Experimental

Materials and Instruments

Ethanol was purified by distilation after refluxing with sodium metal and ethylphthalate for 2 hours. Conductance measurement were carried out with BARNSTED Model PM-70 CB conductivity bridge.

Preparation of Reagents. Substituted Thiobenzamides were prepared from their corresponding benzonitrile.[4,8] Hydrogensulfide was bubbled through pyridine solution of benzonitriles using triethylamine as a catalyst. Substituted Phenacyl Arenesulfonates were synthesized as following.[5b] A solution of 0.055 mole of silver arenesulfonate in 500 *ml* of dry acetonitrile was placed in a dry three necked flask fitted with mechanical stirrer, reflux condenser, and thermometer. Substituted phenacyl bromide (0.05 mole) was introduced and then the solution was heated in a water bath at 50℃ for fifteen hours. After filtering silver bromide precipitated and evaporating the solution, white crystals were obtained and recrystallized from benzene-isopropyl alcohol. Thiazoles were prepared as following.[4] A mixture of 0.02 mole thiobenzamide and 0.02 mole substituted phenacyl arenesulfonate dissolved in 50 *ml* of ethanol was refluxed for hours. After evaporating the solution and adding ammonia water, white or yellow crystals were obtained and then recrystallized from ethanol.

Kinetic Measurements. The kinetic apparatus and procedure to measure the rates of the reactions of substituted phenacyl arenesulfonates with substituted thiobenzamides by an electric conductivity method were the same as those used previous study. Reactions were generally run to about 3 to 4 half-lives of substrate. Pseudo first-order rate constants were determined by the Guggenheim method with substituted thiobenzamides in large excess, and second-order rate constants were obtained by dividing the observed first-order rate constants by nucleophile concentration.

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A Synthesis of 4-Phenyl-2-phenylsulfonyl-3-vinylcyclopentanone *via* Palladium-Catalyzed 1,3-Oxygen-to-Carbon Alkyl Shift

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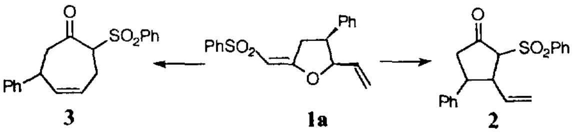
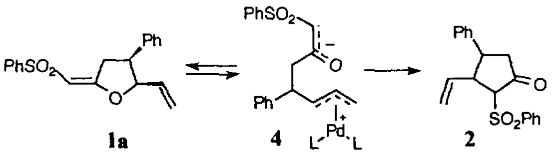
The discovery of natural products that contain five-membered rings has led to increasing investigation of cyclopentanone syntheses.[1] In this respect, a number of synthetic methods were developed over the past years and used to synthesize natural products.[2] In connection with our recent research for Pd-chemistry, we have had an occasion to study the isomerization of **1a** to **2** and it have been found that palladium-catalyzed 1,3-oxygen-to-carbon alkyl shift occurred cleanly to provide cyclopentanone (Eq. 1).[3]



3 **1a** **2** (1)

The fact that an allyl vinyl ether such as **1a** is converted to a cyclopentanone by a Pd(0) catalyst contrasts to the normal chemical reactivity of such compounds which isomerize to cycloheptanones under thermal conditions.[4] In order to find optimum conditions, a variety of Pd(0) catalysts and solvents were tested and these results are shown in Table 1. The use of refluxing 1,4-dioxane under the influence of a $Pd_2dba_3CHCl_3$/dppp catalyst gave cyclopentanone in 51% yield, although many reaction conditions produced only unknowns whose structures may be related to coupling compounds of **1a** and **2** due to two carbonyl peaks (1750 and 1725 cm^{-1}) and many vinyl protons. Thus, cyclopentanone formation proved sensitive to the reaction conditions. Solvent and concentration played a dominant role.

