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RUTHENIUM HYDRIDE-CATALYZED DOUBLE BOND MIGRATION OF 2,5-DIMETHOXY-2,5-DIHYDROFURANS. A NEW PROCESS FOR THE PREPARATION OF γ-KETOESTERS

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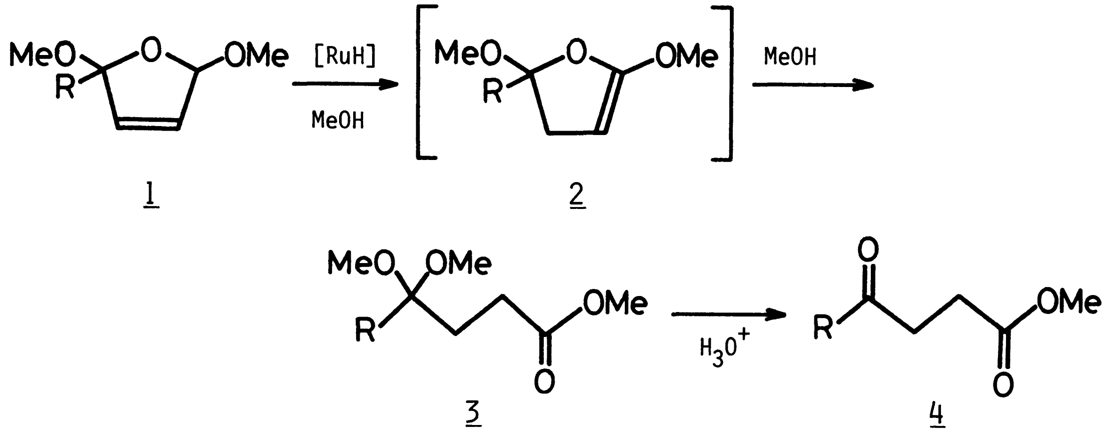
γ-Ketoesters are obtained in excellent yields by means of double bond migration of 2,5-dimethoxy-2,5-dihydrofurans mediated by a ruthenium hydride complex, $HRuCl(PPh_3)_3(C_6H_5CH_3)$ or $HRuCl(CO)(PPh_3)_3$, and subsequent hydrolysis in acidic media.

In our continuing investigation of the synthetic utilization of the ruthenium hydride-catalyzed double bond migration, we showed that allylic trimethylsilyl ethers and allylic acetals were selectively converted to the corresponding vinylic ones.[1] Acid-catalyzed ring opening reactions of substituted furans have been intensively studied for the direct synthesis of 1,4-dicarbonyl compounds, useful precursors for the preparation of cyclopentenone derivatives.[2] In this communication, we report an efficient process for the preparation of γ-ketoesters from 2,5-dimethoxy-2,5-dihydrofurans, which are regarded as cyclic acetals, by means of the ruthenium hydride-catalyzed double bond migration and subsequent acid-catalyzed ring opening reaction. The transformation of 2,5-dimethoxy-2,5-dihydrofurans (1) to γ-ketoesters (4) is outlined in Scheme 1.

Double bond migration of 1 was carried out in methanol solution at 150°C in the presence of catalytic amounts of ruthenium hydride complex, $HRuCl(PPh_3)_3(C_6H_5CH_3)$ or $HRuCl(CO)(PPh_3)_3$, to give protected γ-ketoester (3) as a sole product via an intermediary 2,5-dimethoxy-4,5-dihydrofuran (2).[3] Subsequently, 3 was easily hydrolyzed in acidic media to afford γ-ketoester (4).

Experimentally, chlorohydrido(carbonyl)tris(triphenylphosphine)ruthenium, Scheme 1



$HRuCl(CO)(PPh_3)_3$, (0.103 g, 0.118 mmol) was placed in a pyrex tube equipped with a three-way stopcock. Then the atmosphere was replaced with dry nitrogen. After 2,5-dimethoxy-2,5-dihydrofuran (1a) (5.57 g, 42.8 mmol) and 5 ml of dry methanol were added, the reaction vessel was sealed and heated at 150°C for 6h. ^1H-NMR and GLC analysis of the resulting reaction mixture disclosed the production of methyl 4,4-dimethoxybutanoate (3a). Removal of solvent under reduced pressure followed by distillation afforded 3a in a 90% yield. 3a: bp 109.5-111.0°C/46 mmHg; ^1H-NMR (CCl_4-TMS; ppm) δ1.87(2H, dt, J=6.8 and 6.0 Hz), 2.35(2H, t, J=6.8 Hz), 3.22(6H, s), 3.58(3H, s), 4.28(1H, t, J=6.0 Hz); IR (in CCl_4; cm^{-1}) 1736($^{\nu}$C=O). Two singlet peaks of methoxy protons appeared at 3.22(6H) and 3.58(3H) ppm in ^1H-NMR spectrum and strong absorption band attributable to $^{\nu}$C=O at 1736 cm^{-1} in IR spectrum are well consistent with the structure of the ester 3a.

Deprotection of 3a was achieved by treatment with acetic acid in aqueous methanol at 70°C for 0.5h to give methyl 4-oxobutanoate (4a) quantitatively. In a similar manner, a series of γ-ketoesters (4b-4h) were obtained in excellent yields from the corresponding dimethoxydihydrofurans (1b-1h) and the results are summarized in Table 1.

