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ACYLATION OF ACIDIC NITROGEN COMPOUNDS VIA THEIR *N*-STANNYL DERIVATIVES

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SUMMARY

The tributyltin derivatives of phthalimide, succinimide, imidazole, and isatin have been used as intermediates for the formation of the corresponding *N*-acyl derivatives by reaction with acyl halides under mild conditions. Metathetical reactions of the stannyl derivatives have also been investigated.

Stannylamines are known to undergo easily alkylation reactions, in which the stannyl group is replaced by an alkyl group[1]. Several *N*-stannyl derivatives of compounds having acidic nitrogen have been described, such as *N*-(trialkylstannyl)-phthalimide and *N*-(trialkylstannyl)imidazole, but it seems that these compounds were not utilized as intermediates for the preparation of their *N*-acyl or *N*-alkyl derivatives. Conventional acylation of such acidic nitrogen compounds may be easy or difficult depending on the type of the compound. It seems that use of *N*-stannyl derivatives of such compounds offers a convenient method for synthesizing their *N*-acyl derivatives.

We studied the acylation reaction with *N*-(tributylstannyl)imidazole, -phthalimide, -succinimide, and -isatin. These derivatives were prepared by heating the corresponding nitrogen compounds with bis(tributyltin) oxide under azeotropic conditions (benzene or toluene). These compounds are less sensitive to hydrolysis than the stannylamines[2], and they were found to react almost quantitatively with acyl, aroyl or sulfonyl chlorides to give the corresponding *N*-substituted acyl derivatives.

The reactions were carried out at room temperature in solvents such as light petroleum or ether. The solvents for the reaction were chosen so that the derivative precipitated out on formation. This method is thus convenient and mild for the preparation of the above *N*-acyl derivatives and is clear cut, unlike conventional acylations in which side reactions such as oxidation, may occur. Of special interest is the preparation of *N*,*N'N''*-triacetyl-, -tripropionyl- or -tribenzoylcyanuric acids, which are difficultly accessible[3]. These were obtained by reaction of the appropriate acyl halides with the *N*-tributylstannyl derivative of cyanuric acid.

We investigated the possibility of using the *N*-stannyl compounds as active intermediates for the preparation of the corresponding *N*-alkyl derivatives. However no reaction occurred between benzyl chloride and *N*-(tributylstannyl)imidazole or *N*-(tributylstannyl)phthalimide. Failure of the stannyl compounds to react shows

that the reactivity of the Sn–N bond in these compounds is less than that of the corresponding stannylamines. Specially reactive halogen compounds nevertheless reacted. Thus 2,4-dinitrofluorobenzene reacted with *N*-(tributylstannyl)phthalimide, giving the corresponding *N*-(2,4-dinitrophenyl)phthalimide.

The stannyl derivatives reacted with bromine with loss of the tributyltin group, and formation of the *N*-bromo derivative; for example, *N*-(tributylstannyl)phthalimide gave *N*-bromophthalimide.

The *N*-tributylstannyl derivatives were found to undergo metathesis with arylstannyl halides. Thus *N*-(tributylstannyl)imidazole reacted on heating with triphenyltin chloride in benzene to give a quantitative yield of *N*-triphenylstannylimidazole. Similar substitutions occurred on treatment of the *N*-stannyl derivatives with compounds having an acidic nitrogen. Thus when imidazole was heated with *N*-(tributylstannyl)phthalimide, the phthalimide was replaced and *N*-(tributylstannyl)imidazole was formed. These substitutions are selective. For example, when *N*-stannylimidazole was heated with phthalimide no substitution occurred.

EXPERIMENTAL

N-(Tributylstannyl)imidazole[4], *N*-(tributylstannyl)phthalimide[5], and *N*-(tributylstannyl)succinimide[5] were prepared as previously described.

N-(Tributylstannyl)isatin

Isatin (14.7 g, 0.1 mole) and bis(tributyltin) oxide (29.8 g, 0.05 mole) were heated in toluene (100 ml) and water was removed continuously as an azeotrope. The reaction mixture was heated for 2 h, the toluene was evaporated *in vacuo*, and the *N*-(tributylstannyl)isatin was collected at 215°/0.1 mm, yield 4.1 g (94%). (Found: C, 55.28; H, 7.23; N, 3.24; Sn, 27.10. $C_{20}H_{31}O_2NSn$ calcd.: C, 55.07; H, 7.16; N, 3.21; Sn, 27.22%.)

N-Acetylisatin

N-(Tributylstannyl)isatin (17.45 g, 0.04 mole), prepared as above but not distilled, was dissolved in dry ether (100 ml), and acetyl chloride (3.4 g, 0.043 mole) was added. *N*-Acetylisatin began to crystallize after 1 h. The product was collected and washed with ether; yield 5.2 g (69%); m.p. 143 (lit.[6] 142°). (Found: C, 63.51; H, 3.66; N, 7.54. $C_{10}H_7O_3N$ calcd.: C, 63.49; H, 3.73; N, 7.40%.)

N-(p-Nitrobenzoyl)imidazole

To a solution of *N*-(tributylstannyl)imidazole (2.0 g, 0.0056 mole) in dry ether (75 ml), *p*-nitrobenzoyl chloride (1.04 g, 0.0056 mole) was added with strong stirring. The mixture was stirred for 30 min, and the white precipitate which formed was filtered, yield, 0.75 g (69%); m.p. 119 (lit.[7] 120–122). (Found: C, 55.20; H, 3.49; N, 19.22. $C_{10}H_7N_3O_3$ calcd.: C, 55.30; H, 3.25; N, 19.35%.)

