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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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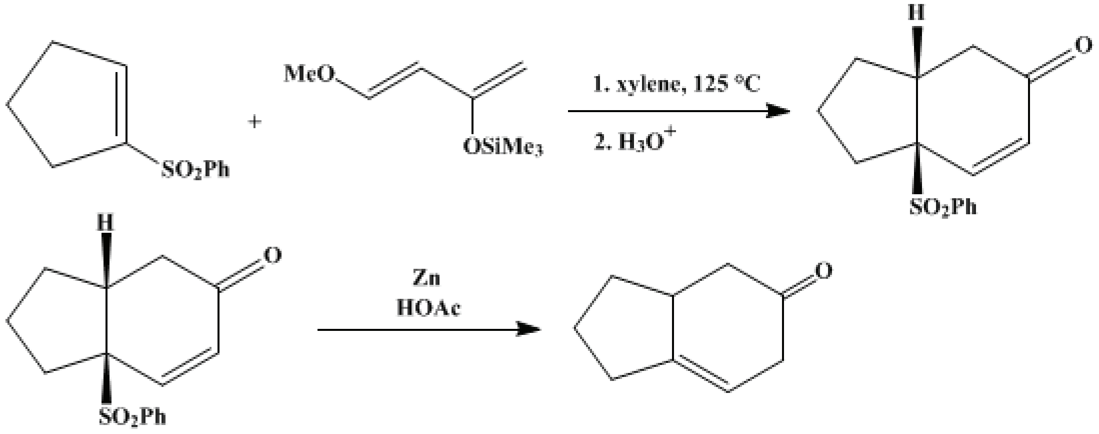
Organic Syntheses, Coll. Vol. 8, p.38 (1993); Vol. 67, p.163 (1989).

REDUCTIVE ANNULATION OF VINYL SULFONES: BICYCLO [4.3.0.]NON-1-EN-4-ONE

[5*H*-Inden-5-one, 1,2,3,3a,4,6-hexahydro-]



Submitted by Ho-shen Lin and Leo A. Paquette[1].
Checked by Edward J. Adams and Edwin Vedejs.

1. Procedure

A. *4-Oxo-1-(phenylsulfonyl)-cis-bicyclo[4.3.0]non-2-ene.* A 250-mL, one-necked flask equipped with a Teflon-coated magnetic stirring bar, a condenser, and a nitrogen inlet tube is charged with 8.76 g (42.1 mmol) of 1-(phenylsulfonyl)cyclopentene (Note 1), 8.75 g (50.9 mmol) of 1-methoxy-3-(trimethylsiloxy)-1,3-butadiene and 8 mL of xylene (Note 2). The stirred reaction mixture is blanketed with nitrogen and heated in an oil bath at 123–125°C in the dark for 3 days. After the solution is cooled, it is diluted with 80 mL of tetrahydrofuran and 30 mL of 2 *N* hydrochloric acid and heated at the reflux temperature for 24 hr. Most of the tetrahydrofuran is removed on a rotary evaporator. The residue is transferred to a 1-L separatory funnel and diluted with ether (200 mL) and dichloromethane (100 mL). The organic phase is washed with two 50-mL volumes of half-saturated sodium bicarbonate solution and a mixed solution of saturated sodium bicarbonate (10 mL) and half-saturated sodium chloride (40 mL). The organic layer is dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue is subjected to flash column chromatography on silica gel (250 g). Elution with a mixture of ethyl acetate–dichloromethane–petroleum ether (1 : 25 : 25) returns 3.56 g (41%) of unreacted 1-(phenylsulfonyl)cyclopentene. Subsequent increase in the solvent polarity to 3 : 25 : 25 provides the cycloadduct as a yellowish solid. This material is dissolved in the minimum amount of dichloromethane to which is added 25 mL of ether; 4.33 g of colorless crystals precipitate. Concentration of the filtrate and crystallization from ether–petroleum ether afford an additional 0.77–1.34 g of light-yellow crystals (combined yield of 44–49%) (Note 3).

