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Synthesis of 1,3−bis\(2,4,6−trimethylphenyl)−imidazolinium salts : **SIMes.HCl**, **SIMes.HBr**, **SIMes.HBF$_4$** and **SIMes.HPF$_6$**.

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Method Article

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Abstract

N,N’–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide is obtained in a single step through the dialkylation of dibromoethane. It serves as a versatile starting material for the synthesis of imidazolium salts: SIMes.HBr, SIMes.HCl, SIMes.HPF$_6$ and SIMes.HBF$_4$.

Introduction

Azolium salts have become indispensable starting materials in N–heterocyclic carbene \(NHC) chemistry. From being a laboratory curiosity, NHCs occupy now an important position in contemporary organometallic chemistry as powerful ligands for many catalytic reactions \(ie: Negishi, Kumada–Tamao–Corriu, Sonogashira and Suzuki–Miyaura cross–coupling reaction, Buchwald–Hartwig amination, aerobic oxidation, CuAAC reaction …) as well as organocatalysts. Although diverse strategies have been developed to synthesize imidazolinium salts, they generally require the reduction of an intermediate diimine. This usually involves stoechiometric borohydride in a exothermic process which could present difficulties and hazards to scale–up. We report a simple gram scale synthesis of several imidazolinium salts \(Br, Cl, PF$_6$ and BF$_4$). Through a direct double alkylation of 1,2–dibromethane, the corresponding diamine is obtained which serves as convenient starting material for the salts described above using convenient known procedures.

Reagents

• 2,4,6-Trimethylaniline • 1,2–Dibromoethane • Methanol \(technical) • Ethanol \(technical and absolute) • Aqueous HBF4 \(60%) • Aqueous HPF6 \(60%) • Diethyl ether • Sodium carbonate • Acetyl chloride • Ethyl acetate • Anhydrous Na2SO4 • Formic acid • Triethyl orthoformate

Equipment

• Round-bottomed flasks \(250 mL, 500 mL and 1 L) • Teflon-coated stirring bars • Filtration funnels • Thermally controlled stirring plate • A distillation apparatus • A thermometer. • A separation funnel.

Procedure

Synthesis of N,N’–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide. 1| Weigh out 40.5 g \(0.3 mol) of 2,4,6–trimethylaniline in a 250 mL round–bottomed flask equiped with a stirring bar. 2| Add 22.5 g \(0.125 mol) of 1,2–dibromoethane. 3| Add 30 mL of methanol. 4| Stir the reaction mixture under reflux for 24 h. ▯ PAUSEPOINT : a solid forms during the reaction, usually after 18 h. 5| The solution is cooled down to room temperature and stirred for an additional 2 h. 6| Filter off the formed brownish precipitate, wash it with 50 mL of methanol, 100 mL of ethyl acetate, 100 mL of diethyl ether and dry under an air flux for one hour to obtain a white powder. **Synthesis of N,N’–bis–\(2,4,6–trimethylphenylamino)ethane dihydrochloride.** 1| Weigh out 37.8 g \(82.5 mmol) of N,N’–bis–\(2,4,6–

trimethylphenylamino)ethane dihydrobromide in a 1 L round–bottomed flask. 2| Add 500 mL of diethyl ether and 25 g \(235.8 mmol) of solution of sodium carbonate in 200 mL water. 3| Stir vigorously the solution for 2 h. 4| Separate the organic layer, extract the aqueous phase with 100 mL of diethyl ether and dry the combined phases over anhydrous Na_2SO_4. 5| Add 200 mL of ethanol in a 500 mL round–bottomed flask immerged in a water bath. 6| Add 19.0 g \(242 mmol) of acetyl chloride dropwise while maintaining the temperature close to room temperature. Then stir the solution for 30 minutes at room temperature. 7| Add the ethanolic HCl solution to the ether. □ PAUSEPOINT : A white solid forms immediately. 8| Filter off the solid and dry it to constant weight in an oven \(90°C). **1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium bromide or chloride [1]** 1| Weigh out 20.0 g of N,N'–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide \(43.7 mmol) or chloride \(58.3 mmol) in a two–necked 250 mL round–bottomed flask equipped with a distillation apparatus and a thermometer. 2| Add 150 mL of triethyl orthoformate and seven drops of formic acid. 3| Heat the white suspension until the internal temperature reaches 115°C and maintain at this temperature for 30 minutes. □ PAUSEPOINT : Ethanol is collected during the heating, as indicated by the temperature of vapors. During the heating, the white solid dissolves to re–precipitate only a few minutes later. 4| Cool down the reaction mixture to room temperature and wait for 2 h. 5| Filter the white powder, wash it with 2×100 mL of diethyl ether and dry under an air flux. **Synthesis of 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium tetrafluoroborate or hexafluorophosphate.[2]** 1| Weigh out 5.0 g \(13 mmol) of 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium bromide in a 100 mL round–bottomed flask. 2| Add 30 mL of ethanol. 3| Add 4.0 mL of 60% aqueous HBF_4 or HPF_6. 4| A white solid forms immediately. In the case of the tetrafluoroborate salt, 5 mL of ethanol are added. Stir the reaction in an ice bath for 45 minutes. 5| Filter the solid, wash it with 5 mL of cold ethanol and 5 mL of diethyl ether. 6| Dry the white solid in a desiccator under reduced pressure.

Timing

N,N'–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide: 30 h. N,N'–bis–\(2,4,6–trimethylphenylamino)ethane dihydrochloride: 5 h. 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium bromide \(**SIMes.HBr**): 4 h. 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium chloride \(**SIMes.HCl**) : 4 h 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium tetrafluoroborate \(**SIMes.HBF_4**) : 2 h. 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium tetrafluoroborate \(**SIMes.HPF_6**) : 2 h.

Troubleshooting

The batch of N,N'–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide might contain up to 7% of 2,4,6–trimethylaniline hydrobromide. Solution: the batch was stirred for 10 minutes in boiling methanol; the solution was allowed to stand at room temperature overnight and filtered to afford pure diamine dihydrobromide as a white solid.

Anticipated Results

Typical isolated yield N,N’–bis–\(2,4,6–trimethylphenylamino)ethane dihydrobromide should be 45–55% \(37.8 g). Typical isolated yield N,N’–bis–\(2,4,6–trimethylphenylamino)ethane dihydrochloride should be 93% \(28.4 g). Typical isolated yield for 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium bromide \(SIMes.HBr) should be 95–99% \(16.7 g). Typical isolated yield for 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium chloride \(SIMes.HCl) should be 93–99% \(18.68 g). Typical isolated yield for 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium tetrafluoroborate should be 97% \(4.98 g). Typical isolated yield for 1,3–bis–\(2,4,6–trimethylphenyl)imidazolinium hexafluorophosphate should be 95% \(5.61 g).

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