Tetrahedron Letters No. 23, pp 2009 - 2012, 1977. Pergamon Press. Printed in Great Britain.

NOVEL AND CONVENIENT ROUTE TO SUBSTITUTED SUCCINATES. THE DIMERIZATION OF KETENE SILYL ACETALS PROMOTED BY TITANIUM TETRACHLORIDE

Shin-ichi Inaba and Iwao Ojima*
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara 229, Japan

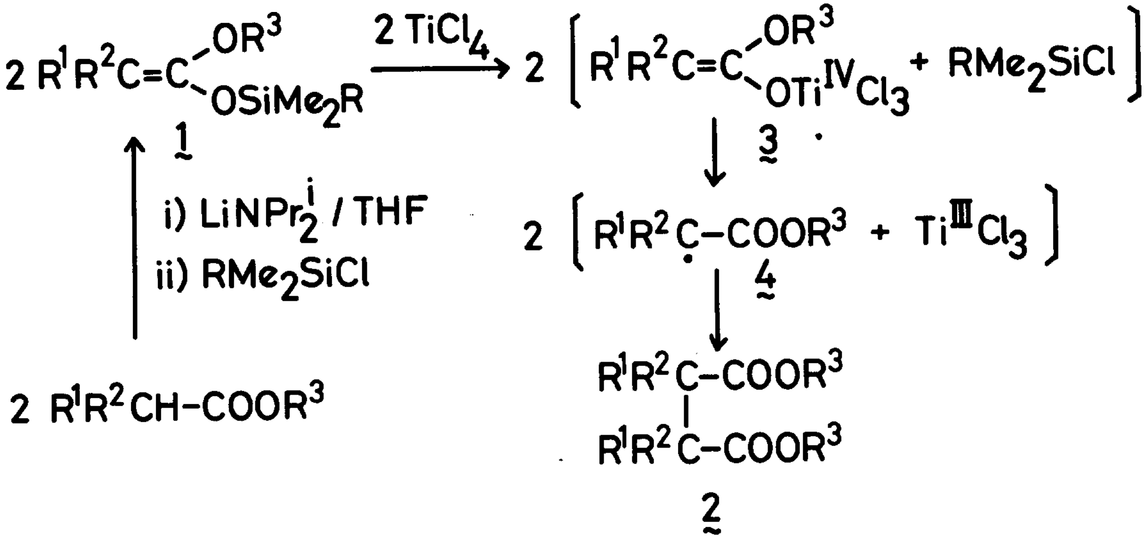
(Received in Japan 4 April 1977; received in UK for publication 28 April 1977)

The oxidative coupling of organosilver and organocopper compounds has been extensively studied for a long time.[1] Nevertheless, as for the metal-promoted coupling of enolate anions only few examples are known.[2,3,4] For instance, Rathke and Lindert reported the dimerization of lithium ester enolates promoted by copper(II) salts,[3] and Ito *et al.* presented the regiospecific coupling of silyl enol ethers by the action of silver oxide in dimethyl sulfoxide.[4] We wish to describe here the facile synthesis of substituted succinates by the dimerization of ketene silyl acetals promoted by titanium tetrachloride, in which titanium(IV) enolates (3) are assumed to be a reactive intermediate.

A typical procedure is described for the reaction of dimethylketene methyl trimethylsilyl acetal with titanium tetrachloride: To a dichloromethane solution (10 ml) of dimethylketene methyl trimethylsilyl acetal (1a, 1.74 g, 10 mmol) was added dropwise 10 ml (10 mmol) of an 1*M* solution of titanium tetrachloride in dichloromethane at ambient temperature. The reaction mixture was stirred for 60 minutes at ambient temperature, and the resulting dark brown solution was poured into ice-water for hydrolysis. The organic layer was separated, washed with water, dried over anhydrous magnesium sulfate, and distilled to afford 0.81 g (80 %) of dimethyl tetramethylsuccinate (2a).