B. *Bicyclo[4.3.0]non-1-en-4-one.* The preceding enone (5.64 g, 20.4 mmol) is dissolved with magnetic stirring in 120 mL of glacial acetic acid contained in a 500-mL, one necked flask. Zinc powder (13.3 g, 0.203 mol) (Note 4) is introduced and the capped reaction mixture is stirred vigorously at room temperature for 1 hr. The zinc is removed by suction filtration through a Celite pad (Büchner funnel) and washed with 200 mL of ether. The combined filtrates are transferred to a 2-L separatory funnel, diluted with 300 mL of petroleum ether, and washed with 200 mL of water. The aqueous phase is reextracted with 300 mL of a 1 : 1 mixture of ether and petroleum ether. Finally the combined organic layers are washed with 100 mL of water and 200 mL of saturated sodium bicarbonate solution prior to drying over anhydrous magnesium sulfate and filtration. The solvents are removed on a rotary evaporator to leave a pale-yellow oil that is purified by chromatography on silica gel (elution with 14% ethyl acetate in petroleum ether). There is isolated 1.81–1.98 g (65–71%) of the β,γ-enone as a colorless oil (Note 5) and (Note 6).

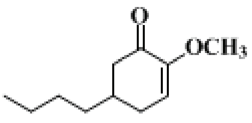
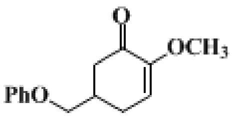
2. Notes

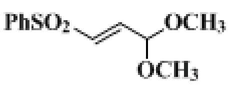
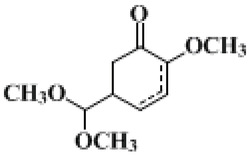
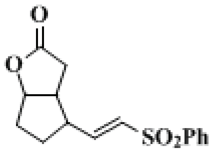
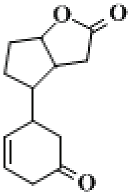
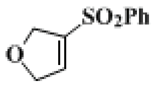
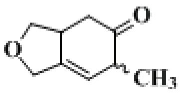
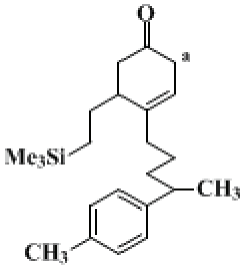
1. See *Org. Synth., Coll. Vol. VIII*, **1993**, 543 for preparation of this intermediate.
2. The reagents were purchased from the Aldrich Chemical Company, Inc.; the diene was used without further purification, and xylene was dried by azeotropic removal of water and distillation from calcium hydride. 1-Methoxy-3-trimethylsiloxy-1,3-butadiene can be prepared by the method of *Org. Synth., Coll. Vol. VII*, **1990**, 312.
3. The product can be further purified by crystallization from dichloromethane and ether. The crystalline modification that is obtained melts at 122.5–126°C. Melting and resolidification provides a second modification that melts at 122.5–123.2°C. The product has the following spectral properties: IR (CH_2Cl_2) cm^{-1}; 1680, 1310, 1150, 1090; ^1H NMR ($CDCl_3$) δ: 1.27–1.49 (m, 1 H), 1.55–1.87 (m, 3 H), 1.95–2.15 (m, 1 H), 2.16–2.31 (m, 2 H), 2.59–2.76 (m, 1 H), 2.93–3.13 (m, 1 H), 6.08 (d, 1 H, J = 10.2), 6.49 (dd, 1 H, J = 10.0, 1.7), 7.53 (br t, 2 H, J = 7.3), 7.64 (br t, 1 H, J = 7.2), 7.83 (br d, 2 H, J = 7.2); ^{13}C NMR ($CDCl_3$) δ: 22.76, 32.34, 35.68, 37.91, 38.73, 70.46, 129.05, 129.64, 131.89, 134.19, 136.38, 143.54, 196.27; *m/z* calcd. for $M^+-C_6H_5SO_2$: 135.0801. Found: 135.0835. Anal. calcd. for $C_{15}H_{16}O_3S$: C, 65.19; H, 5.84. Found: C, 65.28, H, 6.85.
4. Fresh Mallinckrodt zinc dust was used without purification.
5. The product has the following spectral properties: IR (CH_2Cl_2) cm^{-1}: 2960, 2880, 1710; ^1H NMR ($CDCl_3$) δ: 1.08–1.35 (m, 1 H), 1.43–1.68 (m, 1 H), 1.68–1.91 (m, 1 H), 1.91–2.15 (m, 2 H), 2.15–2.38 (m, 2 H), 2.38–2.65 (m, 2 H), 2.65–2.94 (m, 2 H), 5.38–5.53 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ: 24.86, 29.78, 33.80, 39.09, 40.40, 45.07, 113.22, 146.32, 211.05; *m/z* calcd. for $C_9H_{12}O$: 136.0888. Found: 136.0896.
6. The product may be isolated by distillation, although two complications arise. First, because of the volatility of the enone, some material loss is incurred (yields of 57–60% result), bp 68–78°C (19 mm). More critically, heating induces some equilibration (generally ca. 10–15%) to the α,β-enone isomer. Thus, distillation should be avoided if pure β,γ-enone is desired. The spectral properties of the conjugated ketone, which can be obtained in a pure state by silica gel chromatography, are as follows: IR (CH_2Cl_2) cm^{-1}: 2950, 2875, 1670; ^1H NMR ($CDCl_3$) δ: 1.31–1.49 (m, 1 H), 1.57–2.08 (m, 5 H), 2.40 (dd, 1 H, J = 17.8, 7.4), 2.47–2.62 (m, 2 H), 2.72–2.84 (m, 1 H), 5.92 (dd, 1 H, J = 10.2, 2.1), 6.70 (dd, 1 H, J = 10.2, 3.5); *m/z* calcd. for $C_9H_{12}O$: 136.0888. Found: 136.0864.

