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SYNTHESIS OF AROMATIC THIOLS FROM ARYL IODIDES AND THIOUREA BY MEANS OF NICKEL CATALYST[1)]

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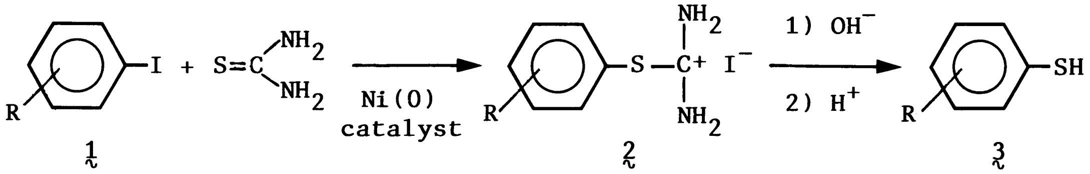
Nickel(0) complex, generated in situ from bis(triethylphosphine)nickel(II) chloride and sodium cyanoborohydride, catalyzed the nucleophilic displacement of aryl iodides with thiourea. S-Arylisothiuronium salts or aromatic thiols were obtained in good yields after simple work-up procedures.

Owing to the well-known reluctance of sp^2C-halogen bond, the utility of aryl halides in organic synthesis is considerably limited. Thus, the reaction of alkyl halides with thiourea, followed by alkaline hydrolysis of resulting S-alkyl-isothiuronium salts, provides a useful method for the preparation of alkyl thiols, whereas a similar sequence is inapplicable to the preparation of aromatic thiols because of the inertness of nonactivated aryl halides toward a nucleophilic displacement.[2)] Here, we will report that this difficulty can be overcome by the usage of nickel(0) complex as a catalyst.



In the presence of a catalytic amount of nickel(0) complex, generated in situ from bis(triethylphosphine)nickel(II) chloride and sodium cyanoborohydride as a reducing agent,[3)] iodobenzene (1) was reacted with thiourea in N,N-dimethylformamide (DMF) at 60 °C for 3 h. Subsequent treatment of the resulting clear solution containing S-phenyl-isothiuronium iodide (2) with 0.5 mol dm^{-3} aqueous sodium hydroxide at ambient temperature, followed by acidification with hydrochloric acid afforded benzenethiol (3) in a quantitative yield. Representative results are summarized in Table 1. Polar solvents such as acetonitrile, acetone, and 1,4-dioxane were also effective, while in hydrocarbon solvents, deposition of metallic nickel occurred rapidly and the reaction stopped before completion. It should be noted that electron-donating substituents such as amino and alkoxy groups did not affect the reactivities of aryl iodides. Under the identical conditions used above, bromobenzene and chloro-substituent in aryl iodides did not react with thiourea, but bromo-substituent in aryl iodides was partly displaced with thiourea, suggesting that an isothiuronium group increased the reactivity of the halides.

Table 1. Synthesis of Aromatic Thiols **3** and/or S-Aryl-Isothiuronium Salts **2**

Run	Aryl Iodides **1** R	Solvent	Temp/°C	Time/h	Yield/% **2**b)	 **3**c)
1	H	DMF	60	3	95	98
2	H	DMF	40	25		98
3	H	Acetonitrile	60	4		97
4	H	Acetone	60	10		70
5	H	1,4-Dioxane	60	4		92
6	H	Benzene	60	10		16
7	p-CH_3	DMF	60	3		97
8	o-CH_3	DMF	60	10		91
9	p-CH_3O	DMF	60	3	85	98
10	p-NH_2	DMF	60	3	91	98
11	p-Cl	DMF	60	3		98
12	p-Br	DMF	60	24		73d)

a) Displacement reaction was carried out under nitrogen. Molar ratio of each component ($ArI/Thiourea/NiCl_2(PEt_3)_2/NaBH_3CN$) was 1.0/1.5/0.02/0.03.
b) Isolated yields of tetraphenylborate (Runs 1 and 10) or iodide (Run 9).
c) Yields were determined by GLC using internal standards.
d) p-Benzenedithiol was obtained in a yield of 20%.

For a sake of simplification, in most runs, S-aryl-isothiuronium salts were converted into aromatic thiols, immediately after the proceeding of the displacement reaction. However, the salts could be isolated intact4) or in the form of tetraphenylborate derivatives after the treatment of the reaction mixture with aqueous sodium tetraphenylborate. Therefore, the present nickel-catalyzed displacement of aryl iodides with thiourea affords not only a convenient "one-pot" procedure for the synthesis of aromatic thiols but also a new synthetic method of S-aryl-isothiuronium salts, not starting from diazonium salts.2)

References

1) Nucleophilic Displacement Catalyzed by Transition Metal. Part VI. Part V: K. Takagi, N. Hayama, and S. Inokawa, Chem. Lett., 1978, 1435.

2) J. L. Wardell, "Preparation of Thiols," in "The Chemistry of the Thiol Group," ed by S. Patai, John Wiley & Sons, London (1974), p. 189. See also L. Testaferri, M. Tingoli, and M. Tiecco, Tetrahedron Lett., 21, 3099 (1980).

3) Uses of other nickel compounds like bis(triphenylphosphine)nickel(II) chloride (reaction time, 2 h; conversion, 30%) and nickel(II) bromide (2 h; 55%) or other reducing agents like zinc powder (15 h; 40%), sodium borohydride (6 h; 17%), and 9-borabicyclo[3.3.1]nonane (4 h; 45%) were found to be less effective.

4) When the reaction of p-iodoanisole (2.0 mmol) with thiourea in the presence of a nickel(0) catalyst in DMF (1 mL) was completed, the resulting solution was cooled down (-10 °C) to crystallize 525 mg of S-p-anisyl-isothiuronium iodide (85%). Recrystallization from ethanol afforded pure salt. Mp 185-189 °C. Found: C, 31.01; H, 3.52; N, 9.12%. Calcd for $C_8H_{11}IN_2OS$: C, 30.98; H, 3.57; N, 9.03%.

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