The present coupling reaction is extremely sensitive to the metal salt employed, e.g., under similar conditions described above except employing a prolonged period of time (24 hr), the succinate 2a was obtained in only 13 % yield on using ferric chloride, and only a trace of 2a was detected by GLC analysis on using cupric bromide or cuprous chloride and moreover, no reaction occurred at all on using titanium trichloride. Thus, titanium tetrachloride is an exceedingly effective agent for the reaction.

Results obtained with a variety of ketene silyl acetals using titanium tetrachloride are summarized in Table 1. As evident in Table 1, the yield of the dimer is not influenced by the extent of the steric congestion on the reacting carbon. The fact is of particular interest since the coupling of either silver(I) enolates[4] or lithium ester enolates promoted by copper(II) salts[3] is known to be very sensitive to the steric hindrance, e.g., diethyl tetramethylsuccinate was obtained in only 25 % yield by the copper(II)-promoted coupling of the lithium enolate of ethyl isobutyrate whereas di-t-butyl succinate was produced in 85 % yield from t-butyl acetate under the same set of reaction conditions.[3]



Scheme 1.

Table 1. The dimerization of ketene silyl acetals promoted by titanium tetrachloride

	Ketene silyl acetal (1) R	 R^1	 R^2	 R^3	Product (2)[a]	Yield (%)[b]
a	Me	Me	Me	Me	Dimethyl tetramethylsuccinate	80
b	Me	H	Me	Me	Dimethyl 2,3-dimethylsuccinate	79
c	Me	H	Ph	Me	Dimethyl 2,3-diphenylsuccinate	73
d	Me	$\leftarrow CH_2 \rightarrow_5$		Me	Dimethyl bicyclohexyl-1,1'-dicarboxylate	78

[a] Usually obtained as a mixture of stereoisomers. The identity of all products was verified by spectral and elemental analyses and/or by comparison with published physical properties. [b] Isolated yield after distillation or recrystallization.

Although a detailed understanding of the reaction mechanism must await further investigation, for the present, our results can be accommodated by a radical-coupling mechanism via titanium(IV) enolates (3) as key-intermediate, which may generate an enolate radical (4) together with the formation of titanium(III) trichloride.

As the preparation of ketene silyl acetals from esters is a well-established reaction,[5] the present reaction may furnish a convenient route to succinate derivatives, especially to highly substituted succinates, from the corresponding esters. This method also has the advantage of requiring neither special polar solvents nor special set of reaction conditions.

Further studies on the titanium(IV)-promoted coupling of enolates are under active investigation.

REFERENCES

1. For example, G. M. Whitesides, D. E. Bergbreiter, and P. E. Kendall, J. Amer. Chem. Soc., 96, 2806 (1974); M. Tamura and J. Kochi, ibid., 93, 1483, 1485 (1971); T. Saegusa, T. Tsuda, K. Isayama, K. Nishijima, and Y. Isegawa, Tetrahedron Lett., 1641 (1968); T. Kauffmann and D. Berger, Chem. Ber., 101, 3022 (1968).

2. T, Kauffmann, G. Beissner, H. Berg, E. Köppelmann, J. Legler, and M. Schönfelder, Angew. Chem. internat. Edit., 7, 540 (1968); H. C. Volger, W. Brackman, and J. W. F. M. Lemmers, Recl. Trav. Chem. Pays-Bas, 84, 1203 (1965).

3. M. W. Rathke and A. Lindert, J. Amer. Chem. Soc., 93, 4605 (1971).

4. Y. Ito, T. Konoike, and T. Saegusa, J. Amer. Chem. Soc., 97, 649 (1975).

5. C. Ainsworth, F. Chen, and Y.-N. Kuo, J. Organometal. Chem., 46, 59 (1972); M. W. Rathke and D. F. Sullivan, Syn. Commun., 3, 67 (1973).