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α-ALKYLATION OF KETONES, ESTERS, AND LACTONES: ZINC BROMIDE-CATALYSED ALKYLATION OF *O*-SILYLATED ENOLATES, A SYNTHESIS OF (±)-*AR*-TURMERONE[1]

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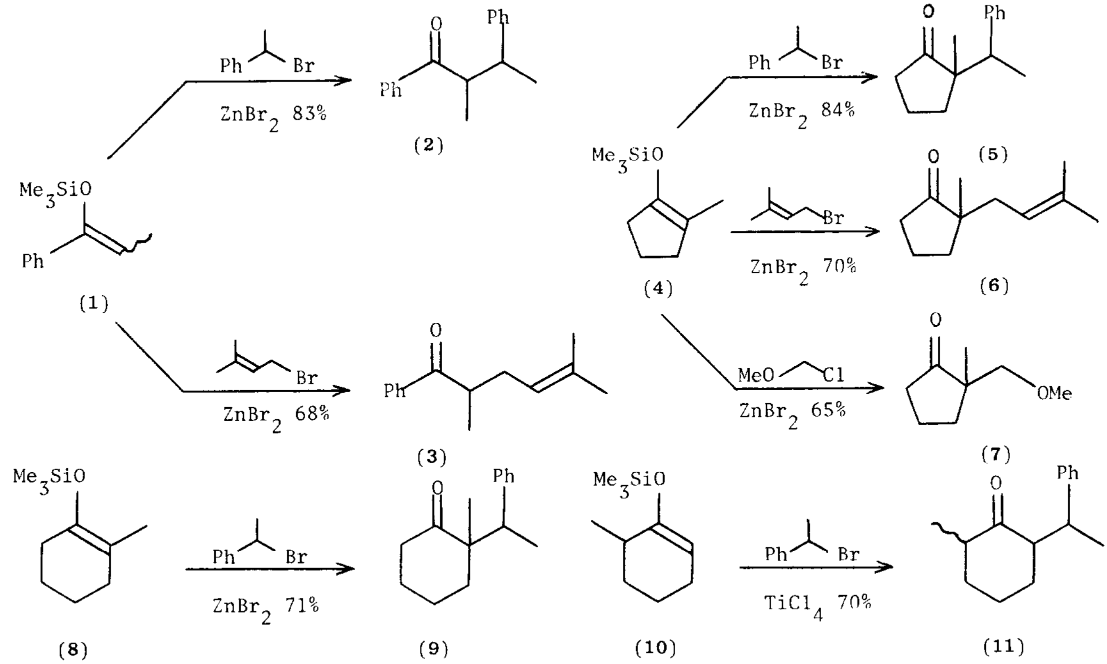
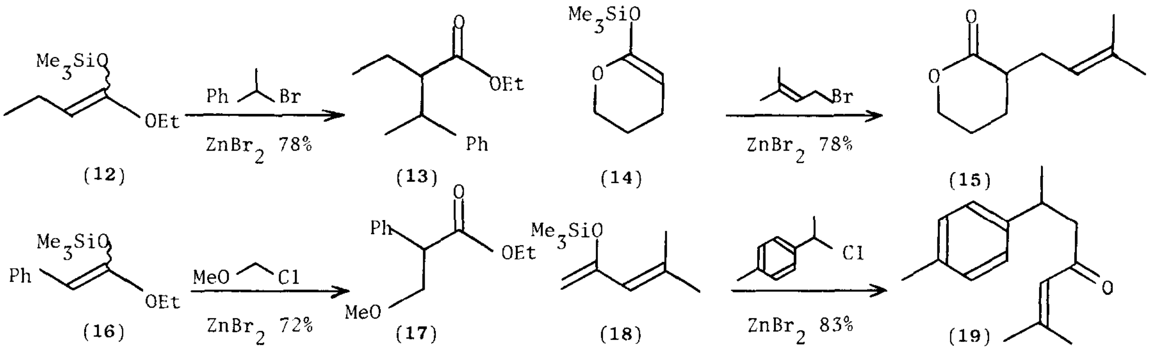
O-Silylated ketone enolates can be alkylated regiospecifically with t-alkyl halides in the presence of an equivalent of titanium tetrachloride;[2] for the alkylation of lithium enolates, in general, dialkylation,[3] loss of regiospecificity,[3] and self-condensation[4] are common problems. Alternative methods[3,5] for the specific alkylation of ketones are best suited for alkylation at the less-substituted side.



