Efficient Coupling of Tertiary Alkyl Halides with Dialkylzinc and Titanium Compounds

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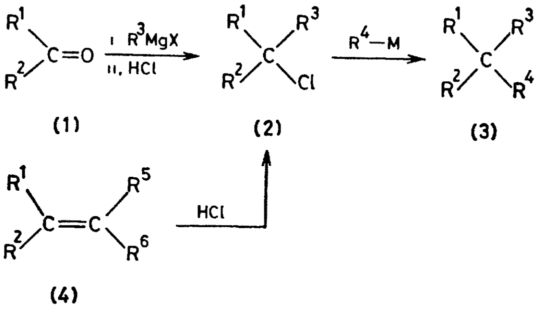
Summary Dialkylzinc compounds react with tertiary alkyl halides to afford the corresponding coupling products containing a quaternary carbon atom, thereby making geminal dialkylation of ketones or hydroalkylation of olefins possible

TECHNIQUES for the synthesis of compounds containing quaternary carbon atoms are of current interest [1] Geminal dialkylation of ketones *via* the sequence (**1**) → (**2**) → (**3**) or hydroalkylation of the olefins (**4**) → (**2**) → (**3**) appear attractive (Scheme 1), but have rarely been exploited



SCHEME 1 M = metal

because of the general inefficiency of the coupling reaction between tertiary halides and organometallic reagents.[2]†

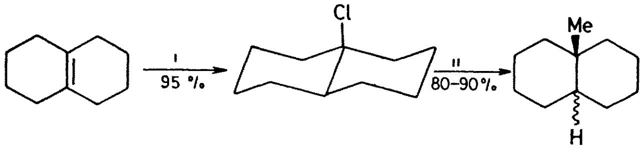
Our recent discovery that $MeTiCl_3$ and Me_2TiCl_2 are excellent methylating agents[3] [70—95% yields of (**3**), R^4 = Me] prompted us to extend the method to more complex systems. We now report two new developments: (i) The introduction of angular methyl groups *via* hydromethylation is possible, and (ii) dialkyl- and diaryl-zinc compounds are useful alkylating agents, if the proper solvent is chosen.

TABLE. Geminal dialkylation of ketones (Scheme 1).[a]

(**1**)	R^3	R^4	(**3**)	Yield[b]/% (**2**) → (**3**)
Cyclohexanone	Me	Me	1,1-Dimethylcyclohexane	90
Cholestan-3-one	Me	Me	3,3-Dimethylcholestane	89
Tricyclo[5.2.1.$0^{2,6}$]decan-8-one	Me	Me	8,8-Dimethyltricyclo[5.2.1.$0^{2,6}$]decane	72
Acetone	C_6H_4Me-*m*	Me	*m*-Methyl-t-butylbenzene[c]	84
Pinacolone	Me	Me	2,2,3,3-Tetramethylbutane	80
Hexane-2,4-dione	Me	Me	2,2,4,4-Tetramethylhexane	81
Cyclohexanone	Me	Bu^n	1-Butyl-1-methylcyclohexane	70
Cyclohexanone	Et	Et	1,1-Diethylcyclohexane	41
Cyclohexanone	Et	Bu^n	1-Butyl-1-ethylcyclohexane	46
Cyclododecanone	Me	Bu^n	1-Butyl-1-methylcyclododecane	45
Nonan-2-one	Me	Bu^n	5,5-Dimethyldodecane	46
Nonan-2-one	Me	Ph	2-Methyl-2-phenylnonane	31
Benzophenone	Ph	Ph	Tetraphenylmethane	54

[a] Reactions were carried out at −20 to −50 °C for 2—4 h in methylene chloride in the presence of catalytic amounts of zinc chloride. The starting tertiary alkyl chlorides were prepared by conventional means. [b] Yields refer to the isolated products. [c] Reaction carried out at −78 °C for 0·5 h.

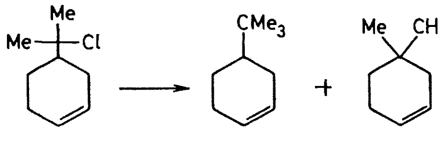
Conversion of Δ^9-octalin (**5**) under conditions of kinetic control into *trans*-9-chlorodecalin (**6**)[4] followed by reaction with $MeTiCl_3$[5] or $ZnMe_2$[6] in methylene chloride affords 80—90% of 9-methyldecalin (**7**) having a *trans*- *cis*-isomer ratio of 1 : 1. In pentane, the reaction with $ZnMe_2$ is slower and not as efficient (70% yield), but the *trans*- *cis*-ratio is about 1 : 2. The thermodynamic equilibrium over a wide temperature range is known to be about 55 : 45 in favour of the *trans*-isomer.[7] $Me(OPr^i)_3Ti$ is ineffective.



(**5**) (**6**) (**7**)

SCHEME 2. *Reagents and conditions*: i, HCl–ether, 0 °C; ii, Me_2Zn–$ZnCl_2$ or $MeTiCl_3$, −40 °C, 0·5 h.

We also carried out geminal dialkylation of ketones using dimethyl-, diethyl-, dibutyl-, and diphenyl-zinc in the final step (**2**) → (**3**). Whereas previous reactions between a number of simple tertiary halides and dimethylzinc were performed in tetralin as the solvent, affording only 20—50% of alkylation products,† the use of methylene chloride causes a large increase in the yield. For example, the conversion of 1-chloro-1-methylcyclohexane into 1,1-dimethylcyclohexane is essentially quantitative, compared with the previous yield of 37%.[2] Also noteworthy is the smooth formation of other methylated compounds (Table), including *m*-methyl-t-butylbenzene, which is inaccessible by Friedel–Crafts alkylation of toluene, and 2,2,3,3-tetramethylbutane containing two neighbouring quaternary carbon atoms. The yields are comparable to those when $MeTiCl_3$ is used.[3] However, the ready availability of dimethylzinc makes the present method particularly attractive. A further advantage is seen in the high positional specificity in systems in which the corresponding tertiary carbonium ions may undergo rapid 1,2-hydride shifts to generate different tertiary ions. For example, at −78 °C $ZnMe_2$ reacts with (**8**) to afford a 96.2 : 3.8 mixture of (**9**) and (**10**) (total yield 81%) [equation (1)], whereas in the previous study the titanium reagent resulted in a positional specificity of only 89·7%.[4] The zinc system constitutes a milder Lewis acid less prone to induce rearrangements.



(1)

(**8**) (**9**) (**10**)

The reactions of other dialkylzinc compounds are generally not as smooth (Table), reduction of the tertiary alkyl halide *via* hydride-ion abstraction being an important side reaction. The corresponding titanium[8] or aluminium[9]

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† Low yields with sodium, magnesium, or zinc reagents: F. Asinger and H. H. Vogel, 'Methoden der Organische Chemie,' Houben-Weyl-Muller, 4th Edn., Vol. 5/1a, p. 347 ff., Thieme, Stuttgart, 1970. There is no coupling with cuprates: G. M. Whitesides, *J. Am. Chem. Soc.*, 1969, **91**, 4871. Trimethylaluminium appears to be better suited, but has not been studied extensively on a preparative scale: J. P. Kennedy, U. V. Desai, and S. Sivaram, *J. Am. Chem. Soc.*, 1973, **95**, 6386, and earlier literature; exhaustive methylation of ketones with trimethylaluminium: A. Meisters and T. Mole, *Aust. J. Chem.*, 1974, **27**, 1665.

derivatives are even less useful alkylating agents Finally, the reaction of trityl chloride with diphenylzinc constitutes the currently best synthesis of tetraphenylmethane [10]

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