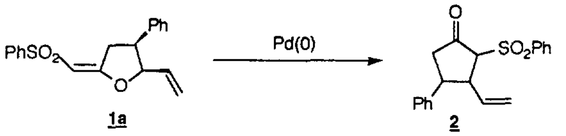
The mechanism of this 1,3-shift can be thought to involve an oxidative addition of palladium(0) catalyst to the allyl ether as in Eq. 2 to form a zwitterion **4**. This intermediate collapses by C-alkylation to form the observed product. The regiochemistry of the collapse is quite interesting in that a five-membered ring product is observed. This reaction illustrates an ability of a transition metal to change the normal rules of reactivity of an organic system.



1a **4** **2** (2)

The experimental procedure for cyclopentanone formation is as follows. To a solution of $Pd_2dba_3CHCl_3$(4.1 mg, 4×10^{-3} mmol) and 1,3-bis(diphenylphosphino)propane (8.3 mg, 0.02 mmol) in 2 *ml* of 1.4-dioxane was added **1a** (52.2 mg, 0.08

Table 1. A Synthesis of 4-Phenyl-2-phenylsulfonyl-3-vinylcyclopentanone (**2**)

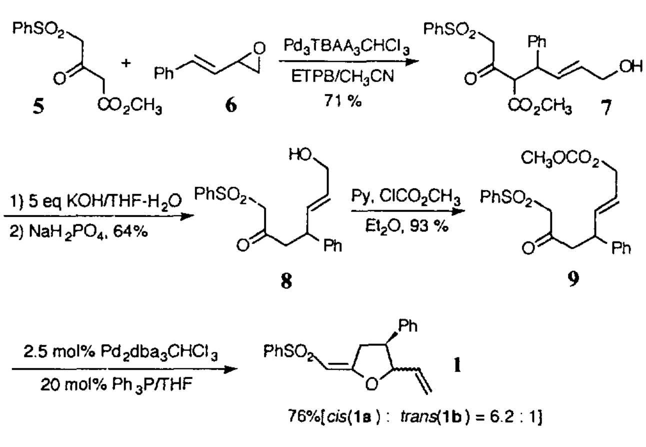


Pd	Ligand[a]	Solvent	Temp (℃)	Time (℃)	Conc (M)	Yield (%)
1.5 $Pd(OAc)_2$	12 $(i\text{-PrO})_3P$	THF	25	2.0	0.1	[b]
	20 $(i\text{-PrO})_3P$	1,4-dioxane	100	16	0.1	[b]
	10 dppp/5*n*-BuLi	1,4-dioxane	100	4.0	0.1	[c]
10 $Pd_2dba_3CHCl_3$	80 Ph_3P	1,4-dioxane	90	8.0	0.01	0[d]
2.5 $Pd_2dba_3CHCl_3$	20 $n\text{-Bu}_3P$	1,4-dioxane	100	8.0	0.1	0[d]
5.0 $Pd_2dba_3CHCl_3$	40 $(i\text{-PrO})_3P$	THF	70	24	0.04	0[d]
2.5 $Pd_2dba_3CHCl_3$	12 dppp	DMSO	80	19	0.02	[c]
	12 dppp	1,4-dioxane	100	1.5	0.1	31+[c]
	12 dppp	1,4-dioxane	100	3.0	0.02	51
	12 dppe	DMSO	130	3.0	0.1	[c]
	12 dppe	1,4-dioxane	90	0.4	0.02	31+[c]

[a] dppp: 1,3-bis(diphenylphosphino)propane. dppp: 1,2-bis(diphenylphosphino)ethane. [b] Mixture of **1a**, **1b** and 1-oxa-4-phenyl-2-phenylsulfonylmethylidene-5-cycloheptene. [c] Unknown. [d] Starting material was recovered.

mmol) in 1m*l* of 1,4-dioxane over 30 min at 100℃. After being stirred for 3 h, the yellow solution was concentrated under reduced pressure. Purification by flash chromatography using ethyl acetate/hexane (1 : 5) gave **2** (26.7 mg, 51%).

