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SELECTIVE REACTIONS OF THIOLATE ANIONS WITH 4-HYDROXY-E-2-ALKENOIC ESTERS OR 4-METHANESULFONYLOXY-E-2-ALKENOIC ESTERS. SYNTHESIS OF 2-ALKEN-4-OLIDES ($\Delta^{\alpha,\beta}$-BUTENOLIDES) AND E,E-2,4-ALKADIENOIC ESTERS

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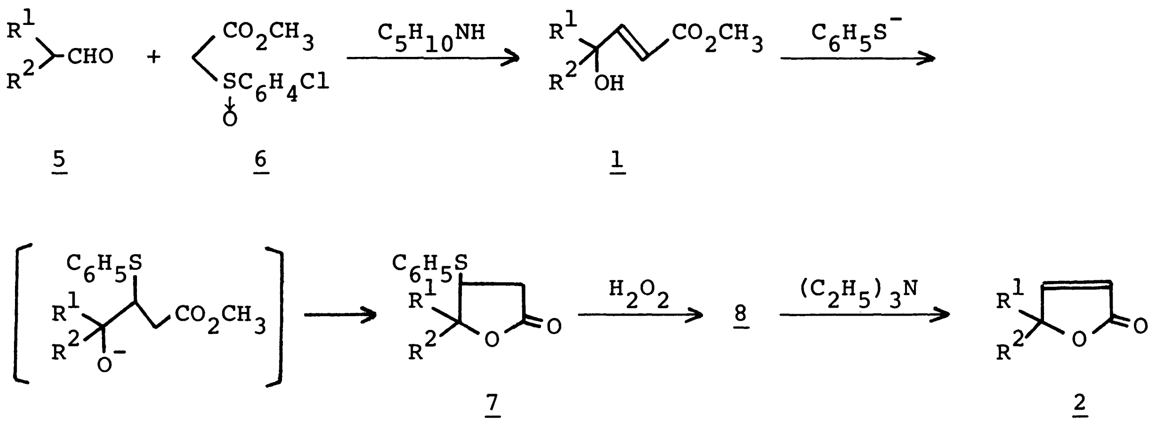
Methyl 4-hydroxy-E-2-alkenoates prepared from aldehydes in one step, undergo the Michael reactions with thiolate anions to give 4-alkanolide derivatives, which are converted into 2-alken-4-olides. Methyl 4-methanesulfonyloxy-E-2-alkenoates undergo the substitution reactions, and subsequent treatments give methyl E,E-2,4-alkadienoates.

The skeletons of 4-hydroxy-E-2-alkenoic esters (1), 2-alken-4-olides ($\Delta^{\alpha,\beta}$-butenolides) (2), and E,E-2,4-alkadienoic esters (3) are widely found as a moiety in many naturally occurring compounds, and there are a variety of methods available for preparing these compounds.[1-3] We now present our results on simple synthesis of 2 and 3 through the selective reactions of thiolate anions with 1 and 4-methanesulfonyloxy-E-2-alkenoic esters (4).

We previously reported that the condensation of ethyl 2-phenylsulfinylacetate and aldehydes (5) in the presence of a catalytic amount of piperidine produced ethyl 2-phenylsulfinyl-2-alkylideneacetates.[4] On the other hand treatment of methyl 2-(p-chlorophenylsulfinyl)acetate (6) and 5[5,6] with excess piperidine gave 1 in high yields, stereoselectively.[7,8] Interestingly the reaction of 1 with benzenethiolate anion lead to the formation of 3-phenylsulfenyl-4-alkanolides (7). Although 1 contains a hydroxy group at the 4-position, the Michael reaction occurs probably because a thiolate anion is a good nucleophile and a soft base.[9] The lactones (7) were quantitatively oxidized to the corresponding sulfones (8) which were converted into 2 in high yields by treatment with triethylamine.[10]



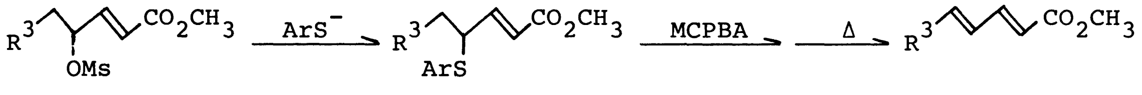
In a typical procedure, a solution of butanal (5a; $R^1=C_2H_5$, $R^2=H$)(18 mmol), 6 (15 mmol), and piperidine (18 mmol) in acetonitrile was stirred at room temperature for 3 h. The ester (1a) was obtained by distillation. A solution of 1a (12.5 mmol), benzenethiol (30 mmol), and piperidine (13 mmol) in acetonitrile was refluxed for 2 h. The lactone (7a) was isolated by column chromatography on silica gel. The direct treatment of 5a with 6 in the presence of piperidine and benzenethiol also produced 7a in reasonable yield (60 %). After oxidation to the corresponding sulfone (8a) with H_2O_2-acetic acid, 2a was obtained by treating 8a (10 mmol) with triethylamine (20 mmol) in chloroform at room temperature for 12 h.11) The other results are shown in the following Table.

Table. Synthesis of 1, 7, and 2

	R^1	R^2	Isolated Yields (%) 1	 7	 212)
a	C_2H_5	H	85	81	77
b	n-C_5H_{11}	H	76	84	74
c	n-C_6H_{13}	H	80	81	76
d	CH_3	CH_3	64a)	85	93
e	n-C_4H_9	C_2H_5	73b)	73	85
f	$-CH_2CH=CH(CH_2)_2-$		72a)	85	68

a) Reflux for 2 h. b) Reflux for 10 h.

