialkylborane——The mixture of the anhydride **3** or **6** (4 mmol) and trialkylborane (in the molar ratios shown in Chart 1) was heated in the absence of solvent for 2 h over a metal bath at the reaction temperature shown in Chart 1. The reaction mixture was brought to room temperature, 5 ml of water was cautiously added, followed by 3 ml of 3 M sodium hydroxide, and oxidation of unreacted trialkylborane was carried out by the slow addition of 3 ml of 30% hydrogen peroxide, maintaining the temperature below 30 to 40 °C. The reaction mixtures of the anhydride **3** using 2.0 mol eq (at 280—300 °C) and 4.0 mol eq (at 200 °C) of trialkylborane **1** were acidified by the addition of 10% hydrochloric acid. The acidic solution was extracted with ether, then the extract was dried over anhydrous magnesium sulfate, and evaporated. The residue was chromatographed over silica gel (column) using pet. ether as the eluent. The eluate was evaporated, and the residue was recrystallized from ether to give 2-hydroxymethylbiphenyl-2′-carboxylic acid lactone **4** as colorless needles, mp 135—136 °C (lit.[7] mp 136—136.5°C). IR ν_{max}^{Nujol} cm^{-1}: 1705 (C=O). UV $\lambda_{max}^{methanol}$ nm: 250. ^{1}H-NMR (10% solution in $CDCl_3$) δ: 5.0 (2H, s, OCH_2), 7.2—8.2 (8H, m, arom. protons). This product was identical with an authentic sample on the basis of mixed melting point determination and IR, UV and NMR spectral comparisons. In the experiment with the anhydride **3** and 4.0 mol eq of trialkylborane **1** or **2** at 300—320 °C (Chart 1), after the treatment with hydrogen peroxide, the precipitate was collected and recrystallized from ether to give the diol **5** as colorless needles, mp 105 °C (lit.[8] mp 110.5—111.5 °C). IR ν_{max}^{Nujol} cm^{-1}: 3240 (OH), 3320 (OH). UV $\lambda_{max}^{methanol}$ nm: 223. MS *m/e*: 214 (M^+). *Anal.* Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.18, H, 6.42. This product was identical with a product which was obtained by the reduction of **3** with $LiAlH_4$. The crude crystals obtained from the reaction mixture of the anhydride **6** and 4.0 mol eq of trialkylborane **1** or **2** at 300—320 °C were recrystallized from chloroform to give the diol **8** as colorless needles, mp 156—158 °C (lit.[9] mp 157—158 °C). IR ν_{max}^{Nujol} cm^{-1}: 3230 (OH), 3330 (OH). UV $\lambda_{max}^{methanol}$ nm: 226, 284. MS *m/e*: 188 (M^+). ^{1}H-NMR (10% solution in $CDCl_3$) δ: 3.22 (2H, s, OH), 5.17 (4H, s, benzyl protons), 7.3—7.9 (6H, m, arom. protons). This product was identical with a sample obtained by reduction of the anhydride **6** with $LiAlH_4$.

The yields of products are shown in Chart 1.

Reaction of Phthalic Anhydride (7) with Trialkylborane——The mixture of **7**(0.59 g, 4 mmol) and **1** (4 mmol) was heated directly for 5 h in a metal bath (bath temperature 300 °C). After treatment of the reaction mixture (unreacted trialkylborane) with hydrogen peroxide, the basic solution was acidified by the addition of 10% hydrochloric acid, and extracted with ether. The extract was dried over anhydrous magnesium sulfate and evaporated, and the residue was chromatographed over a silica gel column using pet. ether as the eluent. The eluate was evaporated, and the residue was recrystallized from ether to give the lactone **9** as colorless prisms, mp 73 °C (lit.[10] mp 71—73 °C), 80 mg (14.9%). IR ν_{max}^{Nujol} cm^{-1}: 1765 (C=O). This product was identical with an authentic sample on the basis of mixed melting point determination and comparisons of IR and UV spectra. Similarly, after the reaction of the anhydride **7** (0.59 g, 4 mmol) and trialkylborane **2** (4.16 g, 16 mmol), the residue was chromatographed over an alumina column. The fraction eluted with chloroform was evaporated, and the residue was recrystallized from ether to give 118 mg of the diol **10** as colorless needles, mp 63 °C (lit.[11] mp 64 °C). This product was identical with an authentic sample on the basis of mixed melting point determination and comparisons of IR and UV spectra.

Reaction of Benzoic Anhydride (11) with Trialkylborane (2)——A mixture of **11** (0.90 g, 4 mmol) and **2**(4.26 g, 16 mmol) was heated directly for 2 h at 300 °C (bath temperature). The reaction mixture was treated as described above, and trace amounts of the ester **14** were obtained from the fraction eluted with pet. ether. IR ν_{max}^{film} cm^{-1}: 1720 (C=O). This product was identical with an authentic sample, based on IR and UV spectral comparisons. The fraction eluted with benzene was evaporated, and the residue was distilled *in vacuo* to afford 17 mg (2.0%) of the ester **13**, bp 188—191 °C (16 mmHg) (lit.[12] bp 185 °C (15 mmHg)). This was identical with an authentic sample, based on comparisons of IR and UV spectra. The fraction eluted with chloroform was evaporated, and the residue was distilled to give 145 mg (33.5%) of benzyl alcohol (**12**), bp 204 °C.

