110. An Improved Preparation of β -Chloropropionaldehyde Acetal

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The work, now under way in our laboratory, requires a certain amount of tryptamine derivatives, which we decided to synthesize according to the classical Ewins' method¹⁾:

One of the starting materials, γ -aminobutyraldehyde (a) is a fairly unstable substance, but its more stable acetal (III), which may be used as a substitute for the compound (a) in the Ewins' method, can be obtained from acrolein (I) via the well-known route:

(%-figures show the yield of the products at each reaction stage.)

As can be seen from the %-figures in the above formula only the first stage proceeds with an unsatisfactory yield. Thus we attempted its amelioration.

The authorized preparation of the compound (II) has been described in "Organic Syntheses".²⁾ We traced it's procedure, which consists of slow addition of cold acrolein to cold absolute ethanol saturated with dry hydrogen chloride gas. The yield of 35% of the product (II) obtained was exactly the same as given in the "Organic Syntheses". Besides (II) we obtained a fore-run of an indefinite boiling point roughly in the same amount of the desired product (II).

We deemed that in the above mentioned procedure at least two competitive reactions (A) and (B) are taking place:

It is certain that the desired product (II) is formed via route (B), but not via route (A), because the ethylene bond of acrolein acetal (IV), produced from acrolein and ethanol by proton catalysis, is not active enough to give the aimed product (II) under the reaction conditions.

Prior to scrutinizing the nature of the above-mentioned fore-run, we attempted to work according to the route (B).

Thus dry hydrogen chloride gas was introduced into cold absolute ether to which ethereal solution of acrolein was dropwise added with stirring, followed by addition of absolute ethanol and molecular sieves. On working up was obtained pure product (II) in 87.7% yield, with only a negligible amount of fore-run.

Starting from rectified pure acrolein, in a smaller scale, yield as high as 91% of II was obtained. Since, however, acrolein is a rather hazardous substance its purification by distillation in a large amount appears not advisable.

Experimental. Dry hydrogen chloride gas (ca. 390 g) was introduced into absolute dry diethylether (1.5 l) cooled in an ice-water bath. This solution was then cooled to $-30\sim-35^\circ\text{C}$ (dry-ice: acetone bath). Acrolein (224 g, 3.6 moles, purity 90%)* dissolved in dry absolute diethylether (2 l) was now dropwise added during 2 hrs with stirring. After stirring for an additional 2 hrs at about 20°C absolute ethanol (1.05 l) and molecular sieves (200 g, type 4A, 1/16)** were added. The mixture was stirred overnight at ambient temperature ($15\sim20^\circ\text{C}$), and then neutralized with sodium bicarbonate (ca. 605 g) and anhydrous sodium carbonate (ca. 300 g),*** and filtered by suction. The filter-cake was washed thoroughly with diethylether. Combined organic solution was washed successively with saturated aqueous solution of sodium bicarbonate and sodium chloride, dried and evapo-

* Purity 90% is indicated on the label of a slightly turbid commercial product.

** In one experiment worked without addition of molecular sieves yield dropped to 65.5%.

*** Vigorous effervescence! Strong manual stirring is necessary. When sodium bicarbonate only was used difficultly tractable product was obtained.

rated. The residue gave a colorless distillate boiling at 56~59°C (6 mmHg), with only a negligible amount of fore-run. Yield 521.4 g or 87.7% of the theoretical.

References

- 1) A. J. Ewins: J. Chem. Soc., 270 (1911).
- 2) E. J. Witzemann, W. L. Evans, H. Hass, and E. F. Schroeder: Organic Syntheses Coll. vol. 2, p. 137 (1943).