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**TRIETHYLAMINE BORANE — A STABLE, EFFICIENT AND SAFE  
REDUCTANT FOR TRANSFORMING CARBOXYLIC ACIDS  
TO PRIMARY ALCOHOLS**

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Triethylamine borane,  $(C_2H_5)_3N.BH_3$ , is a stable, safe and readily available reagent which at  $80^\circ C$  reduces carboxylic acids to primary alcohols in high yields; functional derivatives of carboxylic acids such as esters, nitriles or amides are virtually nonreactive with this reagent under the same conditions. Aldehydes, ketones and acid chlorides, however, react readily. No solvent is required for the process.

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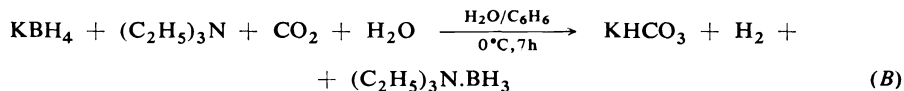
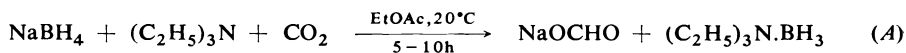
Carboxylic acids can be reduced to primary alcohols only by using very efficient hydride reagents in aprotic solvents. It is particularly complex aluminium hydrides and diborane that exhibit a sufficient reducing capacity. Acids are substantially more difficult to reduce by complex aluminium hydrides than the corresponding esters are<sup>1</sup>, probably on account of formation of low-soluble primary products. Diborane added in appropriate quantities and reacted at temperature below  $20^\circ C$ , on the other hand, reduces preferentially carboxylic acids in the presence of esters, nitriles, epoxides or nitro groups<sup>2-5</sup>. Used in excess and at higher temperatures, diborane easily reduces amides and nitriles of all types. Preparation and handling of free diborane in a conventional laboratory is rather hazardous and the reagent for this must always be fresh. Perhaps this is the reason why this elegant method has not found widespread use.

Dimethylsulfide borane,  $(CH_3)_2S.BH_3$ , is similarly efficient; its solution in excess of dimethyl sulfide is actually used in practice<sup>5</sup>. Although such a solution is appreciably safer to handle, the other safety requirements are the same as with diborane itself, and the reagent has to be prepared by dissolving diborane in dimethyl sulfide anyway<sup>6</sup>. Reduction of carboxylic acids with pyridine borane  $C_5H_5N.BH_3$  has also been reported, the yields, however, are low<sup>7</sup> and the reagent is thermally unstable and decomposes readily during storage.

It is noteworthy that the reducing properties of triethylamine borane,  $(C_2H_5)_3N.BH_3$  (TEB), have not been so far studied systematically, although this substance is easily available in the laboratory<sup>8</sup>, stable in inert atmosphere and withstanding heating at  $80^\circ C$  for 24 h or even at  $150^\circ C$  for several hours. The reagent is also

remarkably resistant to air humidity and oxygen. Its solvolysis only takes place on a long-term action of mineral acids. It is not pyrophoric and is virtually nontoxic.

Triethylamine borane can be synthesized on a large scale from sodium or potassium borohydride (Scheme 1).



#### SCHEME 1

##### Preparation of TEB

The two reactions have been described in patent literature and we tested both of them many times. The yields are about 80% in both cases.

An advantage of the former reaction<sup>9</sup> is that it is not accompanied by evolution of hydrogen, the finest  $\text{NaBH}_4$ , however, must be used. The reverse is true of the latter reaction<sup>10</sup>: it is not sensitive to the texture of the borohydride, the vigorous evolution of hydrogen, however, is a problem.

In the present paper we demonstrate that TEB exhibits remarkable reducing properties. Results of analytical survey experiments, evaluated gas chromatographically, are given in Table I, documenting that not only aldehydes, ketones or acid chlorides but also free carboxylic acids are very well reduced by TEB to the corresponding alcohols. Esters, amides and nitriles, on the other hand, remain unreduced even at 80°C.

