954. *Trisdialkylaminoboranes: New Reagents for the Synthesis of Enamines and Amides*

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In the course of studies on the synthesis of vitamin B_{12},* it became desirable to produce enamines from highly hindered ketones. A basic reagent which would react irreversibly with water and was totally miscible with the reaction mixture was required and, with this in mind, the readily available [1] trisdialkylaminoboranes, $B(NR_2)_3$, were examined. After delineating their activity in this field, their reactions with other organic function groups were examined.

Carboxylic Acids.—When a trisdialkylaminoborane is mixed with a carboxylic acid in an inert solvent, considerable heat is produced, although no amide is present at this stage of the reaction. Depending on the acid involved, either allowing the mixture to stand in the cold, or refluxing it for a period, produces the amide directly. Addition of dilute mineral acid, separation of the organic layer, drying, and removal of the solvent gives the crude amide (Table 1).

For complete reaction, one molecular equivalent of the boron reagent is required. If one-third of this quantity is used, then one-third of the yield is obtained. Obviously, only one of the three dialkylamino-groups is available for the conversion of the acid into the amide. No catalyst is required.

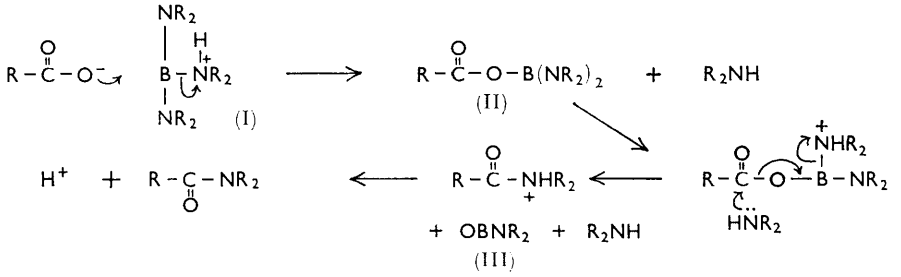
Table 1 †

Acid amides from trisdialkylaminoboranes

Acid	Borane (mole)	Time (hr.)	Conditions	Amide (%)
$PhCH_2 \cdot CO_2H$	Tripyrrolidinyl (1)	40	Room temp.	87
$PhCH_2 \cdot CO_2H$	,, (⅓)	48	Room temp.	33
$Ph \cdot CO_2H$	,, (1)	24	Benzene reflux	78
$Bu^t CO_2H$	,, (1)	20	Benzene reflux	62
$CH_3 \cdot [CH_2]_4 CO_2 \cdot H$	,, (1)	48	Room temp.	78

† The yields shown in all the Tables are those of the isolated purified products.

The mechanism of this reaction is of considerable interest, and studies on this problem are going forward. A working hypothesis is that the first step is salt formation followed by attack by the carboxylate anion on the protonated trisdialkylaminoborane (I) to yield the intermediate (II). Further protonation is followed by nucleophilic displacement, by



the liberated amine, of the metaboric acid amide (III) and more amine. The metaboric acid amide has not been isolated, and whether it reacts further by trimerisation, for example, is unknown.

1,3-*Diketones.*—Trisdialkylaminoboranes react rapidly, in the cold and without catalysis,

* Work being carried out in collaboration with Dr. J. W. Cornforth, Millstead Laboratory, Shell Research, Sittingbourne.

[1] H. A. Skinner and N. B. Smith, *J.*, 1953, 4025.

with 1,3-diketones to give the enamino-ketones. The mechanism may be similar to that given above.

TABLE 2

Enamino-ketones

1,3-Diketone	Borane (mole)	Enamine (%)
$CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$	Trisdimethylamine (1)	75
$CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$	Tripyrrolidinyl (1)	70
$Bu^t \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$	,, (1)	67 *

* Product is one compound, that produced by attack on the least-hindered carbonyl group.