Reaction of the Lactones 4 and 9 with Trialkylborane (1)——The mixture of **4** (1.01 g, 4 mmol) and **1** (4.16 g, 16 mmol) was reacted in the same manner as described above, and the reaction mixture was extracted with ether. The extract was dried over anhydrous magnesium sulfate. The ether and cyclohexanol were evaporated off, and the residue was chromatographed over alumina (column). The fraction eluted with chloroform was evaporated, then the residue was recrystallized from ether to give 609 mg (59.3%) of the diol **5**, mp 105—108 °C. Similarly, treatment of the lactone **9** (1.07 g, 8 mmol) with trialkylborane **1** (4.16 g, 16 mmol) gave 375 mg (34.0%) of the diol **10**, mp 63 °C. The reaction conditions are given in Chart 2.

Reaction of the Esters 14, 15 and 16 with Trialkylborane (2)——A mixture of an ester (4 mmol) and **2** (4.26 g, 16 mmol) was heated at 300 °C for 2 h, and treated as described above to give the alcohol **12** (86 mg, 20.0%), the diol **5** (276 mg, 32.2%) and the diol **5** (230 mg, 26.9%) from **14**, **15** and **16**, respectively (Chart 2).

Reaction of Benzoic Acid (18) and Benzoyl Chloride (19) with Trialkylborane (2)——A mixture of **18** (0.49 g, 4 mmol) or **19** (0.56 g, 4 mmol) and **2** (4.26 g, 16 mmol) was reacted as described above, and the reaction mixture was chromatographed over an alumina column. The reaction of the acid **18** gave 120 mg (30.0%) of the alcohol **12** (the fraction eluted with chloroform), a trace of the ester **13** (the fraction eluted with benzene) and a trace of the ester **14** (the fraction eluted with pet. ether). Similar reaction of **19** gave 50 mg (12.0%) of **12**, 10 mg (3.1%) of **13** and 40 mg (5.2%) of **14** (Chart 3).

Reaction of the Carboxylic Acid (20) with Trialkylborane (1)——A mixture of **20** (0.49 g, 2 mmol) and **1** (2.08 g, 8 mmol) was reacted similarly, treated with hydrogen peroxide, and extracted with ether. After removal of ether and cyclohexanol, the residue was chromatographed over an alumina column. The fraction eluted with chloroform was evaporated, and the residue was recrystallized from ether to give 260 mg (60.2%) of the diol **5**, mp 107—109 °C (Chart 3).

Reaction of Phthaloyl Chloride (21) with Trialkylborane (1)——Amixture of **21** (1.01 g, 5 mmol) and **1** (2.80 g, 10 mmol) was reacted under the conditions shown in Chart 3 to give 75 mg (11.5%) of the lactone **9**, mp 73 °C.

3-*p*-Toluoylphthalide (23)——A mixture of 2-*p*-toluoylbenzoic acid (**22**) (2.36 g, 10 mmol) and trialkylborane **1** (5.2 g, 20 mmol) was reacted in the same manner as above, and the residue was chromatographed over an alumina column. The fraction eluted with pet. ether–benzene (1 : 1) was evaporated and the residue was recrystallized from ether to give 448 mg (20.0%) of **23** as colorless needles, mp 125 °C (lit.[13] mp 127—128 °C). IR ν_{max}^{Nujol} cm^{-1}: 1755 (C=O). MS *m/e*: 224 (M^+). This product was identical with that obtained by reduction of the acid **22** with $NaBH_4$.

2-Hydroxymethyl-4′-methylbenzhydrol (24)——A mixture of **23** (0.67 g, 3 mmol) and trialkylborane **1** (1.56 g, 6 mmol) was reacted in the same manner as described above, and the residue was chromatographed over an alumina column. The fraction eluted with chloroform was evaporated, and the residue was recrystallized to give 105 mg (15.4%) of **24** as colorless needles (from ether), mp 89—92 °C (lit.[14] mp 98 °C). IR ν_{max}^{Nujol} cm^{-1}: 3240 (OH). MS *m/e*: 228 (M^+). *Anal.* Calcd for $C_{15}H_{16}O_2$: C, 78.94; H, 7.01. Found: C, 79.31; H, 7.11. This product was identical with that obtained by reduction of the lactone **23** with $LiAlH_4$ in THF (Chart 3).

Reaction of the Anhydride (3) with Trialkylborane (2) in the Presence of a Radical Scavenger——A mixture of **3** (1.12 g, 5 mmol), **2** (5.32 g, 20 mmol) and galvinoxyl (molar quantities are shown in Table I) was heated at 300—320 °C for the time shown in Table I, and treated as described above. The product and yield are shown in Table I.

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