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A NEW METHOD FOR SYNTHESIS OF α,β-UNSATURATED δ-LACTONES VIA MICHAEL ADDITION USING METHYL (PHENYLSULFINYL)ACETATE

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Variuos α,β-unsaturated δ-lactones were synthesized via Michael addition of methyl (phenylsulfinyl)acetate to alkyl vinyl ketones in the presence of tributylphosphine. For example, racemic massoia lactone was obtained in 49% overall yield.

δ-Lactones bearing the aroma of butter and cream are isolated in milk.[1] α,β-Unsaturated δ-lactones are also important compounds as a sugar flavor and insect pheromone.[2] Generally, α,β-unsaturated δ-lactones were prepared by α-sulfenylation of δ-lactones and oxidation to the sulfoxides followed by thermolysis.[3] However, we found that Michael addition of methyl (phenylsulfinyl)acetate (1) to 1-octen-3-one (2c) catalyzed by tributylphosphine (TBP)[4] in DMSO afforded methyl 5-oxo-2-(phenylsulfinyl)decanoate (3c), which was reduced by sodium borohydride followed by intramolecular ester exchange reaction and thermolysis to give massoia lactone,[5] isolated from the bark oil of Cryptocarya massoia, in good yield.
A few examples of Michael addition of β-keto sulfoxides to α,β-unsaturated esters have been reported.[6] But, Michael addition of 1 to alkyl vinyl ketones and application to α,β-unsaturated δ-lactones have not been reported yet. In our preceding paper, we reported a new and general method for the synthesis of β-substituted α,β-unsaturated ketones and aldehydes using desulfonylation of tert-alkyl sulfones under acidic conditions.[7] In this paper, we wish to describe a new method for the synthesis of α,β-unsaturated δ-lactones as shown in the following Scheme.

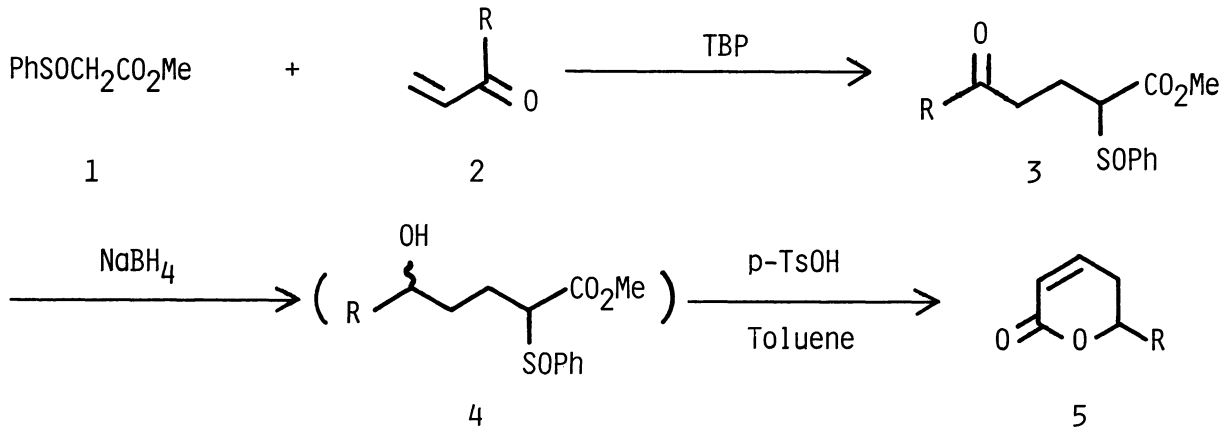


Table 1 Effect of catalysts on reaction of 1 with 1-octen-3-one (2c)

Catalysts	Solvents	Temp. (°C)	Time (h)	3c[a] (%)
NaOMe	MeOH	r.t.	24	—[b]
TBP	DMSO	30	14	86
PPh_3	"	"	"	65
TOP	"	"	"	70
DBU	"	"	"	80
DIPA	"	"	"	—[d]

Table 2 Effect of solvents catalyzed by TBP

Solvents	3c[a] (%)
Benzene	65[c]
Toluene	60[c]
Hexane	5[d]
DMF	82
DMSO	86
t-BuOH	55
MeCN	80

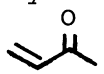
TBP: tributylphosphine, TOP: trioctylphosphine, DBU: 1,5-diazabicyclo[5,4,0]undecene-5, DIPA: diisopropylamine.

(a) The yield of 3c was based on 1. (b) 1-Methoxy-3-octanone was only produced. (c) 7-Methylene-6,10-pentadecanedione was obtained as a by-product in 10 - 30%. (d) Starting materials were almost recovered.