TABLE 3

Enamines

Ketone	Borane	Reflux time	Enamine (%)
Di-isobutyl ketone	Tripyrrolidinyl	30 hr.	84
Acetophenone	,,	30 min.	72
Cholestanone	,,	45 min.	70
Cyclohexanone	,,	3 hr.	85

Ketones.—The reaction of the borane reagents with ketones is slow if free base is absent, or if there is no acid catalyst, but prolonged (three days) refluxing of the reagent, ketone, and free base gives a reasonable conversion (70—80%, estimated spectroscopically) into the enamine. When a mixture of aminoborane, free base, and acid catalyst is allowed to react with a ketone, high yields of enamine are produced. The rate of reaction varies considerably with the ketone used: with acetophenone the beginning of reflux marks the start of an exothermic reaction and, after 30 min. reflux, no ketone is left. With pinacolone, however, spectroscopic evidence indicates the slow production of the enamine, but self-condensation proceeds at a comparable rate, and the preparation of pinacolone enamines by this method is not possible.

β-*Keto-esters.*—With esters in general, trisdialkylaminoboranes react to give amides, but the reaction is slow, has a different stoicheiometry from the reaction with acids, and the results are difficult to reproduce. However, with β-keto-esters, amide production is very rapid, presumably owing to an intermediate chelate compound in which the ester group is attacked intramolecularly. The product is the β-enamino-amide in high yield.

Experimental.—N-*Phenylacetylpyrrolidine.* A solution of phenylacetic acid (1·17 g.) in benzene (10 ml.) was added to tripyrrolidinylborane (1·90 g., 1 mol.) and set aside at room temperature for 40 hr. Dilute hydrochloric acid was added, the organic layer separated, washed with water, and dried (Na_2CO_3). After filtration the solvent was removed and the residue fractionated to give the product (1·40 g., 87%) as a colourless liquid, b. p. 190—192°/18 mm., identical with an authentic sample.

2-*Oxo*-4-(1-*pyrrolidinyl*)*pent*-3-*ene.* Acetylacetone (1·01 g.) in dry chloroform (5 ml.) was added slowly to tripyrrolidinylborane (2·2 g., 1 mol.) in dry chloroform (5 ml.). Heat was produced, the solution turned yellow and a solid was precipitated. After filtration, the chloroform was removed, and the product was recrystallised from benzene–light petroleum, as needles, m. p. 117·5°, identical with an authentic specimen.

Pyrrolidine enamine from di-isobutyl ketone. A mixture of di-isobutyl ketone (1·85 g.), tripyrrolidinylborane (3·17 g., 1·1 mol.), pyrrolidine (1·39 g.), toluene *p*-sulphonic acid, and benzene (5 ml.) were refluxed for 30 hr. The volatile liquids were removed by a water-pump, and the residue was fractionated to give the enamine (2·1 g., 84%) as a colourless liquid, b. p. 96—100°/10 mm., infrared spectrum identical to that of our authentic sample.

Pyrrolidine enamine of acetophenone. Acetophenone (2·28 g.), tripyrrolidinylborane (4·48 g., 1·05 mol.), pyrrolidine (1·45 g.), toluene-*p*-sulphonic acid (5 mg.), and benzene (10 ml.) were mixed and refluxed for 30 min., after which no ketone could be detected. When the product was worked up as described above, it gave the unstable enamine (2·24 g., 70%) as a colourless liquid, b. p. 82—90°/10^{-3} mm., rapidly darkening. Analysis was not possible but the infrared

(1610 $cm.^{-1}$); ultraviolet $\lambda_{max.}$ 238, 275mμ (sh); with acid $\lambda_{max.}$ 247, 270 mμ (sh) [styrene $\lambda_{max.}$ 244 mμ, and nuclear magnetic resonance spectrum multiplets centred at 8·25(4-H), 7·05(4-H), 6·1(2-H), 2·7(5-H)] are all in agreement with the assigned structure.

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