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Tetrahedron Letters 48 (2007) 4395–4398

Tetrahedron Letters

$SiCl_4$–Zn induced reductive coupling of carbonyl compounds: novel and efficient routes for one-pot syntheses of 1,2,3-triaryl-2-propen-1-ones and pinacolones at room temperature

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Received 8 March 2007; revised 5 April 2007; accepted 17 April 2007
Available online 22 April 2007

Abstract—An unprecedented one-pot reductive trimerization of aromatic aldehydes to 1,2,3-triaryl-2-propen-1-ones as well as tandem reductive coupling-rearrangements of aryl ketones to pinacolone analogues was efficiently achieved using tetrachlorosilane–zinc at room temperature.

The development of versatile methods for carbon–carbon bond formation is a central objective of synthetic organic chemistry. Reductive coupling of carbonyl compounds is a powerful method for accomplishing this task.[1] A number of reagents have been used with carbonyl compounds for achieving pinacol coupling or McMurry reactions, however, only a few reports have described the reductive coupling-rearrangement of ketones to pinacolones. For example, low valent titanium species generated in situ by the reduction of $TiCl_3$[2] or $TiCl_4$[3] have been used for such reductive coupling-rearrangements of ketones, even though certain difficulties arose with reproducibility of the titanium slurries with a lack of selectivity giving intermolecular radical dimerization. The relatively expensive $NbCl_3$(DME) also promoted the conversion of acetophenone to pinacolone along with the corresponding stilbene derivative.[4] Diaryl ketones such as benzophenones were converted to benzopinacolones with Al or Zn/$AlCl_3$ in CH_3CN under ultrasonic irradiation while aryl methyl ketones and cyclic ketones such as acetophenone and cyclohexanone gave only aldol-condensation products under the same reaction conditions.[5] Two recent reports showed that treatment of aryl methyl ketones with Zn/$AlCl_3$ in CH_3CN under reflux gave olefins[6] or pinacolones[7] and reasoned that the difference observed might be due to using a different grade of $AlCl_3$ or a sample with a different storage history. On the other hand, the reductive coupling of aldehydes to olefins and/or pinacols is well documented, but to our knowledge, the reductive trimerization of aromatic aldehydes to 1,2,3-triaryl-2-propen-1-ones is hitherto unknown. In the course of our studies[8] on the development and applications of new reagents derived in situ from tetrachlorosilane (TCS)[9] in organic synthesis, we have developed a new protocol for the tandem reductive coupling-rearrangement of ketones to pinacolones using the inexpensive and readily available tetrachlorosilane–zinc reagent in dichloromethane at room temperature. Using these very mild conditions, we also present a unique route for the one-pot conversion of aromatic aldehydes to 1,2,3-triaryl-2-propen-1-ones which are useful as anti-estrogenics.[10]

A number of aryl ketones were treated with a mixture of zinc and tetrachlorosilane in the ratio 1:6:4 in dichloromethane at room temperature to afford pinacolone analogues as the major products along with small amounts of substituted stilbenes in most reactions (Scheme 1, Table 1).

As shown from the results in Table 1, the reaction proved to be general and quite efficient for a variety of ketones with preferable aryl migration rather than methyl in each case. It is well known that the substituents on acetophenones have no effect on the course of such molecular rearrangements.[11] Electron-donating groups accelerate coupling while electron-withdrawing

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Keywords: Tetrachlorosilane; Zinc; Carbonyl compounds; Reductive-coupling; Rearrangement; Pinacolones; 1,2,3-Triaryl-2-propen-1-ones.

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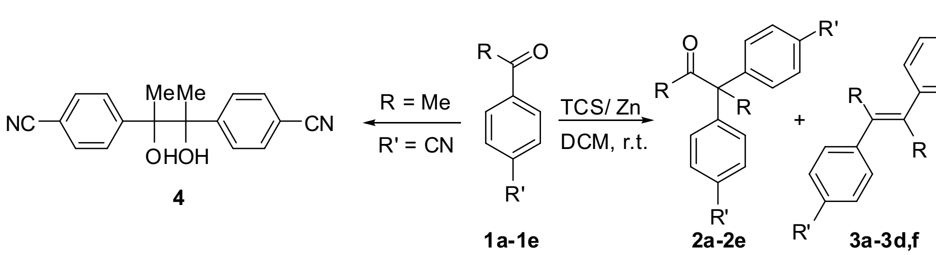
doi:10.1016/j.tetlet.2007.04.092



1a, 2a, 3a; R = Me, R'= H
1b, 2b, 3b; R = Me, R'= Cl
1c, 2c, 3c; R = Me, R' = Br
1d, 2d, 3d; R = Me, R' = OMe
1e, 2e; R = Me, R' = Ph
1f, 2f, 3f; R = Ph, R' = H

Scheme 1.