The preparation of **1a** is illustrated below. Addition of the vinyl epoxide **6** to a mixture of the nucleophile **5** and Pd(0) catalyst derived from tris(tribenzylideneacetylacetone)tripalladium chloroform and 4-ethyl-2,6,7-trioxa-1-phosphabicyclo [2,2,2]octane (ETPB) in acetonitrile afforded **7** in 71% yield as the sole alkylation product.[5] Treatment of the ester **7** with potassium hydroxide in aqueous THF led cleanly, after acidification with sodium dihydrogen phosphate, to the sulfonyl ketone **8** in 64% yield. Alkyl carbonate **9** was prepared from the corresponding allylic alcohol and methyl chloroformate with pyridine in 93% yield.[6] Finally, allyl vinyl ether **1** was produced by Pd-catalyzed cyclization of **9** in 76% yield.



Experimental

cis-4-Phnyl-2-phenylsulfonylmethylidene-5-vinyltetrahydrofuran (1a) and trans-4-phenyl-2-phenylsulfonylmethylidene-5-vinyltetrahydrofuran (1b). To a solution of $Pd_2dba_3CHCl_3$ (2.2 mg, 2.2×10^{-3} mmol) and triphenylphosphine (4.5 mg, 0.017 mmol) in 0.5 m*l* of THF was added **9** (34.9 mg, 0.086 mmol) in 0.36 m*l* of THF. After 12 h at room temperature, the yellow solution was concentrated under reduced pressure. The crude product was purified by flash chromatography using ethyl acetate/hexane (1 : 6 and 1 : 3) to give **1a** (17.5 mg, 63%) and **1b** (3.6 mg, 13%).

1a (*cis*) R_f 0.45 (33% Ethyl acetate in hexane). IR (film): 1630, 1300, 1140 cm^{-1}. ^{1}H-NMR (400 MHz. $CDCl_3$): 7.90-7.87 (m, 2H), 7.60-7.49 (m, 3H), 7.36-7.18 (m, 5H), 5.90-5.79 (m, 1H), 5.86 (s, 1H), 5.26 (d, J=17.03 Hz, 1H), 5.24 (d, J=9.95 Hz, 1H), 4.74 (dd, J=7.90, 6.65 Hz, 1H), 3.84-3.72 (m, 1H), 3.32-3.17 (m, 2H). **1b** (*trans*) R_f 0.26 (33% Ethyl acetate in hexane). IR (film): 1600, 1280, 1120 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): 8.05-8.02 (m, 2H), 7.62-7.50 (m, 3H), 7.33-7.25 (m, 3H), 7.12-7.09 (m, 2H), 5.76 (ddd, J=17.24, 10.68, 5.58 Hz, 1H), 5.58 (s, 1H), 5.20 (d, J=10.68 Hz, 1H), 5.15 (d, J= 17.24 Hz, 1H), 4.92 (dd, J=7.10, 5.58 Hz, 1H), 3.21-3.15 (m, 1H), 3.10-3.03 (m, 1H), 2.91 (ddd, J=16.67, 9.15, 1.52 Hz, 1H).

4-Phenyl-2-phenylsulfonyl-3-vinylcyclopentanone (2). R_f 0.21 (33% Ethyl acetate in hexane). IR (film): 1750, 1300, 1150 cm^{-1}. ^{1}H-NMR (400 MHz $CDCl_3$): 7.93-7.90 (m, 2H), 7.72-7.52 (m, 3H), 7.38-7.28 (m, 5H), 5.71 (ddd, J=17.45, 10.18, 7.27 Hz 1H), 4.99 (d, J=10.18 Hz, 1H), 4.90 (d, J=17.45 Hz 1H), 3.78 (d, J=9.40 Hz, 1H), 3.62-3.55 (m, 1H), 3.06-2.98 (m, 1H), 2.83-2.69 (m, 2H).

