Lewis Acid promoted Additions of Cyclopropanes to Iminium Salts: A New Possibility for α-Methylene-γ-Butyrolactone Synthesis

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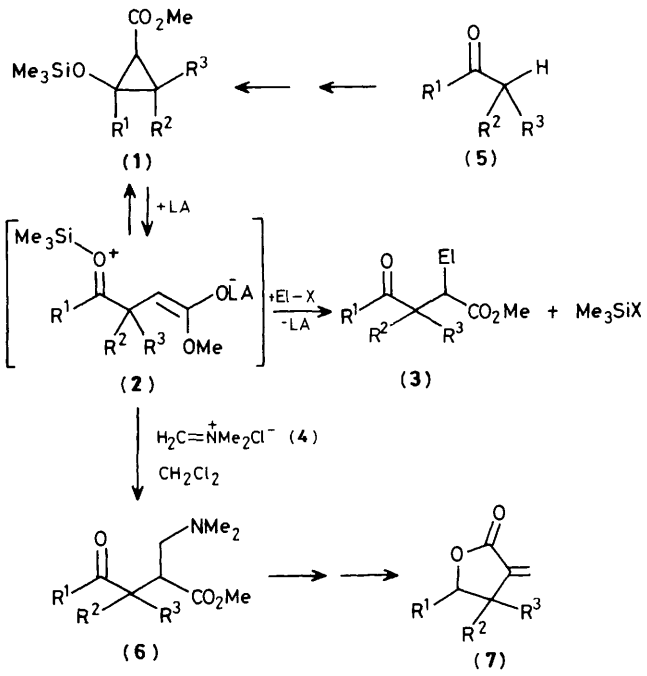
Methyl 2-siloxycyclopropanecarboxylates (**1**) smoothly add to dimethylmethyleneammonium trifluoromethanesulphonate, generated *in situ*, or to the corresponding iminium chloride (**4**) in the presence of $TiCl_4$, giving α-aminomethylated γ-oxoesters (**6**) in good yield; these can serve as precursors for α-methylene-γ-butyrolactones (**7**) as well as for acrylic ester derivatives (**8**).

Addition of electrophiles, El–X, to methyl 2-siloxycyclopropanecarboxylates (**1**) activated by an appropriate Lewis acid (LA) according to (**1**) → (**2**) → (**3**) (Scheme 1) should be a general process.[1] Selenenylation and sulphenylation of (**1**) can occur under extremely mild conditions employing $TiCl_4$ as *catalyst*. However, stoicheiometric quantities of $TiCl_4$ are necessary for the addition of carbonyl compounds and imines to cyclopropanes (**1**).[2] Here we report our results concerning reactions of (**1**) with iminium salt (**4**) which open a new route to α-methylene-γ-butyrolactones (**7**).

Treatment of a mixture of cyclopropane (**1**) and iminium chloride (**4**) (1.1—1.5 equiv.) in dry methylene chloride with $TiCl_4$ (1.1.—1.5 equiv.) for 20 min at −78 °C and 2—48 h at room temperature gives moderate to good yields of α-amino-



a; R^1 = Bu^t, R^2 = H, R^3 = H
b; R^1 = Ph, R^2 = H, R^3 = H
c; R^1, R^2 = -[CH_2]$_4$-, R^3 = H
d; R^1, R^2, R^3 = Me
e; R^1 = H, R^2, R^3 = Me

Scheme 1

methylated γ-oxoesters (**6**) (method A).† However in some cases reproducibility is poor, probably owing to the heterogeneous character of the reaction. Fortunately addition of (**1**) to dimethylmethyleneammonium trifluoromethanesulphonate‡ generated *in situ* by treatment of (**4**) (1.5 equiv.) with trimethylsilyl trifluoromethanesulphonate (1.5 equiv.) in dry methylene chloride at 0 °C, is more reliable providing products (**6**)[3] usually in good yield (method B).§¶ Entries 1—4 in Table 1 demonstrate the wide scope of this novel C–C bond forming process. This method did not work with (**1e**), entry 5. However, using an alternative anionic approach for closure of the crucial C–C bond, the lithium enolate generated from (**1e**)[4] reacts with the iminium trifluoromethanesulphonate

† In the absence of Lewis acid no reaction between (**1**) and (**4**) is observed. The structure of the titanium intermediate involved has so far not been determined.