In the present method, high overall yield of 4 from 1 could be realized by the one-pot reaction without isolation of the intermediate 3. That is, the reaction mixture of 1 with ruthenium hydride complex in methanol was treated with aqueous acetic acid at ambient temperature for several hours to afford γ-ketoester (4) in 75-91% isolated yield.

As mentioned above, γ-ketoesters are useful precursors for the synthesis of various cyclopentenone derivatives. Preparation of dihydrojasmone (6) was performed

Table 1. Double Bond Migration of 1 to 3 and Subsequent Acid-Catalyzed Ring Opening Reaction to 4

1		Double Bond Migration[a]		3	Hydrolysis[d]		4
	R	[1]/[RuH][b]	Time(h)	Yield(%)[c]	Temp(°C)	Time(h)	Yield(%)[e]
a	H	360	12	100(90)	70	0.5	100
b	CH_3	250	8	100(67)	25	3	100(91)
c	C_4H_9	200	15	100(82)	25	3	100(83)
d	C_6H_{13}	150	24	100(90)	25	3	100
e	C_7H_{15}	120	22	100(75)	25	3	100(75)
f	CH_2OH	180	20	80	25	3	72
g	$CH(CH_3)OH$	150	15	90	25	3	77

a) Double bond migration of 1 was carried out in dry methanol at 150°C.

b) $HRuCl(CO)(PPh_3)_3$ was employed as catalyst.

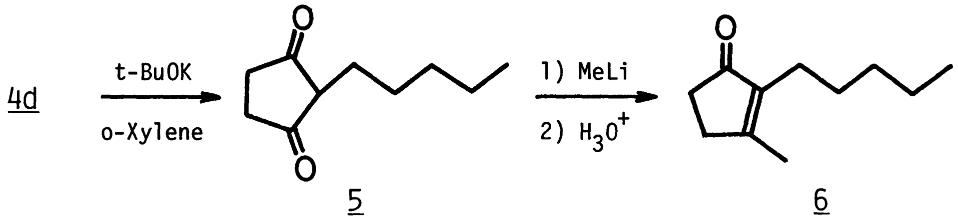
c) Yields were determined by means of ^1H-NMR spectra and GLC analyses, and those shown in parentheses are the isolated yields.

d) Hydrolysis was conducted without isolation of 3 (one-pot reaction).

e) Yields shown in parantheses are the isolated yields based on the starting 2,5-dimethoxy-2,5-dihydrofurans (1).

via the Dieckmann type condensation of 4d. Cyclization of 4d with potassium t-butoxide in xylene and subsequent methylation with methyllithium followed by usual aqueous work-up afforded dihydrojasmone (6) in a 30% yield (Scheme 2).[4]

Scheme 2



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3. Reaction path by way of 2 was confirmed in the reaction of 1a using benzene as solvent. In the following experiment, characterization of the products and determination of isomeric ratio were done by means of ^{1}H-NMR. Treatment of 1a with catalytic amounts of $HRuCl(CO)(PPh_3)_3$ in dry benzene at 150°C for 6h gave an isomeric mixture of 2,5-dimethoxy-2,5-dihydrofuran (2a), (Z)-methyl 4-methoxy-3-butenoate (7Z), and (E)-methyl 4-methoxy-3-butenoate (7E) in the ratio of 1.3:1:1.2. As time goes by, integral intensity of resonance peaks for 7Z and 7E increased in proportion as decrease of that for 2a. Formation of 7Z and 7E as final products in the ratio of 3:2 was observed after heating for an additional 6h at 150°C. 7Z and 7E were purified by chromatography on silica gel and identified as isomeric mixture by means of ^{1}H-NMR, IR, and elemental analysis. These results suggest that 2a is the primary product and then isomerizes to 7Z and 7E. But it is still ambiguous whether 3a is directly derived from 2a or by way of 7 in methanol solution.

2a: ^{1}H-NMR (measured as mixture with 7Z and 7E. CCl_4-TMS; ppm) δ2.20(1H, m), 2.43(1H, m), 3.20(3H, s), 3.31(3H, s), 4.80(1H, m), 5.25(1H, dd, J=7.0 and 3.0 Hz). 7: ^{1}H-NMR (CCl_4-TMS; ppm) δ3.05(2H, dd, J=7.0 and 1.5 Hz), 3.53(3H, s), 3.57(3H, s), 4.47(1H, dt, J=6.0 and 7.0 Hz), 5.88(1H, dt, J=6.0 and 1.5 Hz) for 7Z and 2.87(2H, dd, J=7.0 and 1.0 Hz), 3.47(3H, s), 3.57(3H, s), 4.71(1H, dt, J=12.0 and 7.0 Hz), 6.29(1H, dt, J=12.0 and 1.0 Hz) for 7E. IR(CCl_4; cm^{-1}) 1746(νC=O). Anal. Calcd for $C_6H_{10}O_3$: C, 55.38; H, 7.75. Found: C, 55.56; H, 8.03.

4. Reaction conditions are not optimized.

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