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A Short Synthesis of Dihydrojasmone, *cis*- and *trans*-Jasmones

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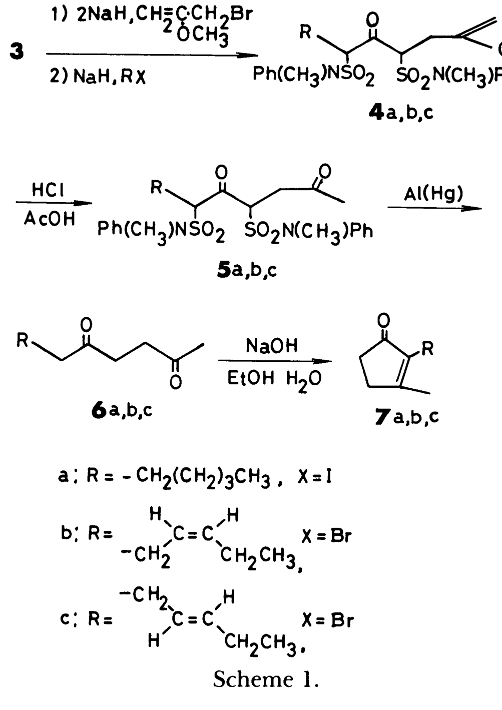
Synopsis. The titled jasmones were synthesized from *N,N'*-dimethyl-2-oxo-1,3-propanedisulfonanilide, a new three carbon building block for organic preparation.

2-Oxo-1,3-propanedisulfonic acid (**1**), which is easily accessible from acetone, has three kinds of reactive groups (sulfonic acid, carbonyl, and methylene groups) and seems to be a promissing intermediate for routine synthesis. But little is known about its synthetic utilization. Recently we have reported an application of the dialkyl sulfonates as practical alkylating reagents.[1] To show the utility of **1**, we now report a new synthesis of dihydrojasmone, *cis*- and *trans*-jasmones from *N,N'*-dimethyl-2-oxo-1,3-propanedisulfonanilide (**3**) through undecane- and 8-undecene-2,5-diones. The sulfonanilide can be prepared easily from the corresponding sulfonyl chloride (**2**)[1] and *N*-methylaniline and it behaves as an acetone with highly activated methylenes.

$$O{=}C(CH_2X)_2 \quad \begin{array}{l} \textbf{1},\ X{=}SO_3H \\ \textbf{2},\ X{=}SO_2Cl \\ \textbf{3},\ X{=}SO_2N(CH_3)Ph \end{array}$$

The process of synthesis was outlined in Scheme 1. In the case of dihydrojasmone, introduction of two necessary carbon fragments, pentyl and acetonyl groups, into **3** was conducted in one pot reaction with a high yield. Thus, the dianion generated from **3** with two equivalents of sodium hydride was allowed to react first with 3-bromo-2-methoxypropene[2] and the resulting reaction mixture was treated with one more equivalent of NaH. The unsymmetrical dianion formed was then alkylated with 1-iodopentane. The product enol ether (**4a**) was easily hydrolysed with HCl in acetic acid to the diketone (**5a**), which was desulfonated with aluminum amalgum in THF to afford 2,5-undecanedione (**6a**). The aldol cyclization of **6a** with NaOH in aq ethanol yielded dihydrojasmone (**7a**).[3] By the essentially same procedure, using *cis*- and *trans*-1-bromo-2-pentenes in place of 1-iodopentane, *cis*- and *trans*-jasmone were synthesized, respectively.



Scheme 1.

As illustrated above, the sulfonanilide (**3**) seems to be a good synthetic part for nucleophilic introduction of acetone unit. Particularly it is noteworthy that the smooth introduction of two electrophiles into the both methylene carbons of **3** is possible in one pot reaction, involving the successive generation of dianions.[4]

Experimental

The melting points were not corrected. The solvents were of a reagent grade. All the known compounds were confirmed by a comparison of the melting points and spectroscopic data with those of the authentic samples or the reported data. The reaction products were fractionated with a JAI LC-08 gel permeation liquid chromatograph (GPLC) using chloroform as eluent. The ^1H NMR spectra were recorded on a JEOL PMX-60 spectrometer in $CDCl_3$ and the shifts were given in δ unit from internal TMS. The IR spectra were measured on a Hitachi 260-30 spectrometer. The boiling points shown were bath temp.