Table I demonstrates that the result of the process is primarily dependent on the substrate-to-TEB ratio and that various unexpected by-products are formed. For instance, hexanal gives not only hexanol but also ethyl and hexyl hexanoates. This indicates that the starting aldehyde undergoes disproportionation in the sense of Tishchenko's reaction. The only conceivable source of ethyl groups for ethyl hexanoate is the triethylamine part of TEB, hence, the reaction is complicated by ethyl group transfer from the nitrogen. It is interesting that in the case of sterically unhindered aldehydes, dimerization plays a role at TEB/substrate ratios higher than 1; so, 1-dodecanol and dodecyl hexanoate were found in the products of reaction of hexanal with TEB.

Hexanoic acid and the sterically more demanding 2-ethylhexanoic acid were used as model substrates for optimizing the conditions of reduction of carboxylic acids. Tables II and III demonstrate that the side products (esters) are formed particularly at TEB/RCOOH ratios lower than 1 and at temperatures below 80°C. The formation

of unwanted esters then is very marked particularly in the case of the linear acid; with the sterically more hindered branched acid it is appreciably lower,

On the other hand, at the ratio  $\text{TEB}/\text{RCOOH} = 1.5$  and temperature  $80^\circ\text{C}$ , primary alcohols are virtually the sole products, formed in exceedingly high yields. Additional increase in the  $\text{TEB}/\text{RCOOH}$  ratio is undesirable. As in the reduction of aldehydes, dimerization products were also found in the reaction mixture. Higher polymerization is not ruled out, as the distillation residue indicates.

We suggest that the effects observed can be interpreted in terms of Schemes 2 and 3.

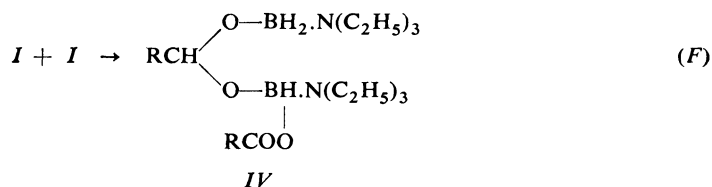
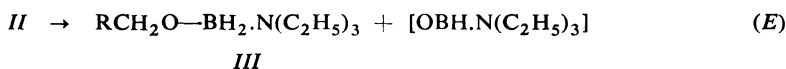
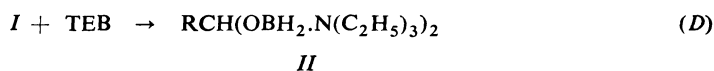
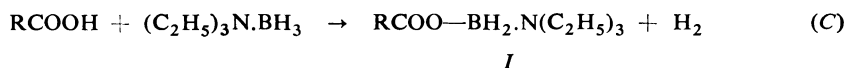
The assumed occurrence of the intermediate II can well account for even a slight excess of TEB having a substantial effect on the good yield of the alcohol, particularly if reaction (D) is assumed to proceed at a sufficient rate at temperature about  $80^\circ\text{C}$  only. Excess TEB may also counteract the formation of the intermediate IV, which

TABLE I  
Reduction of aldehydes, ketones and carboxylic acid derivatives with triethylamine borane (TEB) at  $80^\circ\text{C}$  and TEB/substrate ratio  $r$

Compound	$r$	Time h	Unreacted %	Products	Yield %
Hexanal	0.5	2	—	1-hexanol	58
				ethyl hexanoate	27
				hexyl hexanoate	15
Hexanal	0.67	15	—	1-hexanol	64
				ethyl hexanoate	28
				hexyl hexanoate	8
Hexanal	1	0.5	1	1-hexanol	62
Benzaldehyde	1	15	11	benzyl alcohol	85
Cyclohexanone	0.5	2	15	cyclohexanol	83
Cyclohexanone	1	2	—	cyclohexanol	95
Methyl phenyl ketone	1	15	24	2-phenylethanol	75
Hexanoic acid	1	15	2	1-hexanol	56
				ethyl hexanoate	22
				hexyl hexanoate	20
Benzoic acid	1	15	20	benzyl alcohol	80
Benzoyl chloride	1	15	1	benzyl alcohol	97
Methyl benzoate	1	15	96	benzyl alcohol	1
Benzonitrile	1	15	97	<sup>a</sup>	
Benzoic amide	1	15	<sup>b</sup>	<sup>a</sup>	

<sup>a</sup> Neither benzyl alcohol nor benzylamine found; <sup>b</sup> amount of amide was not measured.

is assumed by us to be the direct precursor of, e.g., hexyl hexanoate from hexanoic acid.



