Tetrahedron Letters, Vol.22, No.31, pp 2981 - 2984, 1981
Printed in Great Britain

0040-4039/81/312981-04$02.00/0

LEWIS-ACID-PROMOTED ADDITIONS OF CARBONYL COMPOUNDS TO DONOR-ACCEPTOR SUBSTITUTED CYCLOPROPANES: A NEW SYNTHESIS OF 2,3-DIHYDROFURANE DERIVATIVES

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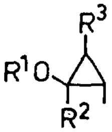
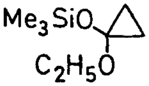
Summary: Methyl 2,3-dihydrofurane-3-carboxylates are synthesized from siloxycyclopropaneesters and ketones in the presence of $TiCl_4$ with good yields.

During the last decade cyclopropanes have attained remarkable importance for the construction of carbon skeletons [1]. The "oxycyclopropanes" (1) - (3) are very useful intermediates in organic synthesis [2]. To our knowledge, there is only one publication describing the use of the strain energy inherent in a compound of type (1) - (3) for the formation of a C-C bond; according to KUWAJIMA and NAKAMURA [3] 1-ethoxy-1-trimethylsiloxycyclopropane (4) smoothly adds to aldehydes R-CHO under $TiCl_4$ activation affording the γ-lactones (5). Therefore (4) can be regarded as homoenolate anion equivalent.



(1) $R^1 = SiMe_3$; $R^2, R^3 =$ Alkyl, H
(2) $R^1 =$ Alkyl ; $R^2, R^3 =$ Alkyl, H
(3) $R^1 =$ Alkyl ; $R^2 = CO_2C_2H_5$, COAlkyl



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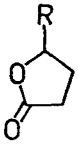

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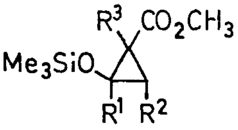
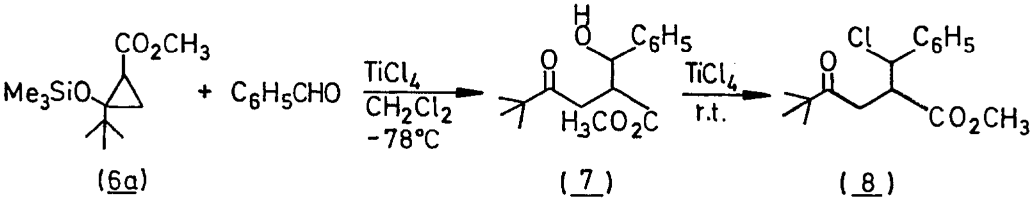


(6)

Currently we are investigating the reactivity of donor-acceptor-substituted cyclopropanes (6), which are conveniently accessible in good yields from trimethylsilylenolethers and methyl diazoacetate [4]. These siloxycyclopropaneesters (6) feature very high reactivity towards electrophilic species. In this communication we present our first results concerning the lewis-acid-promoted additions to carbonyl compounds.

Cyclopropane (6a), treated in dichloromethane with equimolar amounts of benzaldehyde/$TiCl_4$, after aqueous workup and bulb-to-bulb distillation provides the chlorinated 4-oxoester (8) in 76 % yield [5]. Alcohol (7), the likely precursor of (8), is obtained if the reaction is stopped at -78^{0}C after 20 minutes, although only in low quantitiy (16 %).



From (6a) and benzophenone the analogous procedure followed by aqueous workup affords crystalline γ-lactol (10a) in 95 % yield, whereas quenching of the reaction mixture with methanol and stirring at room temperature for 6 hours gives 82 % of the olefin (9a). With methanol ($BF_3 \cdot Et_2O$ catalysis) γ-lactol is converted to the ketal (12a), which can be further transformed into the methyl 2,3-dihydrofurane-3-carboxylate (11a) by pyrolysis (2 h, 150^{0}C, 0.1 mm). Both steps are almost quantitative (overall yield (6a)→(11a): 88 %).