N,N'-Dimethyl-2-oxo-1,3-propanedisulfonanilide (3). *N*-Methylaniline (149.7 g, 1.397 mol) was added dropwise to a benzene (60 cm^3) suspension of 2-oxo-1,3-propanedisulfonyl chloride (**2**, 118.9 g, 0.466 mol)[1] at 13—15 °C with stirring. After stirring was continued for 4 h at the same temperature, benzene was removed under reduced pressure and the residue was poured into aq MeOH (500 cm^3, 1 : 1 v/v). The mixture was made acidic with HCl and the precipitated crystals were collected by suction filtration, washed with water, and dried. Recrystallization from methanol yielded colorless crystals (122.6 g, 71%, mp 77—78 °C).[5] IR: 1725 ($\nu_{C=O}$) cm^{-1}. ^1H NMR: 3.30 (s, 6H, CH_3), 4.27 (s, 4H, CH_2), 7.35 (s, 10H, Ph). Found: C, 51.76; H, 4.96; N, 7.04%. Calcd for $C_{17}H_{20}N_2O_5S_2$: C, 51.50; H, 5.08; N, 7.07%.

N,N'-Dimethyl-2,5-dioxo-4,6-undecanedisulfonanilide (5a). Sodium hydride (60% in mineral oil, 1.20 g, net 30.0 mmol) was washed twice with hexane and suspended in DMSO 30 cm^3) under N_2. The sulfonanilide (**3**) was added to the mixture with stirring at the room temp and stirring was continued for 1 h. 3-Bromo-2-methoxypropene[2] (3.0 g, 45 mmol) was added dropwise with stirring and the mixture was stirred for 3 h at the ambient temp. Sodium hydride (60% in mineral oil, 0.60 g, net 15 mmol) was added and the mixture was stirred for 0.5 h. 1-Iodopentane (2.37 g, 12.0 mmol) was added to the mixture and stirring was continued for further 3 h at the room temp. The reaction mixture was decomposed with water (10 cm^3) and made acidic with HCl. The mixture was extracted with $CHCl_3$ and the combined extracts were washed with water and dried ($MgSO_4$). The crude product obtained on concentration under reduced pressure was subjected to GLPC fractionation. The enol ether (**5a**) was effectively separated by means of the recycle technique and hydrolyzed with AcOH (20 cm^3) containing 1 M[†] HCl (10 cm^3). The diketone (**5a**) was extracted with ether and the combined extracts were washed with 5% aq NaHCO$_3$ and water, successively, and dried (Na$_2$SO$_4$). On the vacuum concentration, **5a** was obtained as a colorless viscous oil (4.47 g, 85.5%). IR (neat): 1726 (sh, $\nu_{C=O}$), 1720 ($\nu_{C=O}$) cm^{-1}. ^{1}H NMR: 0.55—1.57 (m, 11H, pentyl), 2.0 (s, 3H, CH$_3$ of acetyl), 2.87 (d, *J*=6 Hz, 2H, CH$_2$ of acetonyl), 3.27 (s, 6H, CH$_3$–N), 4.76 (dd, *J*=10 and 4 Hz, 1H, pentyl side methine), 5.8 (t, *J*=6 Hz, 1H, acetonyl side methine), 7.32 (s, 10H, Ph). Found: C, 57.62; H, 6.62; N, 4.58%. Calcd for C$_{25}$H$_{24}$N$_2$O$_6$S$_2$: C, 57.45; H, 6.56; N, 4.36%.

