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Tetraalkynylstannanes in Synthesis of α,β-Acetylenic Ketones †

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Abstract: Akynyl ketones were synthesized from tetraalkinylstannanes and both aliphatic and aromatic acyl chlorides under Lewis acid catalysis. The structure of products was confirmed by means of NMR, IR, GC-MS. The method is suitable for the synthesis of long-chain acetylenic ketones.

Keywords: organotin compounds; tetraalkynylstannanes; acyl chlorides; α,β-acetylenic ketones

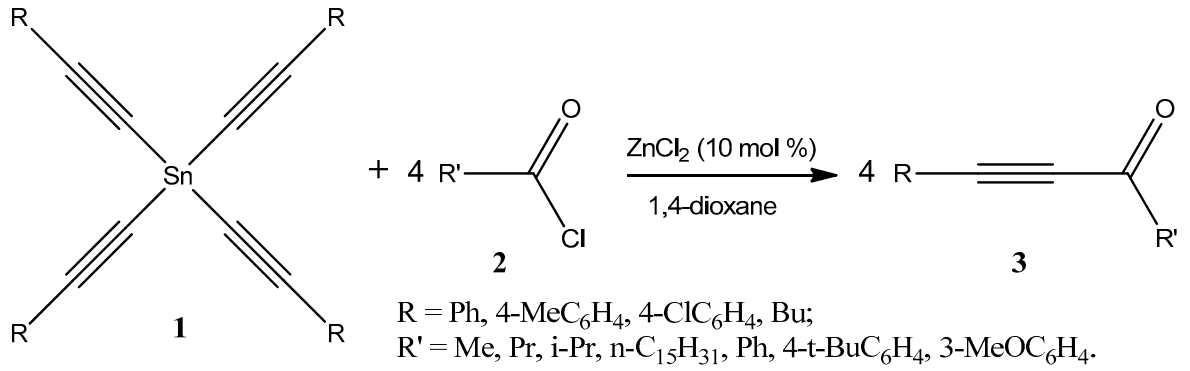
1. Introduction

α,β-Acetylenic ketones are widely used in organic synthesis as starting reagents for the preparation of indenones [1], benzodiazepines [2], chromones [3], frutinones [4], pyrazoles [5], and phosphonylated indenones [6]. Such ketones can be prepared by Sonogashira coupling of terminal alkynes and acyl halides. However, this reaction requires expensive palladium catalysts [7] or sophisticated mesoporous silicates [8]. To date, the most frequently used approaches for the synthesis of acetylenic ketones are based on the reaction of metal acetylides with acyl chlorides. Lithium, sodium, and potassium acetylides are among the most attractive organometallic reagents for the synthesis of functionalized acetylenes. However, due to their high reactivity with acyl halides, this reaction is difficult to control and cannot be stopped precisely at the stage of alkynyl ketone formation. Special interest has been given to trialkyltin acetylides, since these mild reagents are tolerant towards a number of functional groups and react smoothly in the presence of Pd catalysts to give functionalized acetylenes in high yields [9–11]. However, severe toxicity of trialkyltin species and high E-factor (mass ratio of waste to desired product) make the use of these acetylides unattractive for both laboratory and large-scale synthesis.

These drawbacks can be avoided with the replacement of monoalkynylstannanes with tetraalkynyltin reagents, as they are far less toxic and the molecular weight of the tin residue is significantly lower in comparison with trialkyltin reagents. Recently, we reported the Stille-type coupling reaction of tetraalkynylstannanes with aryl halides leading to aryl acetylenes and $SnHal_4$ [12] and aldehydes leading to alkynyl ketones [13,14]. Earlier, we developed convenient methods for preparation of tetraalkinyltin species from either $SnCl_4$ [15] or tin tetra(*N*,*N*-diethylcarbamate) [16].