N-Acetylsuccinimide

To a solution of *N*-(tributylstannyl)succinimide (2.1 g, 0.0054 mole) in dry ether (10 ml) acetyl chloride (0.42 g, 0.0054 mole) was added with stirring. The reaction mixture was left in the cold overnight, and the *N*-acetylsuccinimide was collected;

yield 0.51 g (67%); m.p. 38°. After recrystallization from ether, the m.p. rose to 40–41° (lit.[8] 40–41). (Found: C, 50.85; H, 4.95; N, 9.93. $C_6H_7NO_3$ calcd.: C, 51.07; H, 5.00; N, 9.92%.)

N,N'-Adipoyldiimidazole

N-(Tributylstannylimidazole (7.14 g, 0.02 mole) was dissolved in petroleum ether (150 ml), adipoyl chloride (1.83 g, 0.01 mole) was added, and the reaction mixture was stirred for 15 min. The precipitate that formed was washed with light petroleum (yield 2.3 g, 93.5%) and recrystallized from ethanol, m.p. 161 (lit.[9] 158), (Found: C, 58.03; H, 5.83; N, 23.05. $C_{12}H_{14}N_4O_2$ calcd.: C, 58.52; H, 5.73; N, 22.75%.)

N,N',N''-Triacetyl-s-triazine-2,4,6-trione

To a solution of 1,3,5-tris(tributylstannyl)-s-triazine-2,4,6-trione[10] (4.98 g, 0.005 mole) in light petroleum (50 ml) acetyl chloride (2.5 g, 0.0032 mole) was added, and the mixture was heated under reflux for 30 min. The solution was left in the cold for 1 h and the product was filtered and washed with light petroleum, yield 1.2 g (94.5%); m.p. 142–3°. (Found: C, 42.32; H, 3.87; N, 16.66. $C_9H_9N_3O_6$ calcd.: C, 42.36; H, 3.55; N, 16.46%.)

N,N',N''-Tripropionyl-s-triazine-2,4,6-trione

The compound was prepared as above in 91% yield, m.p. 78–79°. (Found: C, 48.14; H, 5.11; N, 14.62. $C_{12}H_{15}N_3O_6$ calcd.: C, 48.49; H, 5.09; N, 14.12%.)

N,N',N''-Tribenzoyl-s-triazine-2,4,6-trione

The reaction with benzoyl chloride was carried out as above in benzene, reflux time 1 h; yield 98%; m.p. 240–241°. (Found: C, 65.41; H, 3.75; N, 9.39. $C_{24}H_{15}N_3O_6$ calcd.: C, 65.30; H, 3.42; N, 9.52%.)

N-(p-Toluenesulfonyl)imidazole

N-(Tributylstannyl)imidazole (3.57 g, 0.01 mole) and *p*-toluenesulfonyl chloride (1.91 g, 0.01 mole) were dissolved in light petroleum (50 ml). The reaction mixture was shaken for about 15 min. A heavy oily phase separated out, which on cooling and inoculation with a crystal of *N*-(p-toluenesulfonyl)imidazole crystallized out; yield 2.1 g (95.5%); m.p. 78° (lit.[11] 78°) after recrystallization from benzene/cyclohexane (1/3). (Found: C, 54.11; H, 4.78; N, 12.40; S, 14.47. $C_{10}H_{10}N_2O_2S$ calcd.: C, 54.03; H, 4.54; N, 12.61; S, 14.42%.)

N-Bromophthalimide

N-(Tributylstannyl)phthalimide (4.35 g, 0.01 mole) was dissolved in carbon tetrachloride (50 ml) and bromine (1.6 g, 0.01 mole) in carbon tetrachloride (10% solution) was added. *N*-Bromophthalimide separated out; yield 2.2 g (97%); m.p. 206°.

N-(2,4-Dinitrophenyl)phthalimide

N-(Tributylstannyl)phthalimide (4.35 g, 0.01 mole) was dissolved in dry DMF (50 ml), 2,4-dinitrofluorobenzene (1.86 g, 0.01 mole) was added, and the reaction mixture was gently heated for 1 h. The solution became red in a few minutes, and tri-

butyltin fluoride separated out. The DMF was evaporated *in vacuo*, petroleum ether was added slowly to the residue and *N*-(2,4-dinitrophenyl)phthalimide precipitated out; yield 2.3 g (73%); m.p. 195° (lit.[12] 192°). (Found: C, 53.40; H, 2.25; N, 13.61. $C_{14}H_7N_3O_6$ calcd.: C, 53.68; H, 2.25; N, 13.42%.)

N-(Triphenylstannyl)imidazole

N-(Tributylstannyl)imidazole (1.78 g, 5 mmoles) was dissolved in benzene (25 ml) and triphenyltin chloride (1.92 g, 5 mmoles) was added with stirring. The reaction mixture was heated under reflux, and the *N*-(triphenylstannyl)imidazole separated out and was collected; yield 1.9 g (91%); m.p. 310° (lit.[4] 310°).

Metathesis reaction between N-(tributylstannyl)phthalimide and imidazole

N-(Tributylstannyl)phthalimide (4.35 g, 0.01 mole) and imidazole (0.68 g, 0.01 mole) were dissolved in benzene (25 ml) and heated under reflux for 2 h. On cooling, phthalimide separated out; yield 1.3 g (88%); m.p. 237°. The benzene filtrate was evaporated to dryness, methanol was added, and on cooling to −15° (tributylstannyl)imidazole (2.35 g, 66%) crystallized out; m.p. 64–65°.

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