2, 5-Undecanedione (6a). The sulfonanilide (**5a**, 2.66 g, 5.09 mmol) was dissolved in the mixture of THF (170 cm^3) and water (10 cm^3). Aluminum amalgum prepared from Al foil (4.12 g, 0.15 mol) was added to the solution and heated to reflux[6)] for 3 h. After cooling down, the reaction mixture was digested with cold dil HCl and THF was removed under reduced pressure. The residue was extracted with ether and the combined extracts were washed with brine, dried (Na$_2$SO$_4$), and concentrated under reduced pressure. The crude diketone was purified by GPLC and bulb to bulb distillatin (bp 99—101 °C/1 Torr, 1 Torr=133.322 Pa) to yield a faintly yellow oil (0.45 g, 47.9%). IR (neat): 1703 ($\nu_{C=O}$) cm^{-1}. ^{1}H NMR: 0.87 (deformed t, *J*=5 Hz, 3H, CH$_3$ of hexyl), 1.07—1.85 (m, 8H, internal tetramethylenes of hexyl), 2.17 (s, 3H, CH$_3$ of acetyl), 2.27 (t, *J*=7 Hz, 2H, terminal methylene of hexyl), 2.67 (s, 4H, methylenes between carbonyls). Found: C, 70.70 H, 10.94%. Calcd for C$_{12}$H$_{20}$O$_2$: C, 70.90; H, 10.77%. Desulfonation could also be done by 6% Na(Hg) in MeOH containing Na$_2$HPO$_4$ (21% yield).

3-Methyl-2-pentyl-2-cyclopentenone (Dihydrojasmone, 7a). The diketone (**6a**, 0.560 g, 3.04 mmol) was submitted to the aldol cyclization according to the reported method[3)] to yield dihydrojasmone as a colorless oil (bp 110—112 °C/10 Torr, 0.39 g, 77.3%). IR (neat): 1700 ($\nu_{C=O}$), 1645 ($\nu_{C=C}$) cm^{-1}. ^{1}H NMR: 0.55—1.85 (m, 9H, methyl and internal trimethylenes of pentyl), 1.95—2.90 (m including s at 2.07 for CH$_3$ at C$_3$, 9H, CH$_3$, ring methylenes, and the terminal methylene of pentyl). Found: C, 79.53; H, 10.69%. Calcd for C$_{11}$H$_{18}$O: C, 79.46; H, 10.91%. 2,4-Dinitrophenylhydrazone melted at 120—121 °C.[7)] Found: C, 58.92; H, 6.17; N, 16.12%. Calcd for C$_{17}$H$_{22}$O$_4$N$_4$: C, 58.95; H, 6.40; N, 16.17%.

cis- *and* trans-N,N′*-Dimethyl-2,5-dioxo-8-undecene-4,6-disulfonanilides (5b and 5c).* By the essentially same procedure, **3** was allowed to react first with 3-bromo-2-methoxypropene[2)] and then with *cis*- or *trans*-1-bromo-2-pentene[8)] in place of 1-iodopentane. Working up in the same way as in the case of **5a** yielded **5b** or **5c** as a faintly yellow viscous oil (both 86%).

