CATALYST-FREE SYNTHESIS OF SYMMETRICAL DIARYL KETONES FROM ARYLSTANNANES AND OXALYL CHLORIDE

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Abstract

A novel regioselective synthesis of symmetric ketones using oxalyl chloride as C1 carbonyl synthon, under catalyst-free conditions is described. An attractive feature is that these reactions go, exclusively, through an *ipso*-substitution of the stannyl group overcompensating the directing influences of the aryl substituents. A reaction mechanism is suggested.

Keywords: Arylstannanes, Oxalyl chloride, Symmetrical diaryl ketones

Introduction

Oxalyl chloride has been known to be involved as C1 carbonyl synthon for ketone synthesis,[1] as an alternative route for carbonylation with CO gas. Given the importance of ketones in pharmaceutical and industrial applications, there is a permanent interest in finding new ways for their synthesis.

Based on the exceptional leaving group ability of the trialkylstannyl group in EAS, we have recently proposed an efficient catalyst-free and regioselective synthesis of unsymmetrical ketones using different acyl chlorides, in 1,2-dichlorobencene (*o*-DCB) as solvent at 180°C.[2] Driven by these results we initiated studies on the reaction of arylstannanes with oxalyl chloride.

Now, we describe a novel regioselective synthesis of symmetrical diaryl ketones using oxalyl chloride as C1 carbonyl synthon, under catalyst-free conditions. These results are significant from the point of view of its simplicity, the wide range of synthetically[3] or commercially available arylstannanes and the associated convenience in the utilization of oxalyl chloride as carbonyl synthon, instead of specific acyl chlorides.

All the reactions studied went, exclusively, through an *ipso*-substitution independently whether the directing influences of the aryl substituents and the trialkylstannyl group are either matched or mismatched. We suggest a mechanism by which oxalyl chloride acts as C1 synthon on these reactions.

Furthermore, we report the special workup carried out in order to recover the trialkyltin chlorides generated (see the Experimental Section).

Experimental Section

Oxalyl chloride was commercially available and fractionally distilled under nitrogen before use. Aryltrimethylstannanes **1a** and **1d** were obtained from the corresponding commercial aryl chlorides by photostimulated reaction with Me_3SnNa in liquid ammonia, according to the literature procedures.[3] Aryltributylstannanes **1b**, **1c** and **1e** were prepared by transmetalation of the appropiate Grignard reagents with tributyltin chloride in anhydrous THF. Physical and spectroscopic characteristics of compounds are consistent with those previously reported.

General procedure for the carbonylations of $ArSnR_3$ with oxalyl chloride. A 25 mL oven-dried Schlenk tube was charged with $ArSnR_3$ (1.0 mmol) and anhydrous *o*-DCB (1 mL) under nitrogen atmosphere. The system was purged with nitrogen by means of three vac-refill cycles and then oxalyl chloride (0.5 mmol) was added. The mixture was stirred at 180 °C to total disappearance of the stannane (monitoring by TLC). After addition of 10% (m/v) solution of NaOH (2 mL), the mixture was stirred at room temperature for 15 min and then diluted with ether (5 mL). The organic phase was successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification was performed by flash chromatography on silica gel doped with 10% of KF. Ketones were characterized by ^1H NMR, ^{13}C NMR and physical properties.

Disposal method for trimethyltin chloride. The aqueous solution (15 mL for 1.0 mmol scale reaction) was saturated with KF, 10 mL of Et_2O was added, and the mixture was vigorously shaken, then the precipitated trimethyltin fluoride (0.297 g, 81%) was removed by filtration at reduced pressure and stored for future reconversion to the chloride by treatment with an excess of NaCl in THF, according to the method reported by Mitchell.[4]

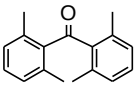
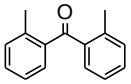
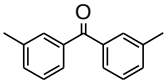
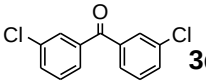
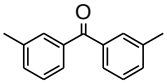
Disposal method for tributyltin chloride. After flash chromatographic procedure (10.0 g of silica gel for 1.00 mmol scale reaction) the column was eluted with 100 mL of THF. The silica was dried using compressed air and poured into a 100 mL round-bottomed flask fitted with a condenser and nitrogen T-joint. Sodium chloride (293 mg, 5.00 mmol) and 50 mL of dry THF were added and the mixture was heated at

reflux with stirring for 4 days. It was then allowed to cool and poured into a chromatography column plugged with a small piece of cotton wool. All of the THF was drained with air pressure and then the column was eluted with ether (2 x 50 mL). The combined ethers were concentrated in vacuo giving tributyltin chloride in ca. 80% with respect to the starting aryltributylstannane.