A typical procedure is as follows: 1-Octen-3-one (0.35 g, 2.78 mmol) in DMSO (5 ml) was added to a mixture of methyl (phenylsulfinyl)acetate (0.5 g, 2.52 mmol) and tributylphosphine (0.1 g, 0.99 mmol) in DMSO (5 ml). The mixture was stirred for 14 h at 30°C. The reaction mixture was poured onto water and extracted with ether. The extract was worked up to give 0.65 g (86% yield) of methyl 5-oxo-2-(phenylsulfinyl)decanoate (3c) after column chromatography over silica gel (60 - 80 mesh) with benzene - ethyl acetate (95 : 5). IR (neat) 2950, 1730, 1710, 1440, 1250, 1145, 1080, 1045, 750 cm^{-1}. NMR (CCl_4) δ 0.86 (3H, t, J = 6.3 Hz), 1.0 - 1.7 (6H, m), 1.8 - 2.7 (6H, m), 3.42 (1H, t, J = 6.0 Hz), 3.53 (3H, s), 7.66 (5H, br s). Sodium borohydride (0.02 g, 0.52 mmol) was added to a stirred solution of 3c (0.15 g, 0.51 mmol) in MeOH (10 ml) and $Na_2HPO_4 \cdot 12H_2O$ (0.4 g, 1.11 mmol) in water (4 ml) at 0°C. The mixture was stirred for every 10 min. at 0°C and at room temperature. Saturated ammonium chloride solution was added to the mixture and extracted with methylene chloride. The methylene chloride layer was dried and concentrated to give the alcohol 4c. After toluene (40 ml) and p-toluenesulfonic acid (10 mg) were added to 4c followed by refluxing for 2 h, massoia lactone (0.05 g, 57% yield) was obtained by column chromatography on silica gel (60 - 80 mesh) with benzene - ethyl acetate (98 : 2). IR (neat) 2950, 1715, 1470, 1390, 1260, 1040, 820, 755 cm^{-1}. NMR (CCl_4) δ 0.93 (3H, br), 1.1 - 1.8 (8H, br), 2.2 - 2.4 (2H, m), 4.15 - 4.5 (1H, m), 5.90 (1H, dd, J_1 = 10, J_2 = 1.5 Hz), 6.78 (1H, dt, J_1 = 10, J_2 = 4.8 Hz).

The results of effects of catalysts and solvents on reaction of 1 with 2c are summerized in Tables 1 and 2. The reaction of 1 with 2c used by NaOMe / MeOH gave only methanol adduct of 2c, 1-methoxy-3-octanone. Diisopropylamine did not gave 3c but starting materials were recovered. The Michael addition did not occur in hexane as solvent. When DMSO, DMF, or MeCN was used, 3c was obtained as a main product in 86 - 80% yield. A combination of TBP and DMSO was the best catalyst and solvent on reaction of 1 with 2c.

Table 3 Preparation of α,β-unsaturated δ-lactones 5

Starting	Alkyl vinyl ketones  R =	5 Products	(%)[a]
1	C_4H_9-	5a	60
"	$(Me)_2CHCH_2$-	5b	61
"	C_5H_{11}-	5c	57
"	C_6H_{13}-	5d	55
"	C_8H_{17}-	5e	54

(a) Yield of isolated product.
(b) All compounds gave satisfactory NMR and IR spectra.

Next, we examined the lactonization of 3c. In a usual manner, hydrolysis of the ester group of 3c and subsequent reduction of the ketone by sodium borohydride did not give 5c but decarboxylation happened to give phenylsulfinylnonan-4-ol Therefore, treatment of 3c with sodium borohydride containing Na_2HPO_4 as buffer at 0°C without hydrolysis of the ester gave 4c in good yield. Without purification, toluene was added to 4c in the presence of p-toluenesulfonic acid and refluxed for 2 h to give the desired 5c in 57% yield after column chromatography. Some kinds of α,β-unsaturated δ-lactones were prepared from the corresponding alkyl vinyl ketones as shown in Table 3.

On the other hand, reaction of methyl (p-tolylsulfonyl)acetate with 1-octen-3-one catalyzed by NaOMe in MeOH gave methyl 5-oxo-2-(p-tolylsulfonyl)decanoate in 90% yield. The reductive elimination of the sulfonyl group followed by lactonization in the usual manner afforded δ-decalactone, butter flavor, in 55% yield after column chromatography.[8)]

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8) The NMR and IR spectra of δ-decalactone synthesized here were identical with those of authentic sample.

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