Synthesis of *cis*-Jasmone *via* the Retroaldol-aldol Condensation of 3-(*cis*-3-Hexenyl)-2-cyclopentenone in an Autoclave

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Synopsis. *cis*-Jasmone was efficiently synthesized from 2-cyclopentenone. The treatment of 2-cyclopentenone with sodium *p*-toluenesulfinate gave 3-(*p*-tolylsulfonyl)cyclopentanone in a 92.5% yield. The alkylation of the sulfone, after the protection of the ketone, with *cis*-1-bromo-3-hexene, followed by desulfonylation with 5% hydrochloric acid in tetrahydrofuran, afforded 3-(*cis*-3-hexenyl)-2-cyclopentenone in a good yield. The retroaldol-aldol condensation of the cyclopentenone in a stainless steel autoclave in presence of 5% sodium hydroxide yielded *cis*-jasmone in a 80% yield.

Among the *cis*-jasmone syntheses, the cyclization of 1,4-diketone employing weak alkali is well known.[1] We reported previously a new synthesis of *cis*-jasmone (**6**) *via* 1,4-diketone prepared by the condensation of *cis*-1-(*p*-tolylsulfonyl)-3-hexene with ethyl 4,4-ethylenedioxypentanoate.[2] On the other hand, 3-(*cis*-3-hexenyl)-2-cyclopentanone (**5**) is also a key intermediate for the synthesis of **6**.[3] Two examples involve the intermediate **5**. McCurry *et al.* reported in 1974 that **5** was synthesized by the addition of alkyllithium to 2-cyclopentenone, followed by chromium-trioxide oxidation,[3] giving **6** in a 29% overall yield by the retroaldol-aldol condensation of **5**. Torii *et al.* reported in 1979 that **5** was obtained by the electrolytic acetoxylation reaction of 1-(*cis*-3-hexenyl)-2-cyclopentene-1-carboxylic acid in several steps.[4] In a previous paper, we ourselves reported that the treatment of the tertiary alkyl sulfones bearing carbonyl groups at the β-position with 5% hydrochloric acid in tetrahydrofuran (THF) at 30—60 °C afforded β-substituted α,β-unsaturated ketones and aldehydes in good yields.[5] Using this method, **5** was obtained from 2-cyclopentenone in a good yield. In this paper, we wish to report a new approach which allows a relatively simple and effective synthesis of **6**.

As shown in Fig. 1, 3-(*p*-tolylsulfonyl)cyclopentanone (**2**) was obtained in a 92.5% yield by the addition of *p*-toluenesulfinic acid to 2-cyclopentenone (**1**). The keto sulfone **2** was treated with ethylene glycol in benzene to give 1,1-ethylenedioxy-3-(*p*-tolylsulfonyl)cyclopentane (**3**) in a 95% yield. The sulfone **3** was alkylated using *cis*-1-bromo-3-hexene to afford 1,1-ethylenedioxy-3-(*cis*-3-hexenyl)-3-(*p*-tolylsulfonyl)cyclopentanone (**4**) in a quantitative yield.

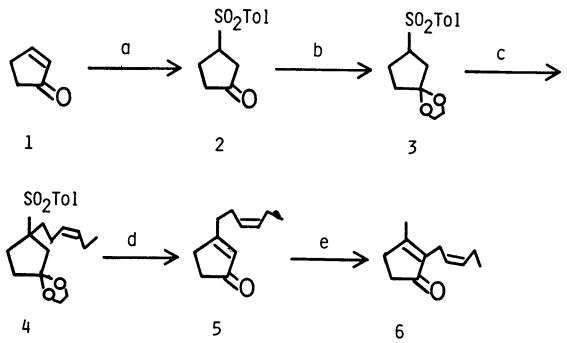

Fig. 1. a: *p*-Toluenesulfinic acid, b: ethylene glycol, c: LDA, −78 °C, *cis*-1-bromo-3-hexene, d: 5% HCl THF, 30 °C, e: 120 °C, (autoclave).