‡ On addition of Me_3SiOTf (Tf = trifluoromethanesulphonate) to a suspension of (**4**) in CH_2Cl_2 the iminium trifluoromethanesulphonate precipitates as a heavy colourless oil. Formation of this species is indicated by spectroscopic data and by its reactions. Owing to its (assumed) higher electrophilicity and miscibility it should be a useful synthetic reagent, although to our knowledge its generation and reactions have so far not been described. Anion exchange of chloride by trifluoromethanesulphonate using Me_3SiOTf could become a useful process.

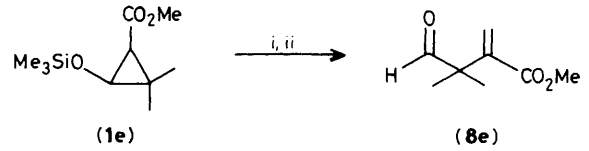
§ Catalytic amounts of Me_3SiOTf induce a fast conversion of (**1**) into the corresponding ring opened ketene silyl acetals: H.-U. Reissig, unpublished results.

¶ *Spectroscopic data* for (**6a**): ^{1}H n.m.r. ($CDCl_3$) δ 3.70 (s, 3H, CO_2Me), 3.3—2.0 (m, 5H, CH_2, CH), 2.21 (s, 6H, NMe_2), and 1.16 (s, 9H, CMe_3); i.r. (CCl_4) 1740 (CO_2Me) and 1710 cm^{-1} (CO).

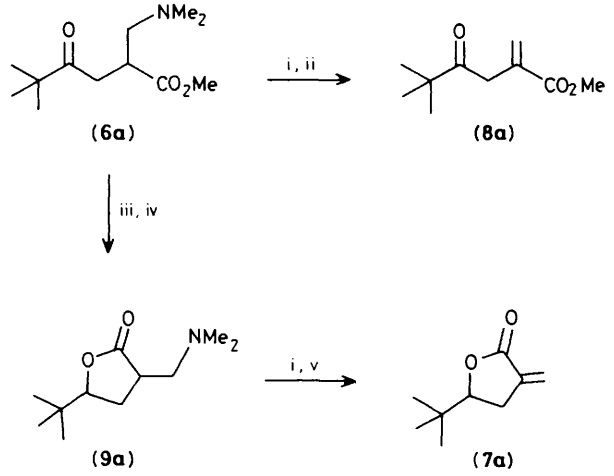
Table 1. α-Aminomethylated γ-oxoesters (**6**) obtained from (**1**).[a]

Entry		% Yield of (**6**) Method A	Method B[b]
1	(**1a**)	73	89
2	(**1b**)	25	56
3	(**1c**)	42	63
4	(**1d**)	66	55
5	(**1e**)	—	—

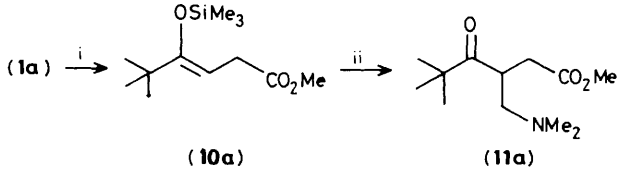
[a] Non optimized yields of isolated purified products; all compounds showed characteristic spectra and satisfactory elemental analysis. [b] Typical procedure for method B: dimethylmethyleneammonium chloride (**4**) (6.00 mmol) in 10 ml CH_2Cl_2 is stirred with trimethylsilyl trifluoromethanesulphonate (6.00 mmol) for 30 min at 0 °C; (**1a**) (4.00 mmol) is added at this temperature, and stirring of the resulting solution is continued for 16 h at 20 °C. The solution is quenched with 10 ml 2 M NaOH. Extraction with CH_2Cl_2 and distillation (90 °C/0.02 mm Hg) yields 89% (**6a**) as a colourless oil.