Table 1. Reductive coupling—rearrangement of ketones utilizing the TCS–Zn reagent

Entry	Substrate	Time (h)	Product	Yield (%)
1	Acetophenone	12	**2a**	82
			3a	7
2	4-Chloroacetophenone	15	**2b**	78
			3b	9
3	4-Bromoacetophenone	17	**2c**	80
			3c	10
4	4-Methoxyacetophenone	10	**2d**	85
			3d	10
5	4-Acetylbiphenyl	11	**2e**	83
6	4-Acetylbenzonitrile	20	**4**	62
7	4-Nitroacetophenone	22	—	
8	3-Nitroacetophenone	23	—	
9	Benzophenone	26	**2f**	69
			3f	24

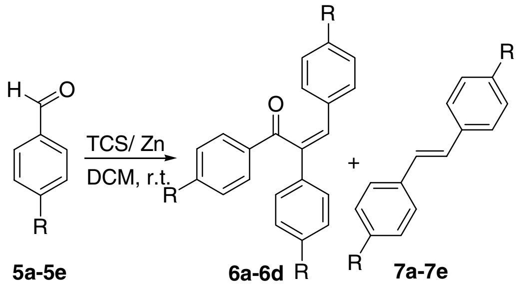
Table 2. Reductive coupling reaction of aryl aldehydes with the TCS–Zn reagent

Entry	Substrate	Time (h)	Product	Yield (%)
1	Benzaldehyde	2	**6a**	71
			7a	23
2	4-Methylbenzaldehyde	2	**6b**	75
			7b	21
3	4-Chlorobenzaldehyde	4	**6c**	66
			7c	18
4	4-Bromobenzaldehyde	5	**6d**	69
			7d	12
5	3,4-Dichlorobenzaldehyde	16	**7e**	33
6	4-Nitrobenzaldehyde	18	—	—

groups have an inhibiting effect. Thus, activated aryl methyl ketones such as 4-methoxyacetophenone and 4-acetylbiphenyl gave the corresponding pinacolones **2d** and **2e** in high yields. Moderately deactivated aryl methyl ketones were transformed into pinacolone derivatives **2b** and **2c** at a slower rate, but in good yield. In the case of 4-acetylbenzonitrile, although similar reaction conditions were used, the corresponding pinacolone was not observed, but rather the reaction stopped at pinacol formation giving 2,3-bis(4′-cyanophenyl)-2,3-butanediol **4**. Moreover, strong electron withdrawing groups inhibit this coupling completely, no reaction was observed with 3′-, or 4′-nitroacetophenone even when using an excess of Zn and TCS for longer times (up to 10 equiv, entries 7 and 8). In contrast, diaryl ketones such as benzophenone reacted slowly under the same conditions to give a mixture of benzopinacolone and tetraphenyl ethylene (entry 7). The slow reaction as well as the increased amount of alkene derivative may arise from steric effects.

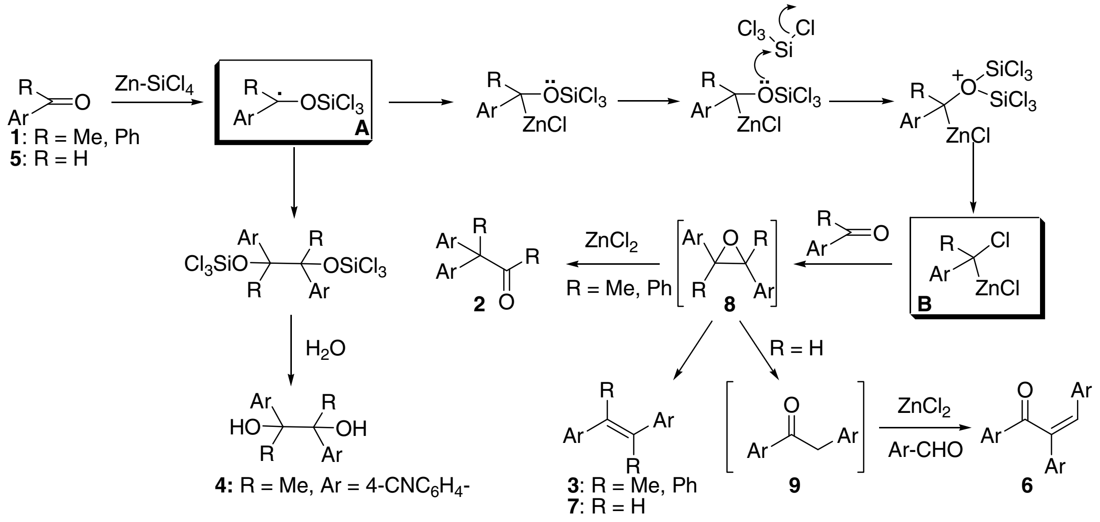
Various aromatic aldehydes were also reacted with the tetrachlorosilane–zinc reagent. Table 2 demonstrates that treatment of aryl aldehydes with TCS–Zn in the ratio 1:2:4 under mild conditions at room temperature in dichloromethane typically gave two products, the major product was identified as 1,2,3-triaryl-2-propen-1-one **6** while the minor one proved to be stilbene derivative **7**. This reaction tolerated several functional groups on the aromatic ring, including bromine, chlorine, and methyl (Scheme 2, Table 2).

