Borch synthesis of secondary amines from aromatic nitriles:

1-[4-(trans-4-Heptylcyclohexyl)phenyl]-N-methylmethanamine

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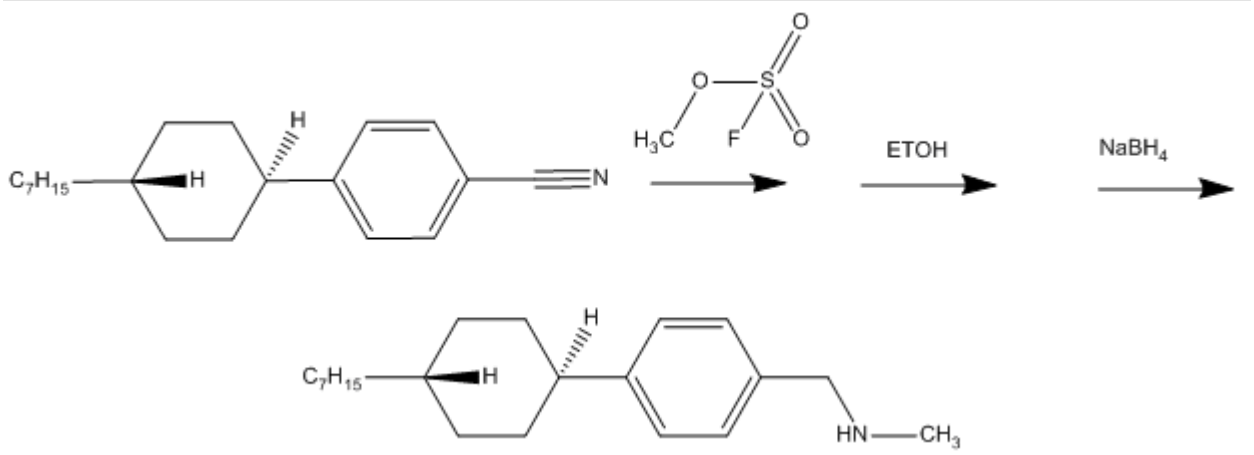

Chemicals Used:

N-(Trans-4-heptylcyclohexyl)-benzonitrile (Chemos group)

http://www.chemos-group.com/productinfo.php?CAS=61204-03-3

"Magic methyl" (methyl fluorosulfonate), BOC sciences, 421-20-5

http://www.bocsci.com/description.asp?cas=421-20-5

Sodium borohydride, Sigma Aldrich, powder, 99%, 21,364-2

Ethyl alcohol, Sigma Aldrich, absolute, 99.5%, 200 proof, A.C.S. reagent, 46,984-4

Methylene chloride (dichloromethane), Sigma Aldrich, 99.9%, A.C.S. HPLC grade 27,056-3

Sodium hydroxide, Sigma Aldrich, Pellets, 97+%, A.C.S. reagent, 22,146-5

Ether, Sigma Aldrich, anhydrous, 99+%, A.C.S. reagent, 44,354-9

Sodium sulfate, anhydrous, granular, 99+%, A.C.S. reagent, 23,931-3

Procedure:

A flame or oven dried 50 ml round bottom three neck flask was equipped with a heating mantle, water condenser, calcium chloride drying tube on top of the condenser, nitrogen inlet, magnetic stirrer and septum cap. The nitrogen flow was commenced and ~2 ml of methyl fluorosulfate was syringed into the flask with stirring. The septum cap was removed and 1.16 g (4.2 mmol) of the nitrile was charged under nitrogen. A thermometer and adapter replaced the septum cap and the mixture was stirred until homogeneous. The reaction was then heated at ~ 100° overnight (~ 12 hours).

Infrared analysis, neat film, at that point indicated complete reaction of the nitrile, as evidenced by total disappearance of the nitrile stretching frequency at ~ 2300 cm^{-1}. A drop of the reaction mixture was pipetted from the reaction and dropped onto a salt plate, and a 2^{nd} plate placed on top for this analysis.

