

THE SYNTHESIS OF O-NITROBENZALDEHYDE-D 1 BY A MODIFIED BROWN-SUBBA-ROW REDUCTION. A SIMPLE ROUTE TO FORMYL DEUTERATION.

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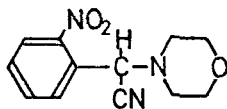
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MATERIALS AND METHODS

Formyl deuterated o-nitrobenzaldehyde has been prepared using a variation of the Brown-Subba-Row reduction.

The synthesis of ortho-nitrobenzaldehyde-d₁, despite its importance as a synthetic intermediate ¹ and interesting photochemistry ², appears not to have been reported ^{3,4}. During the course of investigations into its photochemical rearrangement we found it necessary to prepare the substance in gram quantities.

Of the many methods available ³, two appealed particularly on grounds of their simplicity and reported yields. The method of Bennett et al ⁵, consisting of exchange of the benzylic proton of the corresponding morpholinonitrile (I), though reported successful for meta- and para-nitrobenzaldehydes failed in our hands with the ortho isomer.

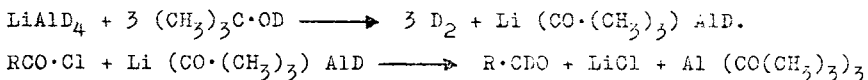


(I)

morpholinonitrile

Attempts to decompose the intermediate iminium perchlorate with aqueous NaCN (the reaction leading to I) yielded an array of fifteen products detectable by t.l.c.

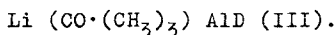
The second method, though reported successful for the preparation of ortho-nitrobenzaldehyde from orthonitrobenzoyl chloride appears not to have been applied to deuteration reactions. The method consists basically of "damping" the activity of LiAlH_4 so that i) nitro groups remain intact and ii) further reduction of the aldehyde to primary alcohol does not occur. The decreased reducing activity results from conversion to the tri-tertbutoxy complex $\text{Li}((\text{CH}_3)_3\text{CO})_3\text{AlH}$. The latter is then allowed to react with the appropriate acyl chloride at low temperature to yield the aldehyde in high yield ⁶.



The experimental procedure described below is that observed as being optimised with regard to yield of aldehyde.

Experimental

a) Preparation of lithium tri-tertbutoxy aluminodeuteride



Despite the possibility of preparing the reagent in situ ⁶ we found it preferable to isolate it in pure form before use, noting that in situ preparations usually led to formation of impurities, probably due to reactions of excess uncomplexed LiAlD_4 .

Lithium aluminium deuteride (1 g 0.024 mole) was suspended in dry ether (20 ml) in a three necked flask fitted with magnetic stirrer

and condenser and stirred for 10 minutes. To the grey suspension tert-butanol d_1 (7.2 ml = 0.072 mole) was added dropwise. Evolution of gas and formation of a white precipitate were observed. After a further 1/2 hr stirring, the ether and excess tert-butanol- d_1 were removed by rotary evaporation and the white complex separated and stored in a desiccator over phosphorus pentoxide.

b) Reduction

Ortho-nitrobenzoyl chloride (IV) (3.71 g = 0.02 mole) was dissolved in dry diglyme (10 ml) and in placed in a round-bottomed flask fitted with magnetic stirrer, low temperature thermometer, dropping funnel and a gas in-and-outlets. The flask and contents were cooled to -80°C under a continuous flow of dry nitrogen and a solution of III (5.9 g = 0.024 mole) added dropwise over a period of 1 hr. The resulting reaction mixture was maintained at -80°C for 24 hr and then allowed to warm naturally to room temperature before subsequent operations. Thereafter the contents were poured onto D_2O ice, whereby aluminium hydroxide and organic material consisting largely of deuterioaldehyde and orthonitrobenzoic acid (derived from hydrolysis of unreacted IV). No *o*-nitrobenzylic alcohol was present. The former was extracted in dichloromethane, the solution rotary evaporated and finally isolated in pure form by column chromatography (Kieselgel column; benzene elutant). Yield = 2,4 g = 78 %.

c) Analysis

Using a column chromatographed sample after vacuum sublimation we confirmed the identity of our isolated product by the following means a) thin-layer chromatography - the R_f value of our product was identical with that of authentic *o*-nitrobenzaldehyde (O-NBA)

in six different solvent systems.

b) gas-chromatography - the retention time of our product was identical with that of authentic o-NBA in temperature-programmed gas chromatography (3 % OV-225 column running at 80° programmed at 2°/min to 220° C)

c) NMR spectroscopy-a 0.1 M solution in showed no trace of an aldehydic proton in the range observed in the case of o-NBA.⁷

We conclude that the method described represents a simple and rapid method for preparation of the title compound which may indeed be more generally applicable.

References

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