The treatment of the sulfone **4** with 5% hydrochloric acid gave 3-(*cis*-3-hexenyl)-2-cyclopentenone (**5**) in a 90% yield. Generally, the desulfonylation for making a variety of double bonds is carried out by the treatment of the allylic sulfones with a strong base. β-Keto sulfones are decomposed by dilute aq alkali. However, we found that the treatment of the sulfone **4** with 5% hydrochloric acid in THF afforded **5** in a good yield[5] when stirring was done at 45 °C for 4 h. When these conditions, **5** and its *trans* isomer were obtained in the ratio of 5 : 5. However, the reaction at a temperature below 30 °C gave pure **5** in a 90% yield.

Next, we investigated the details of the retroaldol-aldol condensation of **5** to **6**. McCurry *et al.* reported that the treatment of 0.160 g of **5** with 160 ml of 0.75 mol dm^{-3} sodium hydroxide by refluxing under argon for 72 h provided **6** in an 80% yield.[3] However, we could obtained the desired **6** by this method, only resinous substances were isolated. Thus, the reaction was carried out in a stainless steel autoclave using a dilute aq sodium hydroxide solution. The product-selectively in the conversion of **5** to **6** in an autoclave mainly depends on the reaction temperature, the reaction time, and the condensation of sodium hydroxide. The reaction conditions at 95 °C for 12 h using 5% sodium hydroxide did not give **6**, only the starting material, **5**, was recovered. When the reaction temperature was kept at 120 °C, the desired **6** was obtained in an 80% yield and in a 94% purity, along with the double-bond isomer, 3-methyl-2-(*trans*-1-penteny)-2-cyclopentenone (**7**) in a 6% yield. The sructure of **7** was determined from the ^1H NMR and IR spectra.[6] The ^1H NMR spectra of the olefin protons of the side chain of **7** appeared at δ 6.00 (d, J=16.5 Hz) and δ 6.78 (dt, J=16.5 and 6.0 Hz). The IR spectra of the compound show a characteristic absorption band at 970 cm^{-1} due to the *trans*-alkene bond. The mechanism produced may be assumed to proceed *via* the migration of the *cis*-olefin of the resulting **6** for the compound **7** was not obtained from 3-(*trans*-2-hexenyl)-2-cyclopentenone under similar conditions, only resinous substances being almost entirely produced. In addition, **6** isomerized to **7** with 5% sodium hydroxide in the autoclave in a ratio of 6%. Under the constant temperature of 120 °C, the employment of 1% sodium hydroxide gave **6** in a 40% yield, whereas 5% sodium hydroxide yielded **6** in an 80% yield. A higher concentration of more than 5% can easily give resinous substances as by-products.

Experimental

All the melting and boiling points are uncorrected. The melting points were taken on a Yanagimoto micro-melting-point apparatus. The infrared spectra were recorded on a Shimadzu IR-27G spectrophotometer. The ^{1}H NMR spectra were measured on a Varian EM-390 spectrometer at 90 MHz, using CCl_4 as solvent and TMS as an internal standard.

3-p-Tolylsulfonylcyclopentanone (2). Sodium *p*-toluenesulfinate tetrahydrate (8 g, 33 mmol) in 30 ml of MeOH, AcOH (2 g, 33 mmol), and 2-cyclopentenone (**1**) (2 g, 24 mmol) were placed in an Erlenmeyer flask and heated to reflux. After 10 h, the reaction product was neutralized by the use of a dilute sodium hydrogencarbonate solution and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and concentrated to give **2**, as solid substances. Recrystallization from benzene–hexane afforded 5 g (92.5% yield) of pure **2** as white needles, mp 58—58.5 °C. IR (Nujol) 2980, 1750, 1600, 1410, 1300, 1140 cm^{-1}. ^{1}H NMR (CCl_4) δ 2.05—2.90 (9H, m), 3.78 (1H, m), 7.45 and 7.85 (4H, an A_2B_2 pattern, J=8.7 Hz). Found: C, 61.11; H, 5.96%. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92%.