3. Discussion

As a group, annulation reactions have been exceedingly valuable to the synthetic organic chemist. Unfortunately, processes of this type involving simple alkenes and cycloalkenes are few. However, the facility with which unactivated olefins can be transformed into vinyl sulfones,[2,3] the high degree to which α,β-unsaturated sulfones are captured regioselectively by unsymmetrical dienes[4] such as those developed by Danishefsky,[5] [6] [7] [8] and the ease with which reductive desulfonylation can be effected[9,10] combine to permit convenient synthetic entry to substituted cyclohexenones. Several representative examples can be found in Table I.

TABLE I
REDUCTIVE ANNULATION OF VINYL SULFONES[4]

Starting material	Diene	Product	α,β:β,γ Ratio
	1b		100:0
	1b		100:0

	1b		60:40
	1a		0:100
	1b		0:100
	1a		0:100

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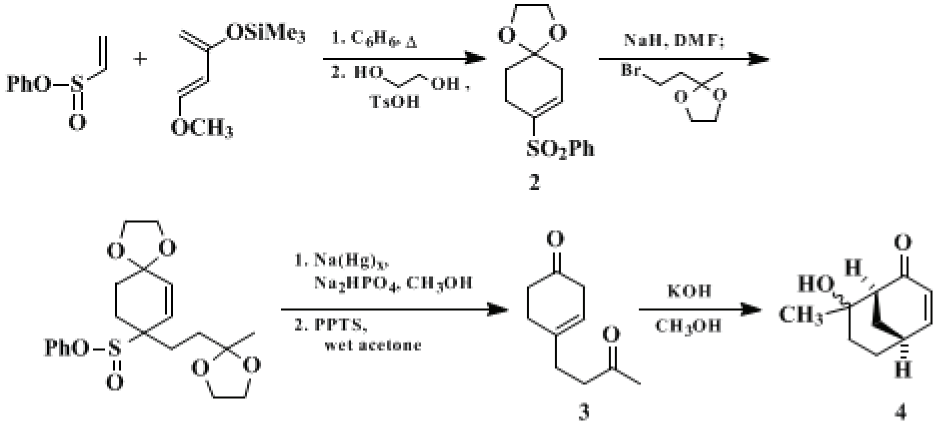
[a]Including an intermediate alkylation step.

Other variants on this theme are possible. Thus, if the initially formed Diels–Alder adduct is directly ketalized as in **2**, the derived α-sulfonyl carbanion can be alkylated. Reductive desulfonylation and acidic hydrolysis [with pyridinium *p*-toluenesulfonate (PPTS)] then deliver a 4-substituted cyclohexenone (e.g., **3**), which in many cases can be made to undergo further useful synthetic transformations (e.g., **4**).[4]



The expendability of the scheme allows one to prepare 4-substituted and 4,5-disubstituted 2(and 3)-cyclohexenones where the nature of the side chains can be widely varied.

References and Notes

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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

silica gel

petroleum ether

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

zinc (7440-66-6)

xylene (106-42-3)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

calcium hydride (7789-78-8)

1-Methoxy-3-trimethylsiloxy-1,3-butadiene,
1-methoxy-3-(trimethylsiloxy)-1,3-butadiene

BICYCLO[4.3.0.]NON-1-EN-4-ONE,
5H-Inden-5-one, 1,2,3,3a,4,6-hexahydro-,
Bicyclo[4.3.0]non-1-en-4-one (131712-16-8)

1-(Phenylsulfonyl)cyclopentene (64740-90-5)

pyridinium p-toluenesulfonate

4-Oxo-1-(phenylsulfonyl)-cis-bicyclo[4.3.0]non-2-ene (131712-15-7)