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A New Synthesis of Solanone

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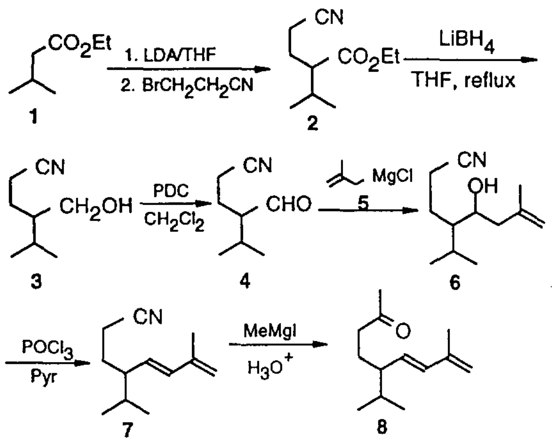
Solanone (**8**), a colorless oil with a faint aroma reminiscent of carrots, has been detected in the Burley,[1] Greek tobacco[2] and marijuana.[3] The synthesis of solanone has been worked out by a few workers. In 1965, Johnson and Nicholson[4] isolated it from tobacco and elucidated the structure, confirming by synthesis. They carried out a relatively short synthesis of solanone starting from isovaleraldehyde. An optically active (*S*)-(+)-solanone has been also synthesized by Kohda and Sato[5] starting from optically active (*R*)-(+)-*p*-menthene.

Although it seems relatively short and convenient, Johnson's synthesis is not suitable for practical purpose, since the starting material (isovaleraldehyde) stinks, seriously contaminating the air for a long time. The Kohda's method, though significant as an asymmetric synthesis, is also inapplicable to perfumery industry. The present paper describes a new synthesis of solanone starting from ethyl isovalerate and/or diethyl malonate, which are inexpensive and smell good.



Scheme 1.

Treatment of ethyl isovalerate (**1**) with lithium diisopropylamide (LDA) at −78℃, and reaction of the resultant ester enolate with 3-bromopropanenitrile in THF/HMPA, for 5 h at −78℃ and for additional 2 h at room temperature, gave ethyl 2-(2′-cyanoethyl)-3-methylbutanoate (**2**) in 69% yield (Scheme 1).

The chemoselective reduction of ester carbonyl[6] of the cyanoester **2**, without attack of nitrile function, could be effectively conducted. Treatment of **2** with lithium borohydride in refluxing THF for 2 days gave the corresponding cyanoalcohol **3** in 78% yield.[7] Oxidation of cyanoalcohol **3** for 18 h with PDC in dichloromethane gave 93% yield of 4-formyl-5-methylhexanenitrile (**4**). Direct conversion of cyanoester **2** to cyanoaldehyde **4** was also attempted using reported reagents, such as diisopropylaluminum hydride (DIBAH),[8] lithium aluminum hydride (LAH),[9] and diaminoaluminum hydride,[10] which were known to be effective for the conversion of ester to aldehyde. However, the chemoselective, direct reduction of **2**-to-**4** was not successful with these reagents, presumably because of the presence of cyano group in **2**.

Treatment of cyanoaldehyde **4** with methallylmagnesium chloride (**5**)[11] at −78℃ under nitrogen, followed by stirring overnight, gave rise to a chemoselective Grignard condensation product, hydroxynitrile **6**, in 67% yield.

Dehydration of **6** with phosphorus oxychloride ($POCl_3$) in refluxing pyridine afforded dienenitrile **7** in 78% yield. Although direct conversion of **4** to **7** can be also possible by Wittig olefination of **4**,[4] it may be less convenient and less economical, since it requires more steps, involving preparation of methally Wittig salt, followed by treatment with base to give the ylide, and olefination with **4**.

Treatment of a solution of dienenitrile **7** in dry benzene with methylmagnesium iodide, followed by refluxing for 20 hours, and hydrolysis of the resulting ketimine with 6 N HCl furnished solanone (**8**) in the yield of 70%.

An alternative route to ester nitrile **2**, which begins with dialkylation of malonate ester, is shown in Scheme 2. Treat-