

REISSERT COMPOUND STUDIES. LIII. A NEW SYNTHESIS OF REISSERT
COMPOUNDS USING TRI-n-BUTYL TIN CYANIDE

Frank D. Popp* and Joydeep Kant

Department of Chemistry, University of Missouri-Kansas City,
Kansas City, Missouri 64110, U. S. A.

Abstract - Reissert compounds were prepared by the reaction of the heterocyclic base and acyl halide with tri-n-butyltin cyanide in methylene chloride.

Reissert compounds (N-acyldihydroazaaromatic- α -nitriles)¹ have been widely used for the synthesis of various heterocyclic compounds. Many methods have been reported for the synthesis of Reissert compounds. The formation of Reissert compounds by the reaction of the heterocyclic base with potassium cyanide and an acyl chloride in methylene chloride-water² (occasionally with a phase transfer catalyst³) is the general method of choice. The reaction of the heterocyclic base and acyl chloride with trimethylsilyl cyanide⁴ in anhydrous methylene chloride (sometimes with an aluminum chloride catalyst) offers certain advantages in some situations.⁵ We now wish to report the use of a convenient new cyanide source in Reissert compound preparation. In a typical experiment, 5 mmole of isoquinoline and 10 mmole of tri-n-butyltin cyanide and a trace of anhydrous aluminum chloride were stirred in 20 ml of anhydrous methylene chloride. A solution of 10 mmole of benzoyl chloride in 5 ml of anhydrous methylene chloride was slowly added and the mixture was stirred at room temperature for 1.5 h. The methylene chloride solution was washed with water, dilute hydrochloric acid, water, dilute sodium hydroxide, and water. The dried (MgSO₄) methylene chloride solution was evaporated and the residue washed with ethanol to give a 96% yield of the isoquinoline Reissert compound (2-benzoyl-1,2-dihydroisoquinolal donitrile) identical in all respects with a pure authentic sample. The reactions shown in the Table were carried out in a similar manner.

Table. Reaction of Benzoyl Chloride and Tri-n-butyltin Cyanide
with Heteroaromatic Compounds

<u>Heterocyclic compound used</u>	<u>Ratio of reactants</u>			<u>AlCl₃</u>	<u>Time</u> h	<u>Yield</u> %
	Het. Cpd.	Bu ₃ SnCN	PhCOCl			
Isoquinoline	1	1	1	yes	1.5	68
Isoquinoline	1	2	2	yes	1.5	96
Isoquinoline	1	1.2	1.4	no	1.5	83
Phthalazine	1	1.2	1.4	no	1.5	79
Phthalazine	1	1.2	1.4	no	18	91
Phthalazine	1	1.2	1.4	yes	1.5	85
Phthalazine	1	2	2	yes	3	95
Quinoline	1	1.2	1.4	no	18	75
Quinoline	1	1.2	1.4	no	2	65
Quinoline	1	1.2	1.4	yes	18	82
Quinoline	1	2	2.5	yes	18	83
Phenanthridine	1	1.2	1.4	no	18	91

Reaction of pyridine, tri-n-butyltin cyanide and ethyl chloroformate in a 1 to 1.2 to 1.4 molar ratio for 2 h in the absence of aluminum chloride gave an 89% yield of the Reissert analog.⁶

The use of tri-n-butyltin cyanide is thus shown to be a very effective source of cyanide for the preparation of Reissert compounds in very good yield. A wide variety of reaction conditions appear to give almost equally good results. It is anticipated that this reagent will prove to be at least as useful as tri-methylsilyl cyanide in the preparation of Reissert compounds from some of the more difficult heterocyclic systems.

REFERENCES

1. W.E. McEwen and R.L. Cobb, Chem. Rev., 1955, 55, 511; F.D. Popp, Adv. Heterocyclic Chem., 1968, 9, 1; idem, ibid., 1979, 24, 187; idem, Heterocycles, 1973, 1, 165; idem, ibid., 1980, 14, 1033; and F.D. Popp and B.C. Uff, ibid., 1985, 23, 731.
2. F.D. Popp and W. Blount, Chem. Ind. (London), 1961, 550; F.D. Popp, W. Blount, and P. Melvin, J. Org. Chem., 1961, 26, 4930; F.D. Popp, W. Blount, and A. Soto, Chem. Ind. (London), 1962, 1022; and F.D. Popp and W. Blount, J. Org. Chem., 1962, 27, 297.
3. B.C. Uff and R.D. Budram, Heterocycles, 1977, 6, 1789; D. Bhattacharjee and F.D. Popp, ibid., 1977, 6, 1905.
4. S. Ruchirawat, N. Phadungkul, M. Chuankamnerdkarn, and C. Thebtaranonth, Heterocycles, 1977, 6, 43.
5. See for example many recent papers by F.D. Popp and co-workers and B.C. Uff and co-workers on Reissert compounds from diaza systems.
6. R.H. Geuss, N.G. Smith, and L.J. Winters, J. Org. Chem., 1974, 39, 2027; J. Kant and F.D. Popp, Chem. Ind. (London), 1985, 125.

Received, 7th May, 1985