On the other hand methyl 4-methanesulfonyloxy-E-2-alkenoates (4) prepared from 1 and methanesulfonyl chloride,13) did not undergo the Michael reaction with benzenethiolate anion, but did the S_N2 reaction to afford methyl 4-phenylsufenyl-E-2-alkenoates(9).[14] Oxidation to the corresponding sulfoxides and pyrolysis lead to the formation of 3 in a high degree of stereoselectivity.



4

9 ($Ar=C_6H_5$)

10 ($Ar=ClC_6H_4$)

3

In a typical procedure a solution of 4a ($R^3=CH_3$)(10 mmol) and sodium p-chlorobenzenethiolate (10 mmol) in tetrahydrofuran was stirred at -20°C for 1.5 h, and 10a was isolated in 83% yield. After oxidation with m-chloroperbenzoic acid, refluxing in xylene for 2 h yielded 3a in 63% yield (E-4/Z-4 = 93/7). Similarly, 3b ($R^3=n-C_4H_9$) was obtained from 4b in 52% yield (E-4/Z-4 = 96/4).[15] Treatment of 4a with benzenethiol and piperidine in acetonitrile gave 9a in 52% yield, but pyrolysis of the sulfoxide afforded 3a in poor yield.

The present synthetic methods of 1 and 2 have the following advantages; (1) the reagents are readily available, (2) the procedures are simple, and (3) the reaction conditions are mild.

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References

1) B. M. Trost and J. H. Rigby, J. Org. Chem., 43, 2938 (1978).

2) P. Brownbridge, E. Egert, P. G. Hunt, O. Kennard, and S. Warren, J. Chem. Soc., Perkin Trans. I, 1981, 2751, and references therein.

3) N. Ono, H. Miyake, Y. Tanabe, K. Tanaka, and A. Kaji, Chem. Lett., 1980, 1365, and references therein.

4) R. Tanikaga, M. Nishida, N. Ono, and A. Kaji, Chem. Lett., 1980, 781.

5) The use of methyl 2-phenylsulfinylacetate caused the yields of 1 to lower because of the competitive self-condensation of 5.

6) Ketones failed to undergo the condensation with 6.

7) S. Yamagiwa, H. Sato, N. Hoshi, H. Kosugi, and H. Uda, J. Chem. Soc., Perkin Trans. I, 1979, 570.

8) Q. B. Cass, A. A. Jaxa-Chamiec, and P. G. Sammes, J. Chem. Soc., Chem. Commun., 1981, 1248.

9) The anion from nitromethane and 1,5-diazabicyclo[5.4.0]undecene-5 underwent the Michael reaction with 1a to give 3-nitromethyl-4-hexanolide in 30% yield.

10) Pyrolysis of the sulfoxide derived from 7a gave 2a and 3-hexen-4-olide in 64% and 11% yields, respectively.

11) 1a: colorless liquid; bp 81-83°C/0.3 mmHg; ^{1}H-NMR (CCl_4) δ 0.93 (t, 3H, J=7 Hz), 1.4-1.8 (m, 2H), 3.4 (br s, 1H), 3.65 (s, 3H), 4.0-4.2 (m, 1H), 5.86 (dd, 1H, J=16, 1 Hz), 6.84 (dd, 1H, J= 16, 4 Hz); IR (neat) 1720 cm^{-1}.

7a: colorless liquid; ^{1}H-NMR (CCl_4) δ 0.95 (t, 3H, J=7 Hz), 1.5-1.8 (m, 2H), 2.40 (dd, 1H, J=18, 7.5 Hz), 2.83 (dd, 1H, J=18, 7.5 Hz), 3.3-3.7 (m, 1H), 3.9-4.3 (m, 1H), 7.1-7.4 (m, 5H); IR (neat) 1770 cm^{-1}; MS (20 eV) *m/e* 222 (M^+).

2a: colorless liquid; bp 100-105°C / 20 mmHg (bp 92-94°C/10 mmHg$^{16)}$).

12) 2a-d are known compounds.$^{16)}$

2e: colorless liquid; bp 97-98°C/2 mmHg; ^{1}H-NMR (CCl_4) δ 0.7-1.0 (m, 6H), 1.0-1.5 (m, 4H), 1.6-2.0 (m, 4H), 6.00 (d, 1H, J=5.5 Hz), 7.31 (d, 1H, J=5.5 Hz), IR (neat) 1745 cm^{-1}; MS (20 eV) *m/e* 168 (M^+).

2f: colorless solid; mp 66-67°C; ^{1}H-NMR (CCl_4) δ 1.7-2.6 (m, 6H), 5.5-5.9 (m, 2H), 5.99 (d, 1H, J=5.5 Hz), 7.50 (d, 1H, J=5.5 Hz); IR (KBr) 1750 cm^{-1}; MS (20 eV) *m/e* 150 (M^+).

13) Treatment of 1d-f with methanesulfonyl chloride yielded methyl alkadienoates besides methanesulfonic esters.

14) The compound 4a underwent the Michael reaction with $LiCH(SC_6H_5)(CO_2C_2H_5)$, while it did the S_N2' reaction with $n\text{-}C_4H_9CuBF_3$. These results will be reported in future.

15) The structures of 3a and 3b were confirmed by comparison with an authentic sample or on the basis of the reported data of 2,4-decadienoic esters.$^{17)}$

16) A. Nobuhara, Agric. Biol. Chem., 11, 1745 (1970).

17) G. Ohloff and M. Pawlak, Helv. Chim. Acta, 56, 1176 (1973).

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