

AN IMPROVED METHOD FOR THE GENERATION OF ORGANOZINC CARBENOIDS AND ITS APPLICATION IN DICARBONYL COUPLING REACTIONS

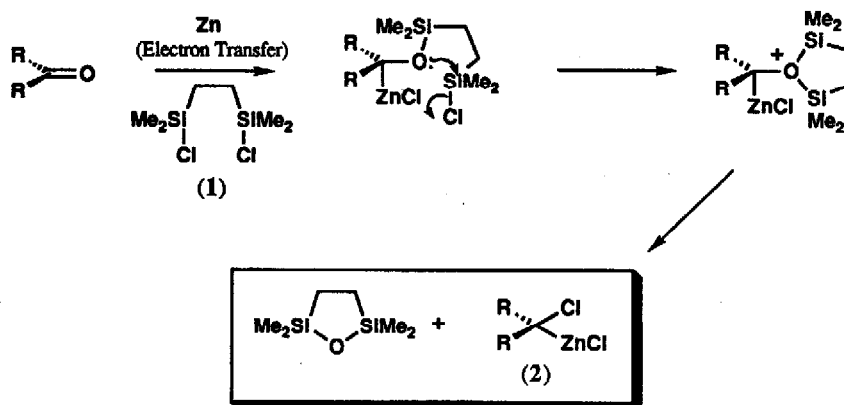
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Abstract: Reaction of aromatic aldehydes and certain α,β -unsaturated carbonyl compounds with 1,2-bis(chlorodimethylsilyl)ethane and zinc leads to products of symmetrical dicarbonyl coupling.

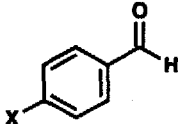
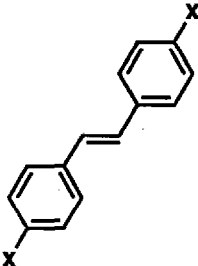
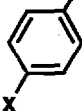
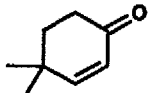
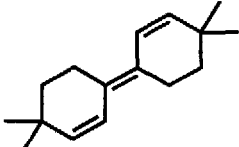
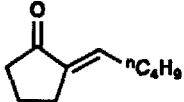
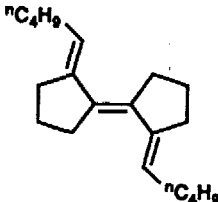
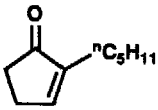
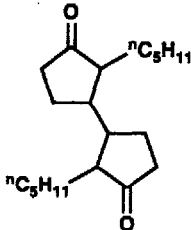
We have previously reported a novel type of symmetrical dicarbonyl coupling reaction of certain aromatic aldehydes and α,β -unsaturated carbonyl compounds using chlorotrimethylsilane and zinc.¹ In contrast to the McMurry reaction,² vicinal diols or their derived trimethylsilyl ethers were inert, thereby precluding the operation of a pathway utilising pinacolic coupling. A mechanism involving the trapping of an organozinc carbenoid³ by a second molecule of carbonyl compound and subsequent deoxygenation of the resulting epoxide was proposed. The formation of stilbene from *trans*-stilbene oxide was demonstrated under the reaction conditions.



Scheme 1

During studies to extend the range of substrates, we became even more aware that pinacolic type coupling or dimerisation of trimethylsilyloxy alkyl radicals, produced at the one electron reduction level, could

Table 1. Reaction of Aromatic Aldehydes and α,β -unsaturated Carbonyl compounds with 1,2-bis (chlorodimethylsilyl)ethane (1) and Zinc.

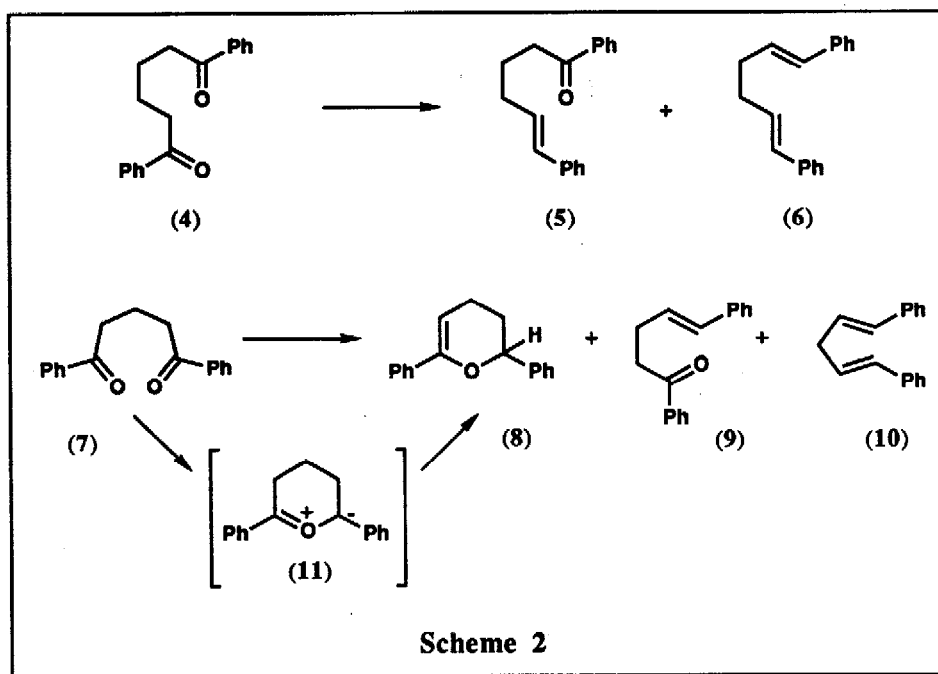
Entry	Substrate	Product	X	Yield*
1.			OMe	79%
2.			Me	86% [†]
3.			H	69%
4.			Cl	26%
5.				76%
6.				72%
7.				18%