## SCHEME 2

## Reduction mechanism

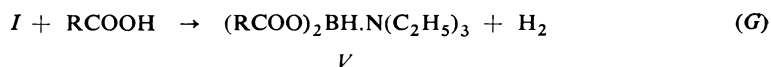
TABLE II

Optimization of reaction conditions of reduction of hexanoic acid RCOOH (R = CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>·CH<sub>2</sub>CH<sub>2</sub>) with TEB

No	<i>r</i> <sup>a</sup>	<i>t</i> °C	<i>τ</i> h	RCOOH <sup>b</sup> %	RCH <sub>2</sub> OH %	RCOOC <sub>2</sub> H <sub>5</sub> %	RCOOCH <sub>2</sub> R %
1	0.5	80	2	10	1	85	3
2	0.5	80	20	1	13	75	10
3	1.0	80	2	9	42	29	15
4	1.0	80	20	3	52	25	19
5	1.5	80	2	8	72	—	—
6	1.5	80	4	—	96	—	—
7	1.5	80	16	—	95	—	—
8	2.0	80	2	—	85	1	1
9	2.0	80	16	—	81	—	—
10	1.0	60	16	10	2	74	14
11	1.0	100	16	—	59	23	18
12	1.0	130	16	—	22	16	62

<sup>a</sup> TEB/acid molar ratio; <sup>b</sup> unreacted fraction.

At lower temperatures and, particularly, at TEB/RCOOH ratios lower than 1, side reactions involving the ethyl group transfer from the nitrogen to the oxygen (Scheme 3) will probably also play a role.



SCHEME 3  
Formation of ester

With regard to the preparative value of the reduction of free carboxylic acids with triethylamine borane, its mechanism deserves more detailed investigation.

Table IV gives the optimized preparative yields of reduction of some monoacids and diacids. The TEB/RCOOH ratio of 1.5, temperature 80°C and reaction time 4 to 16 h emerge as optimal. The yields do not decrease on extending the reaction time to 16 h even for sterically unhindered acids. They are all satisfactory to excellent.

It is favourable from the practical point of view that the reduction with triethylamine borane requires no solvent and that hydrogen (according to Eqs (C) and (G)) only evolves very slowly at temperatures higher than 60°C. Stirring is mostly unnecessary, it is, however, advised for low-soluble dicarboxylic acids.

TABLE III  
Optimization of reaction conditions of reduction of 2-ethylhexanoic acid RCOOH (R = CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH(CH<sub>3</sub>CH<sub>2</sub>)) with TEB

No	$r^a$	$t$ °C	$\tau$ h	RCOOH <sup>b</sup> %	RCH <sub>2</sub> OH %	RCOOC <sub>2</sub> H <sub>5</sub> %	RCOOCH <sub>2</sub> R %
1	0.5	80	20	26	36	36	2
2	1.0	80	2	15	61	12	7
3	1.0	80	20	11	70	7	13
4	1.5	80	4	—	85	—	15
5	1.5	80	15	—	90	—	8
6	2.0	80	15	—	94	1	5
7	1.0	60	15	33	2	54	11
8	1.0	100	15	22	60	3	17
9	1.0	130	15	—	54	9	—

<sup>a</sup> TEB/acid molar ratio; <sup>b</sup> unreacted fraction.

This novel method for the reduction of carboxylic acids will be very suitable for preparation of the corresponding alcohols in higher quantities.

### EXPERIMENTAL

The starting compounds for the reduction as well as the chromatographic standards were of analytical purity. Triethylamine borane was prepared from triethylamine and sodium tetrahydroborate following patent literature<sup>9,10</sup>.

The reaction mixtures were analyzed gas chromatographically using a flame ionization detector. The following columns, all 3 mm i.d., were used: a 1 200 mm glass column packed with Chromosorb W AW DMCS 60/80 mesh with 10% FFAP for the determination of acids and their derivatives at 190°C; a 2 400 mm stainless steel column packed with Chromosorb W 60/80 mesh with 3% PEG 20M (temperature 80–180°C) and a 1 200 mm glass column packed with Porapak QS 100/120 mesh for the determination of alcohols at 220°C. After evaluating the GLC traces, standard solutions of the nonreacted starting substances and reaction products were prepared in the same concentrations (50%, 20% and 5%) as were expected in the samples analyzed. The reaction yields were calculated based on a comparison of the analyses with the calibration curves.