cis- *and* trans-*8-Undecene-2,5-diones (6b and 6c).* The dioxodisulfonanilide (**5b**, 2.42 g, 4.65 mmol or **5c**, 1.99 g, 3.82 mmol) was refluxed in the mixture of THF and water (200 cm^3, 9:1 v/v for **5b** or 130 cm^3, 15:1 v/v for **5c**) with aluminum amalgum, prepared from Al foil (6.27 g, 0.23 mol for **5b** or 3.24 g, 0.12 mol for **5c**) for 3 h under stirring. Working up the reaction mixture in the same way as in the case of **6a** afforded **6b** or **6c** as a colorless oil (**6b**: bp 140 °C/2 Torr, 0.40 g, 47.3%; **6c**: bp 137 °C/4 Torr, 0.11 g, 15.8%). IR: **6b** (neat), 1710 ($\nu_{C=O}$); **6c** (neat), 1712 ($\nu_{C=O}$) cm^{-1}. ^{1}H NMR: **6b**, 0.95 (t, *J*=7 Hz, 3H, CH$_3$ of heptenoyl), 1.27—*ca.* 2.5 (m, 4H, allylic methylenes), 2.18 (s, 3H, CH$_3$ of acetyl), 2.43 (t, *J*=4 Hz, 2H, heptenoyl methylene neighboring to the carbonyl), 2.7 (s, 4H, methylenes between carbonyls), 5.2—5.6 (m, 2H, olefinic); **6c**, 0.95 (t, *J*=7 Hz, 3H, CH$_3$ of heptenoyl), 1.1—2.6 (m, 6H, methylenes of heptenoyl), 2.18 (s, 3H, CH$_3$ of acetyl), 2.68 (s, 4H, methylenes between carbonyls), 5.3—5.6 (m, 2H, olefinic). Found: **6b**, C, 71.98; H, 9.58%; **6c**, C, 72.75; 9.94%. Calcd for C$_{11}$H$_{18}$O$_2$: C, 72.49; H, 9.95%.

*2-(*cis*-2-Pentenyl)-3-methyl-2-cyclopentenone (*cis*-Jasmone, 7b).* The diketone (**6b**, 0.303 g, 1.66 mmol) was refluxed in 0.5 M aq NaOH (5 cm^3) containing ethanol (2 cm^3) for 5 h. The reaction mixture was extracted with ether. The combined extracts were washed with brine, dried (Na$_2$SO$_4$), and concentrated under reduced pressure. The crude product was purified by GPLC and vacuum distillation to yield a colorless oil (bp 82—85 °C/1 Torr, 0.13 g, 50%). IR (neat): 1700 ($\nu_{C=O}$), 1650 ($\nu_{C=C}$) cm^{-1}. ^{1}H NMR: 0.98 (t, *J*=7 Hz, 3H, CH$_3$ of pentenyl), 1.7—2.7 (m, 6H, methylenes), 2.07 (s, 3H, CH$_3$ at C$_3$), 2.94 (d, *J*=5 Hz, 2H, CH$_2$ between double bonds), 5.1—5.7 (m, 2H, olefinic). Found: C, 79.91; H, 9.71%. Calcd for C$_{11}$H$_{16}$O: C, 80.44; H, 9.82%. 2,4-Dinitrophenylhydrazone melted at 115—116 °C.[9)] Found: 59.05; H, 5.96; N, 15.91%. Cacld for C$_{17}$H$_{20}$O$_4$N$_4$: C, 59.29; H, 5.85; N, 16.27%.

*2-(*trans*-2-Pentenyl)-3-methyl-2-cyclopentenone (*trans*-Jasmone, 7c).* The diketone (**6c**, 0.240 g, 1.32 mmol) was heated to reflux for 6 h in the mixture of ethanol (2 cm^3) and 0.5 M aq NaOH (3 cm^3). The reaction mixture was worked up and purified in the same way as in the case of **7b** to obtain **7c** as a colorless oil (bp 87—90 °C/1 Torr, 0.136 g, 63%). IR (neat): 1700 ($\nu_{C=O}$), 1650 ($\nu_{C=C}$) cm^{-1}. ^{1}H NMR: 0.94 (t, *J*=7 Hz, 3H, CH$_3$ of pentenyl), 1.6—2.7 (m, 6H, methylenes), 2.07 (s, 3H, CH$_3$ at C$_3$), 2.88 (d, *J*=4 Hz, 2H, CH$_2$ between double bonds), 5.3—5.6 (m, 2H, olefinic). Found: C, 79.88; H 9.72%. Calcd for C$_{11}$H$_{16}$O: C, 80.44; H, 9.82%. 2,4-Dinitrophenylhydrazone melted at 127—128 °C.[9)] Found: C 59.15; H, 5 62; N, 16.16%. Calcd for C$_{17}$H$_{20}$O$_4$N$_4$: C, 59.29; H, 5.85; N, 16 27%.

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[†] 1 M=1 mol dm^{-3}.