1,1-Ethylenedioxy-3-(p-tolylsulfonyl)cyclopentanone (3). Ethylene glycol (2 g, 31 mmol) was stirred into a solution of **2** (6.5 g, 27 mmol) in benzene (50 ml) in the presence of *p*-toluenesulfonic acid (20 mg), and the mixture was refluxed for 5 h. The reaction mixture was then worked up in the usual manner to give **3** (6.5 g, 95% yield) after recrystallization from hexane–benzene as white crystals, mp 61.5—62 °C. IR (Nujol) 2900, 1600, 1430, 1310, 1140 cm^{-1}. ^{1}H NMR (CCl_4) δ 1.75—2.40 (6H, m), 2.50 (3H, s), 3.45—3.90 (1H, m), 3.96 (4H, s), 7.50 and 7.90 (4H, an A_2B_2 pattern, J=8.7 Hz). Found: C, 60.41; H, 6.53%. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43%.

1,1-Ethylenedioxy-3-(cis-3-hexenyl)-3-(p-tolylsulfonyl) cyclopentane (4). To lithium diisopropylamide, prepared from *n*-BuLi (15% hexane solution, 8.5 g, 20 mmol) and diisopropylamine (2.1 g, 20 mmol) in dry THF (15 ml), was added a solution of **3** (4 g, 16 mmol) in dry THF (15 ml) at −78 °C under nitrogen. After the mixture has been stirred for 1 h, *cis*-1-bromo-3-hexene (2.8 g, 17 mmol) in dry THF (15 ml) was added. The mixture was then stirred for 1 h at −78 °C and an additional 3 h at room temperature. The mixture was then poured onto cold 2% sulfuric acid. The usual workup gave **4** as a viscous liquid in a quantitative yield after purification by column chromatography (SiO_2, 60—80 mesh) with benzene. IR (neat) 2930, 1600, 1460, 1300, 1140 cm^{-1}. ^{1}H NMR (CCl_4) δ 0.99 (3H, t, J=7.2 Hz), 1.6—2.8 (15H, m), 3.90 (4H, s), 5.05—5.60 (2H, m), 7.33 and 7.77 (4H, an A_2B_2 pattern, J=8.7 Hz). Found: C, 66.13; H, 7.75%. Calcd for $C_{20}H_{28}O_4S$: C, 65.90; H, 7.74%.

3-(cis-3-Hexenyl)-2-cyclopentenone (5). To a stirred solution of **4** (3 g, 8.24 mmol) in THF (60 ml) was added 5% hydrochloric acid (18 ml). The mixture was then stirred for 5 h at 30 °C. After the removal of the THF, the mixture was poured into 500 ml of water and worked up to give **5** (1.2 g, 90% yield) as a colorless liquid, bp 104—106 °C/6 mmHg (1 mmHg=133.322 Pa). IR (neat) 2950, 1715, 1620, 1440, 1185 cm^{-1}. ^{1}H NMR (CCl_4) δ 0.95 (3H, t, J=7.2 Hz), 1.8—2.6 (10H,m), 5.15—5.75 (2H, m), 5.93 (1H, br s). The product was identified by comparing its NMR spectrum with the reportedone.[3]

cis-*Jasmone (6).* **5** (0.4 g, 2.24 mmol) and 5% sodium hydroxide (30 ml) were placed in a stainless steel autoclave equipped with a magnetic stirrer. The autoclave was heated in an oil bath maintained at 120 °C for 12 h and then allowed to cool. The reaction mixture was acidified with dilute hydrochloric acid. The organic layer was extracted with ether. The extract was worked up in the usual manner to give 0.32 g (80% yield after being chromatographed, SiO_2 with benzene–hexane (7 : 3)) of **6**, whose gas chromatographic analysis showed a *cis/trans* isomer ratio of 94/6. The NMR and IR spectra of the **6** synthesized here were identical with those of an authentic sample.

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6) Compound **7**: ^{1}H NMR (CCl_4) δ 0.94 (3H, t, J=6.9 Hz), 1.3—1.7 (2H, m), 2.0—2.6 (6H, m), 2.07 (3H, s), 6.00 (1H, d, J=16.5 Hz), 6.78 (1H, dt, J=16.5 and 6.0 Hz). IR (neat) 2960, 1700, 1600, 1435, 1375, 1075, 970 cm^{-1}.