Now 5 ml of dichloromethane was added through the water condenser and the mixture was cooled in an ice bath to ~ 0°. Then 2 ml of absolute ethanol was added through the condenser, and the solution stirred for 2.5 hours at ~ 0° (ice bath). The solution was then treated with 10 ml of 6 N sodium hydroxide solution through the condenser , the apparatus disassembled, and liquid transferred to a 50 ml separatory funnel. The liquid was extracted three times with 5 ml ether portions,

which were combined, transferred to another separatory funnel, and shaken several times with ~ 1 ml portions of distilled water until the water extract was neutral to litmus paper. The combined ether extracts were then dried over ~ 1 g of sodium sulfate, the extracts decanted into a 50 ml beaker, and the ether removed on a steam or water bath.

The residue was taken up in 20 ml of absolute ethanol and the solution transferred to another flame or oven dried 100 ml round bottom three neck flask equipped with a water condenser, calcium chloride drying tube on top of the condenser, nitrogen inlet and magnetic stirrer. 1.5 g of sodium borohydride was added and the solution stirred at room temperature under nitrogen for ~ 48 hours.

After transferring to a 50 ml one neck round bottom flask, the ethanol was removed on a rotary evaporator under water aspirator pressure, with heating via a warm water bath. The residue was taken up in 50 ml of deionized water, transferred to a 100 ml separatory funnel, and extracted three times with ~ 10 ml ether portions. The combined ether extracts were dried over ~ 2 g of sodium sulfate for one hour, and the solution decanted from the sulfate into a 100 ml beaker. The ether was removed on a steam bath and the residue transferred via micro pipette into a 10 ml round bottom flask. The flask was attached to a "Kugelrohr" distilling apparatus, and the amine micro distilled under pump vacuum at 0.1 mm,while heating at ~ 140° in an oil bath, yielding ~ 400 mg (~ 30%) of the secondary amine. The amine exhibited liquid crystalline behavior (see data). Since the material is somewhat hygroscopic, it was converted to the less sensitive hydrochloride salt for combustion analysis. The free amine should be stored in a desiccator.

Author's Comments:

CAUTION! "Magic methyl" is **very toxic**, irritating and moisture sensitive. It reacts violently if exposed to large quantities of water or hydroxylic solvents. Weigh quickly in a glove box if possible. Always manipulate this material in an efficient fume hood! Wear latex gloves.

Sodium borohydride is stable in neutral hydroxylic solvents but reacts violently with acids. Do not mix borohydride waste with acids.

Ether is extremely flammable. Avoid sparks or open flame.

The procedure is applicable for preparing a wide variety of secondary amines from nitriles.

Data:

B.p. ~ 130° (0.1 mm)

m.p K-N (crystal-nematic) -1°, N-I (nematic-isotopic) 2°.

I.r. (neat film) 3300(N-H stretch), 3010(vinylic C-H stretch, 2900 (aliphatic C-H stretch), 1620 (Aromatic C=C stretch),cm^{-1}.

Analysis, hydrochloride salt:

Calculated for $C_{21}H_{35}NCl$:	C, 74.84	H, 10.47	N, 4.15
Found:	C, 75.06	H, 10.52	N, 4.19

Lead references:

1) Richard F. Borch, "Nitrilium salts. New method for the synthesis of secondary amines"

J. Org. Chem., 1969, 34 (3), pp 627–629

DOI: **10.1021/jo01255a031**

http://pubs.acs.org/doi/abs/10.1021%2Fjo01255a031

2) John H. MacMillan and Mortimer M. Labes, "Low Transition Temperature Liquid Crystalline Amines Incorporating the Trans-1,4-Cyclohexane Ring System", Molecular Crystals and Liquid Crystals, Vol. 55, p 61, (1979).

DOI: **dx.doi.org/10.1080/00268947908069791**

http://jhm2.homestead.com/files/13.pdf

Other references:

1) John H. MacMillan and Mortimer M. Labes, "Low Transition Temperature Liquid Crystalline Amines Incorporating the Biphenyl Ring System", Mol. Crystals and Liquid Crystals Letters, Vol. 56, p51, (1979).

DOI: Link: **http://dx.doi.org/10.1080/01406567908071966**

http://jhm3.homestead.com/files/15.pdf

2) John H. MacMillan and Mortimer M. Labes, "Amine Substituted Liquid Crystal Compositions", U.S. Patent 4,293,193, Oct. 6, 1981.

http://jhm3.homestead.com/files/patent1.pdf

3) Chemspider deposition:

http://www.chemspider.com/Chemical-Structure.29354037.html

Keywords: nitrile, amine, aniline, secondary amine, reduction, sodium borohydride, nitrilium, cyano, methylation, Borch, aromatic, benzonitrile.