Results and discussion

We prepared electronically diverse starting trialkylarylstannanes (**1a-e**) and studied their reaction toward oxalyl chloride (**2**) under the optimized reaction conditions that we have previously established, that is, in *o*-DCB as solvent, at 180 °C. The results obtained are summarized in **Table 1**.

Table 1.

Entry	$ArSnR_3$ (2 eq.)	+	$(COCl)_2$ (1 eq.)	*o*-DCB, 180°C, time (h)		Yield (%)[a]
1	 **1a**		**2**	2	 **3a**	80[b]
2	 **1b**			6	 **3b**	52
3	 **1c**			7	 **3c**	20
4	 **1d**			12	 **3d**	35
5	 **1e**			5	 **3c**	45

[a] Determined by GC. [b] Isolated yield as an average of at lest two independet reactions.

First, we carried out a reaction between **1a** and **2**; pleasantly we noticed that the reaction occurred through the *ipso*-substitution of the stannyl group providing the expected ketone **3a** in excellent yield in rather short time (entry 1). The formation of ketone **3a** and not the corresponding diketone indicated the participation of **2** as C1 carbonyl synthon under these reaction conditions.

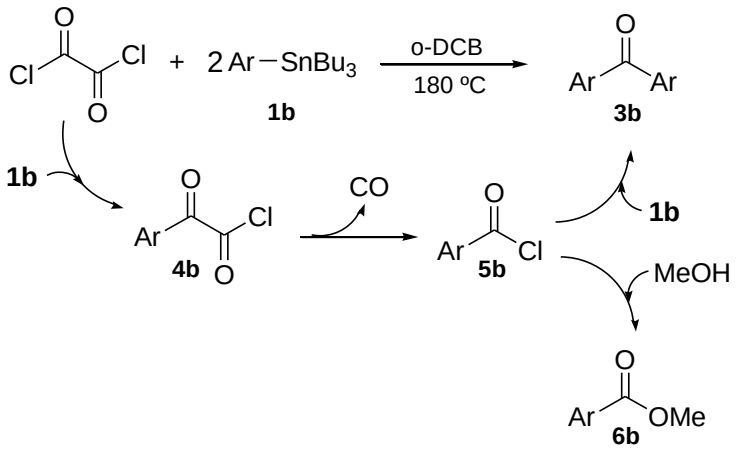
A similar reaction carried out with **1b** and **2** also gives the desired ketone **3b** in acceptable yield (entry 2). On the other hand, either **1c** and **1d** reacted with **2** giving the corresponding ketones **3c** and **3d** in lower yields after longer reaction times, being

detected, also, the presence of the corresponding biaryls (entries 3 and 4). When a similar reaction was carried out with **1e** an increment of the ketone yield was achieved together with a decrease in the reaction time (compare entries 3 and 5). Moreover, even traces of undesired biaryl were not detected.

These preliminary results indicate that reactivity of the arylstannanes is crucial in order to avoid the presence of biaryls, probably due to competitive reactions after longer reaction times.

We think that **2** acts as a C1 carbonyl synthon trough the following mechanism. In a first step the arylstannane reacts with **2** giving an α-oxo acid chloride intermediate which, under the reaction conditions, suffer decarbonylation generating the corresponding aroyl chloride which reacts with a second molecule of arylstannane[5] giving the diarylketone. In order to detect the aroyl chloride intermediate, a model reaction was voluntarily shortened (2 h) and the mixture was quenched with MeOH and was left overnight, under stirring. The presence of **6b** in the product mixture (GC), allow us to propose the mechanism resumed in Scheme 1.

Scheme 1



Conclusions

In summary, we have initiated a study to the reaction of oxalyl chloride with arylstannanes, under catalyst-free conditions. The results obtained to date indicate that oxalyl chloride acts as a C1 carbonyl synthon and that selective symmetric ketones are obtained in rather good to excellent yields. We continued with this study in order to determine the scope and limitations to this protocol to be applied to the selective synthesis of symmetric ketones avoiding the use of catalyst and of specific acid chlorides.

We are currently working on strategies to expand the application range of arilstannanes using oxalyl chloride as C1 or C2 carbonyl synthon.

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References

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[1] Rao, M. L. N.; Venkatesh, V.; Dasgupta, P. *Tetrahedron Lett.* **2010**, *51*, 4975-4980.

[2] Lo Fiego, M. J.; Silbestri, G. F.; Lockhart, M. T.; Chopa, A. B. *J. Org. Chem.* **2011**, *76*, 1707-1714.

[3] Silbestri, G. F.; Lo Fiego, M. J.; Lockhart, M. T.; Chopa, A. B. *J. Organometal. Chem*. **2010,** *695*, 2578-2585 and references therein.

[4] Mitchell, T. N.; Kwetkat, K.; Godry, B. *Organometallics* **1991**, *10*, 1633-1634.

[5] We have proved that the reaction of aroyl chlorides with arylstannanes give the corresponding ketone in good yields. Ref 2.