2. Results and Discussion

Herein, we report an effective and time-saving protocol for the synthesis of acetylenic ketones via the reaction of tetraalkynylstannanes **1** with acyl chlorides **2**. This reaction starts easily in the presence of Lewis acid catalysts and is autocatalytic.



Scheme 1. The reaction of tetraalkynylstannanes with acyl chlorides.

The presence of tin tetrachloride, which is being formed during the reaction, accelerates the acylation process but also leads to some resinification of the acetylenic ketone **3**. The nature of the solvent also exerts a significant influence—thus, the use of 1,4-dioxane, which forms a complex with tin tetrachloride, leads to lower acidity and decreases side-reactions to some extent.

The effects of solvent and catalyst loading on the yield of acetylenic ketones were studied on the model reaction of tetra(phenylethynyl)stannane (TPES) with benzoyl chloride. The use of increased catalyst loading accelerates the reaction but also lowers the yield due to by-product formation. TPES did not react with benzoyl chloride below 80 °C. Meanwhile, the ketone yield tended to decrease with further temperature increases. The use of $ZnCl_2$ as a catalyst was found to be optimal, giving the highest product yields. The reaction did not proceed in the presence of basic catalysts. Another important factor that influences the reaction process is the reactant concentration. Thus, when the concentration of benzoyl chloride was doubled (increased from 1.4 mmol/mL to 2.8 mmol/mL), the yield of the target ketone increased significantly, despite the reaction mixture becoming thick as the reaction reached completion due to the formation of a complex between $SnCl_4$ and 1,4-dioxane. The formation of a thick slurry was taken to indicate that the reaction had proceeded to completion.

In order to avoid hydrolysis, all of the reactions were conducted in dry solvents under an argon atmosphere. The preparative yields of the alkynyl ketones varied from 63% to 99%. Lipophillic acid chlorides were noticeably more active in this reaction than aromatic acid chlorides. Thus, the reaction of TPES with acetyl chloride was complete within 30 min even at 40 °C, affording 4-phenylbut-3-yn-2-one in 99% isolated yield. The reaction of stannanes with other lipophillic acid chlorides required heating at 60 °C; the reaction was complete within 10 to 30 min, furnishing acetylenic ketones in good yields (78% to 95%). It should be noted that long-chain lipophillic acid chlorides also reacted well to give the corresponding long-chain ketones in high yields.

3. Conclusions

In summary, we have proposed a new, fast and atom-economical method for the preparation of α,β-acetylenic ketones, starting from mild nucleophilic reagents—tetraalkynylstannanes. The method is suitable for the synthesis of long-chain acetylenic ketones.

4. Experimental

Typical Procedure for the Synthesis of Alkynyl Ketones

A 2-mL sealable Wheaton vial was charged with anhydrous $ZnCl_2$ (27.3 mg, 0.2 mmol), 1,4-dioxane (0.72 mL), tetra(phenylethynyl)stannane (287.8 mg, 0.55 mmol) and hexadecanoyl chloride (549.7 mg, 2.0 mmol). The reaction mixture was stirred at 60 °C for 30 min, then treated with 1 M aqueous HCl (10 mL). The product was extracted with $CHCl_3$ (3 × 10 mL) and purified by column chromatography (eluent—hexane, then 1:1 hexane-toluene, then toluene) to give 1-phenyloctadec-1-yn-3-one in 95% yield (571.3 mg), as a light yellow solid. After recrystallization from heptane—colorless crystals, m.p. 41.4 to 41.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, CH_3), 1.21 to 1.37 (m,

24H, CH_2), 1.73 (quint, 2H, C^5H_2), 2.65 (t, 2H, C^4H_2), 7.35 to 7.39 (m, 2H, ArH), 7.42 to 7.46 (m, 1H, ArH), 7.55 to 7.57 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.08, 22.66, 24.17, 28.99, 29.33, 29.42, 29.57, 29.63, 29.65, 31.90, 45.54, 87.85, 90.48, 120.08, 128.57, 130.57, 132.99, 188.25.

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