I now report that the alkylation of *O*-silylated enolates[6] of ketones, esters, and lactones can be extended to certain types of primary and secondary alkyl halide, using *a catalytic amount of zinc bromide*, to give the monoalkylated carbonyl compounds in good yield, as summarised in diagrams 1 to **19**. The reaction works well for secondary benzylation (**1**→**2**, **4**→**5**, **8**→**9**, **12**→**13**, and **18**→**19**), prenylation (**1**→**3**, **4**→**6**, and **14**→**15**), and methoxymethylation (**4**→**7** and **16**→**17**), but it could not be extended to less reactive primary and secondary alkyl halides. $ZnBr_2$ is generally a more effective Lewis acid than $TiCl_4$ in these reactions, whereas the latter is better suited for the t-alkylation of silyl enol ethers;[2] $ZnBr_2$ has the important advantages of mildness, catalytic use, and ease of operation.

Typically, a catalytic amount of powdered anhydrous ZnBr$_2$ (*ca.* 25 mg, 0.1 mmol) was added to a solution of the alkyl halide (6 mmol) and *O*-silylated enolate (5 mmol) in dry CH$_2$Cl$_2$ (10 ml) at room temperature. This mixture was briefly shaken every 5-10 min. After 0.5-1.5 h, the solvent was simply evaporated and the residue chromatographed on silica gel to give the α-alkylated carbonyl compound directly.

The method is particularly effective for alkylation at the more-substituted side of unsymmetrical ketones, complementing the alternative methods;[3,5] for instance, the 'thermodynamic' silyl enol ethers (**4** and **8**) were regiospecifically alkylated to give **5**, **6**, **7**, and **9**. For the 'kinetic' silyl enol ether (**10**) the predominant product obtained on ZnBr$_2$-catalysed sec-benzylation was **9**; equilibration of **10** to **8** is evidently faster than alkylation with this particular alkyl halide. In this case, replacing ZnBr$_2$ by TiCl$_4$ allowed regiospecific alkylation (**10**→**11**).[7]



I have used this method in an extraordinarily short synthesis of the sesquiterpene (±)-*ar*-turmerone (**19**).[8] The *O*-silylated dienolate (**18**), prepared from mesityl oxide with LDA in THF at -78° followed by treatment with Me$_3$SiCl (96%), was alkylated in the presence of ZnBr$_2$[9] in CH$_2$Cl$_2$ at room temperature to give **19** in 80% overall yield.

I thank Professor T. H. Chan at the Dept. of Chemistry, McGill University, and Dr. Ian Fleming at Cambridge for helpful discussions.

NOTES and REFERENCES

[1] Reprints of this paper will not be available.

[2] T. H. Chan, I. Paterson, and J. Pinnsonnault, *Tetrahedron Letters*, 4183 (1977); M. T. Reetz and W. F. Maier, *Angew. Chem. Internat. Edn.*, **17**, 48 (1978).

[3] I. Kuwajima and E. Nakamura, *J. Amer. Chem. Soc.*, **97**, 3257 (1975) and references therein.

[4] M. W. Rathke and A. Lindert, *J. Amer. Chem. Soc.*, **93**, 2318 (1971).

[5] G. Stork and S. R. Dowd, *J. Amer. Chem. Soc.*, **85**, 2178 (1963); M. E. Jung, P. A. Blair, and J. A. Lowe, *Tetrahedron Letters*, 1439 (1976); E. J. Corey and D. Enders, *Chem. Ber.*, **111**, 1337 (1978).

[6] J. K. Rasmussen, *Synthesis*, 91 (1977).

[7] Co-addition of **10** and 1-(bromoethyl)benzene was made to TiCl$_4$ (1 equivalent) in CH$_2$Cl$_2$ (-23°, 1 h). After 2 h, the reaction mixture was poured into saturated NaHCO$_3$ solution; extractive work-up and chromatography gave **11** as a mixture of stereoisomers.

[8] For previous syntheses, see: P. A. Grieco and R. S. Finkelhor, *J. Org. Chem.*, **38**, 2909 (1973) and references therein.

[9] When the stronger Lewis acid TiCl$_4$ was used for this synthesis, it was first necessary to protect the double bond of the mesityl oxide.

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