As with ketones, the reaction with aldehydes was strongly retarded by electron-withdrawing groups. Thus, the reaction of 3,4-dichlorobenzaldehyde (Table 2, entry 5) afforded the anticipated stilbene derivative **7e** in low yield from a complex mixture of products whilst the starting material was recovered in the coupling reaction of 4′-nitrobenzaldehyde (Table 2, entry 6). In addition to the coupling of aryl aldehydes, it



5a, 6a, 7a; R = H
5b, 6b, 7b; R = Me
5c, 6c, 7c; R = Cl
5d, 6d, 7d; R = Br
5e, 7e; R = 3,4-di Cl

Scheme 2.



Scheme 3.

should be mentioned that a multi-component mixture was obtained from the reaction using aliphatic aldehydes (i.e., *n*-butyraldehyde) with the TCS–Zn reagent. The radical intermediates from aliphatic aldehydes may be unstable and do not have enough time to react to give distinct products as has been reported in a similar case.[12]

A reasonable pathway for the present reaction may proceed as depicted in Scheme 3 via a carbene mechanism[13] involving the formation of *O*-siloxy radical **A** through the reaction of one molecule of carbonyl compound with TCS–Zn which can be reduced to produce carbene **B**. Subsequent addition of carbene **B** across the carbonyl group of a second molecule of carbonyl compound yields the intermediate *trans*-stilbene oxide **8**. Zinc chloride induced ring opening of this incipient epoxide would account for the formation of *trans*-stilbenes **3** and **7** and rearranged pinacolone **2** or deoxybenzoin **9.** The latter may undergo an aldol type condensation with a third molecule of aldehyde giving 1,2,3-triaryl-2-propen-1-one **6** presumably arising from zinc chloride catalyzed condensation.[14] On the other hand, *O*-siloxy radical **A** stabilized by an electron-withdrawing group may be dimerized to form the *O*-silylated pinacol which upon aqueous workup, yields pinacol **4**. This plausible mechanism is in agreement with the well documented transformation of *trans*-stilbene epoxide to an alkene in the presence of Me_3SiCl–Zn.[15] Besides, deoxybenzoin was isolated through the reaction of benzaldehyde with Me_2SiCl_2/Zn–Cu as well as benzpinacol via a similar pathway.[13b]

In conclusion, we report TCS–Zn[16] as a new reagent for the tandem reductive coupling rearrangement of ketones to pinacolone derivatives under mild conditions. The present method is convenient, inexpensive and applicable to a variety of aryl methyl and diaryl ketones. Moreover, the TCS–Zn reagent has promoted the first direct reductive trimerization of aromatic aldehydes to 1,2,3-triaryl-2-propene-1-ones under very mild conditions. It is noteworthy that only multi-step routes to such compounds from aryl aldehydes through deoxybenzoins have previously been reported.[17]

Acknowledgements

We would like to thank Dr. H. A. Soliman and Dr. E. H. Nashy for their spectroscopic assistance as well as Dr. E. Bouzas for valuable help with the artwork.

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16. A typical procedure for reductive coupling of **1** or **5** with $SiCl_4$/Zn in the ratio 1:4:6 or 1:2:4, respectively: To a stirring mixture of zinc and carbonyl compound (**1** or **5**) in CH_2Cl_2 at room temperature was added $SiCl_4$ and the mixture left to stir until TLC showed disappearance of the starting material. The reaction was then poured onto water and filtered. The filtrate as well as the precipitate was extracted with CH_2Cl_2. The extracts were collected, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography (pet. ether–ethyl acetate 10:1 or 20:1) to give pure **2** or **6**, respectively. Ketones **2** are all known compounds,[4,5,18] except for **2e**, mp 95 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.52–7.57 (m, 8H), 7.23–7.43 (m, 10H), 2.14 (s, 3H, COMe), 1.89 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 205.2, 142.3, 140.1, 137.5, 131.1, 128.2, 127.9, 127.1, 126.7, 58.9, 29.2, 27.1; MS (m/z, %): 333 (M^+−COMe, 100); IR (KBr plate) ν 3025, 2955, 2850, 1700 (CO), 1600 (C=C), 750, 700 cm^{-1}; Anal. Calcd for $C_{28}H_{24}O$ (376.49): C, 89.33; H, 6.43%. Found: C, 89.19; H, 6.51%. α-Aryl chalcones **6a**,**b** are known[17a,b] while **6c**,**d** are unknown. Data for **6c**: mp 136–138 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.74–7.77 (d, $J = 8$ Hz, 6H), 7.28–7.51 (m, 7H, 6 Ar-H + vinyl H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 194.3, 141.1, 137, 135.1, 134.3, 133.2, 131.9, 130.3, 129.8, 128.2, 128.9, 128.3; IR (KBr plate) ν 2930, 1654 (CO), 1586 (C=C), 1484, 1397, 1282, 1011, 851, 754, 688; UV λ_{max} (EtOH 95%) 262 (ε 2000), 223, 211 nm; Anal. Calcd for $C_{21}H_{13}Cl_3O$ (387.65): C, 65.06; H, 3.38%. Found: C, 65.14; H, 3.32%.
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