* Aldehyde and dichlorodisilane slowly added to the zinc.⁶

† Aldehyde slowly added to the dichlorodisilane and zinc.

be an undesirable and even dominant^{1,3} process, as can be found in the mechanistically analogous Clemmensen reduction.⁴ Since the formation of the putative organozinc carbenoid (2) formally requires the delivery of *two* electrons from zinc and sequential attack of *two* silicon electrophiles we reasoned as shown in Scheme 1 that the overall efficiency of carbenoid generation would be improved by selection of 1,2-*bis*(chlorodimethylsilyl) ethane (1) as a *bis* electrophile which would then permit *intramolecular* delivery of the second electropositive silicon atom.⁵

The results for a variety of substrates are shown in Table 1, and confirm that a more efficient dicarbonyl coupling procedure is possible. Several features are worthy of particular comment. Within the series of aromatic aldehydes (Entries 1, 3, 4), the decreasing yields in the series *para* OMe > H > Cl are mirrored by those obtained under classical Clemmensen conditions and are, in all probability, related to the redox potential of the corresponding carbonyl substrate. Of the acyclic enones which have been examined (Entries 5, 6, 7), it is notable that successful dicarbonyl coupling to give oxygen sensitive *s-trans*-trienes⁷ is favoured either by branching and/or by increased hindrance around the β -carbon atom of the enone unit, as demonstrated by the remarkable difference between the *exo* and *endocyclic* cyclopentanoid isomers (Entries 6, 7).



Finally, we have attempted to perform some intramolecular dicarbonyl coupling reactions (Scheme 2). Reaction of (4) gave the open chain products (5) (18%) and (6) (42%), indicating that insertion of the carbenoid into the neighbouring C-H bond was an energetically more favourable outcome than interaction with the second carbonyl group. More interestingly, however, use of the *nor* methylene congener (7) gave dihydropyran (8) (31%) along with open chain products (9) (14%) and (10) (21%). Dihydropyran (8) is formed presumably *via* a carbonyl ylide⁸ like intermediate (11) whose ring closure to the epoxide

necessary for deoxygenation to alkene is effectively retarded by a combination of electronic effects and ring strain. Such an observation is also in keeping with the carbenoid character of intermediates (2), and tends to rule out the possibility of epoxide formation *via* nucleophilic attack at the carbonyl group in a manner reminiscent of intermediate (2) functioning as a Reformatsky like reagent, or as the carbanion in a Darzen's Glycidic Ester condensation.

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References and Notes

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 - The formation and representation of the organozinc carbenoid on a zinc surface may be considered in a variety of ways, as, for example, through evolution of an oxometallocycle as shown below. The organozinc carbenoid may then be viewed as attached to the surface while electrochemical "corrosion" produces zinc chloride. For convenience, we have chosen to feature the intermediate by analogy with the Simmons-Smith reagent.
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- A typical procedure: To a stirring mixture of zinc amalgam (13.2 mmol) and THF (6 ml) at room temperature was added a solution of the carbonyl compound (1.32 mmol), 1,2-bis(chlorodimethylsilyl)ethane (2.64 mmol, 1.4M in THF) and THF (4 ml) dropwise over one hour and then left overnight. The reaction mixture was filtered through florisil, washing with diethyl ether, and the filtrate evaporated *in vacuo*. The residue was dissolved in ether/water and stirred for 30 mins. The ether layer was separated, dried over MgSO₄ and the solvent removed *in vacuo*. The crude product was purified by silica gel chromatography. In the case of *p*-tolualdehyde (entry 3), the carbonyl compound was added to a flask containing both the 1,2-bis(chlorodimethylsilyl)ethane and zinc amalgam, whilst the workup involved washing the ethereal solution with aqueous saturated sodium bicarbonate.
 - The geometries of the trienes were characterised by ultraviolet spectroscopy.
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