Scheme 2. *Reagents and conditions:* i, lithium di-isopropylamide, −78 °C, tetrahydrofuran (THF); ii, H_2C=NMe_2OTf, THF, −78 to 20 °C (21% yield).



Scheme 3. *Reagents and conditions:* i, MeI; ii, $NaHCO_3$, CH_2Cl_2 (66%); iii, KBH_4–MeOH; iv, H^+ (81%); v, $NaHCO_3$, CH_2Cl_2 (67%).



Scheme 4. *Reagents and conditions:* i, $ISiMe_3$ (97%); ii, CH_2=NMe_2Cl, CH_2Cl_2 (79%).

(generated in THF) to give the acrylic ester derivative (**8e**) directly in low yield (Scheme 2).[5]

Quaternization of (**6**) and elimination allows synthesis of the corresponding compound (**8**), whereas transformation to α-methylene-γ-butyrolactones (**7**) can be achieved in a

straightforward manner with good overall yield as illustrated in Scheme 3 with (**6a**) → (**7a**)[6] as an example.

Our approach to the formation of compounds (**7**), some of which display biological activity, should complement existing methodology.[7] By using silyl enol ethers the overall transformation (**5**) → (**1**) → (**7**) (Scheme 1) can proceed in the absence of strong base in a chemo- and regio-selective manner.[8] Rearrangement of (**1a**) with catalytic amounts of Me_3SiI to the ring opened silyl enol ether (**10a**)[9] and addition of (**4**) results in the isomeric β-aminomethylated γ-oxoester (**11a**) in high yield (Scheme 4).[10] Therefore the preparation of β-methylene-γ-butyrolactones[11] should also be achievable, underlining again the versatility of methyl 2-siloxycyclopropanecarboxylates (**1**) as building blocks for organic synthesis.

Generous support by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Universitätsbund Würzburg is appreciated.

Received, 18th September 1985; Com. 1368

References

1 H.-U. Reissig and I. Reichelt, *Tetrahedron Lett.*, 1984, **25**, 5879.
2 H.-U. Reissig, *Tetrahedron Lett.*, 1981, **22**, 2981 and unpublished results.
3 For synthesis of β-aminomethylated esters from ketene silyl acetals see: K. O. Kano, T. Morimoto, and M. Sekiya, *J. Chem. Soc., Chem. Commun.*, 1984, 883.
4 I. Reichelt and H.-U. Reissig, *Liebigs Ann. Chem.*, 1984, 531.
5 The mechanism of this eliminative ring cleavage has not been elucidated, but for the reaction of iminium salts with ester enolates see: J. L. Roberts, P. S. Borromeo, and C. D. Poulter, *Tetrahedron Lett.*, 1977, 1621.
6 G. Schlewer, J. L. Stampf, and C. Benerza, *J. Med. Chem.*, 1980, **23**, 1031.
7 For a recent review see: H. M. R. Hoffmann and J. Rabe, *Angew. Chem.*, 1985, **97**, 96; *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 94.
8 E. Kunkel, I. Reichelt, and H.-U. Reissig, *Liebigs Ann. Chem.*, 1984, 512.
9 This rearrangement is a fairly general process: H.-U. Reissig, *Tetrahedron Lett.*, 1985, **26**, 3943.
10 S. Danishefsky, T. Kitahara, R. McKee, and P. F. Schuda, *J. Am. Chem. Soc.*, 1976, **98**, 6715.
11 O. Moriya, M. Okawara, and Y. Keno, *Chem. Lett.*, 1984, 1437.