#### Preparation of Triethylamine Borane (TEB)

Triethylamine (75 ml, 50.5 g, 0.5 mol) was added to a vigorously stirred suspension of NaBH<sub>4</sub> (19.0 g, 0.5 mol) in 250 ml of ethyl acetate. Carbon dioxide was then fed for 4 h into the mixture cooled to 20–35°C with water, whereafter the reaction mixture was decomposed with 250 ml of water. The slightly effervescent bottom layer was drained off, the top layer was washed with 100 ml of 20% aqueous K<sub>2</sub>CO<sub>3</sub> and dried with solid K<sub>2</sub>CO<sub>3</sub>, and the major fraction of ethyl acetate was evaporated on a rotary evaporator at 50°C/2.5 kPa. The residue was distilled at 95°C/1.3 kPa (52 g, 91%).

TABLE IV

Preparative reduction of carboxylic acids with TEB (80°C, 16 h, TEB/RCOOH molar ratio 1.5)

Acid	Unreacted %	Product	Yield <sup>a</sup> %
Hexanoic acid	—	1-hexanol	95
Dodecanoic acid	—	1-dodecanol	90
Butanedioic acid	10	1,4-butanediol	75
Hexanedioic acid	10	1,6-hexanediol	80
Decanedioic acid	35	1,10-decanediol	53
Benzoic acid	13	benzyl alcohol	75
Phenylethanoic acid	8	2-phenylethanol	77
2-Phenylbutanoic acid	5	2-phenylbutanol	76
Diphenylethanoic acid	35	2,2-diphenylethanol	55
Propionoic acid	36	2-propinol	23

<sup>a</sup> By gas chromatography of the reaction product.

### Reduction of Organic Compounds with TEB

Mixtures of the substances to be reduced and TEB were heated on an oil bath without stirring; the reaction conditions are given in Tables I–IV. The heating was conducted under nitrogen; although the yields were not lower if air was admitted, some of the reaction mixtures turned dark on several hours' heating.

#### Analytical Reduction of Hexanoic Acid

Hexanoic acid (0.46 g, 4.0 mmol) and TEB (0.9 ml, 6.0 mmol) were heated for 4 h under nitrogen. The reaction mixture was diluted with 1.5 ml of ethanol and decomposed with 30% hydrochloric acid, whose total volume of 1.5 ml was added dropwise. After hydrogen ceased to evolve, the mixture was heated to boil and extracted with  $3 \times 5$  ml of chloroform. The extracts were diluted to 20 ml and agitated with 4 ml of 10% NaOH, whereafter the chloroform phase was dried with  $\text{MgSO}_4$  and analyzed by GLC. The alkaline extract was made acidic with 30% HCl, and unreacted hexanoic acid was extracted with  $3 \times 3$  ml of chloroform. The chloroform extracts were combined, diluted to 10 ml, dried with  $\text{MgSO}_4$ , and subjected to chromatographic analysis.

#### Preparative Reduction of 2-Phenylbutanoic Acid

2-Phenylbutanoic acid (2.2 g, 13.3 mmol) and TEB (3.0 ml, 20.0 mmol), protected from air, were heated at 80°C for 16 h under an air condenser. The mixture was diluted with 3 ml of ethanol, decomposed gently with 3 ml of 30% HCl, heated under a reflux condenser to boil, allowed to stand for 2 h, and extracted with  $3 \times 10$  ml of chloroform at room temperature. The chloroform solution was shaken with  $2 \times 3$  ml of 10% NaOH and dried with  $\text{MgSO}_4$ ; after distilling the solvent off, 1.84 g of 2-phenylbutan-1-ol was obtained in a 90% purity (10.1 mmol 76%). The substance was distilled at 98°C/0.2 kPa to obtain 1.35 g (8.2 mmol, 68%) of the pure alcohol; 0.12 g (0.72 mmol, 5%) of the crude unreacted 2-phenylbutanoic acid was reclaimed from the alkaline aqueous phase after acidification and extraction with chloroform.

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