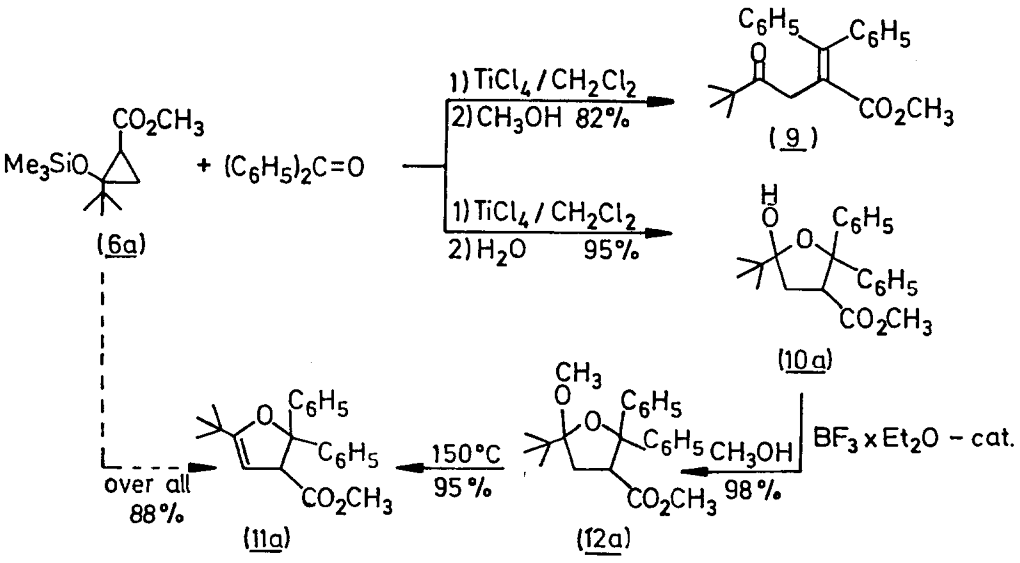
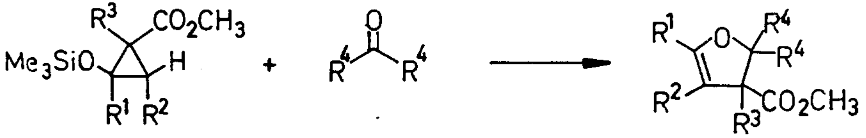


Table: Methyl 2,3-dihydrofurane-3-carboxylate synthesis



(6) (11)

Entry	R^1	R^2	R^3	R^4, R^4	Method[a]	Yield[b] %	mp./bp.
a	t-C_4H_9	H	H	C_6H_5, C_6H_5	A	88	73-75 °C
b	t-C_4H_9	H	H	C_6H_4-C_6H_4 (fluorenone)	B	61	125-126.5 °C
c	t-C_4H_9	H	H	-$(CH_2)_5$- (cyclohexanone)	C	88	60-70 °C/0.01 mm
d	t-C_4H_9	H	H	$C_6H_5CH_2$, $C_6H_5CH_2$	B	58	85-86 °C
e	t-C_4H_9	H	CH_3	C_6H_5, C_6H_5	C	88	150 °C/0.01 mm
f	-$(CH_2)_4$-		H	C_6H_5, C_6H_5	B	51	117-119 °C

Footnotes: [a]A: as described for (11a); B: crude γ-lactol (10) is thermolyzed for 1 h at 150°C/0.1 mm; C: as A but without purification at the stage of (10) and (12). [b]isolated yield of spectroscopically pure compound (11); all new compounds gave satisfactory combustion analysis and characteristic spectra.

This three step procedure (method A) can be simplified, as further examples show (methods B, C; see table). The 2,3-dihydrofurane derivatives (11a-g) are thus obtained in good to very good yield. Enolizable ketones can also be used without difficulties (entries c and d) as is frequently the case with $TiCl_4$-controlled reactions [6]. With benzophenone the 1-methyl-substituted cyclopropane (6e) [7] is transformed into (11e) in 88 % (entry e); this example demonstrates that the ketone can also be connected to quarternary centres. It remains to be clarified why this reaction sequence could not be applied to cyclopropanes (6) with R^1=H. However the bicyclic compound (6f) undergoes the same transformation in satisfying yield (entry f). The product (12f) is a potential precursor for functionalized lactones of medium ring size, as is suggested by the known oxidative cleavage of bicyclic enolethers [8].

Whereas we found that 1-t-butyl-1-trimethylsiloxycyclopropane (1) (R^1= $SiMe_3$, R^2= t-C_4H_9, R^3= H) does not react even with benzaldehyde and while the bisdonor-substituted (4) adds only to aldehydes but not to ketones [3], activation of our cyclopropanes (6) due to the 1-2-arrangement of donor and acceptor substituents is so strong [9] that even relatively sluggish ketones are readily attacked under the influence of lewis acids. Studies concerning the reaction mechanism and the stereoselectivity if aldehydes or unsymmetrical ketones are involved as carbonyl component are under way [10].

References and Notes

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10. The technical assistance of I. Boehm in synthesizing the cyclopropanes (6) is gratefully acknowledged. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

(Received in Germany 21 April 1981)