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A Convenient Method for the Synthesis of Acyclic Ketones. Synthesis of Sex Pheromone of Douglas Fir Tussock Moth

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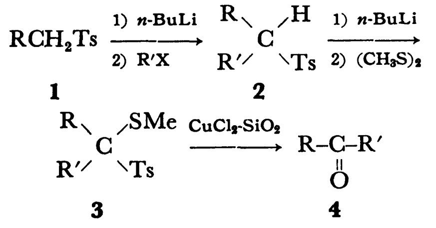
Synopsis. (α-Alkyl-α-methylthio)alkyl *p*-tolyl sulfones derived from the reaction of α-alkylated alkyl *p*-tolyl sulfones with dimethyl disulfide could be easily hydrolyzed by $CuCl_2$–SiO_2 to give the corresponding ketones in fairly good yields. This method was applied to the synthesis of Douglas Fir Tussock Moth Pheromone.

The development of the general method for the synthesis of acyclic ketone is a major point of interest in the organic synthesis and a variety of methods have been reported. In connection with our continuing interest to extend the synthetic utility of sulfones, in the preceding paper,[1)] a new method for the preparation of aromatic ketones *via* chlorination of α-substituted benzyl *p*-tolyl sulfones followed by hydrolysis was described. However, the reaction was limited to the formation of aryl ketones, and drastic conditions using silver perchlorate in refluxing trifluoroacetic acid for hydrolysis were required. Recently, a convenient method for the hydrolysis of a ketone dithioacetal *S*,*S*-dioxide leading to the corresponding carbonyl group has been reported by Ogura and co-workers,[2)] in which hydrochloric acid in refluxing methanol was used for hydrolysis.



Scheme 1.

In this paper, we wish to report a more mild synthetic method of acyclic ketones (**4**) starting from alkyl *p*-tolyl sulfones (**1**), which were subjected to alkylation followed by treatment with *n*-BuLi and $(CH_3S)_2$ to afford α-(methylthio)alkyl *p*-tolyl sulfones (**3**). Subsequently, on treatment of **3** with $CuCl_2$–SiO_2 in dichloromethane at room temperature without further purification, hydrolysis to ketone compounds took place very smoothly to give the desired products (**4**) in fairly good yields as shown in Table 1.

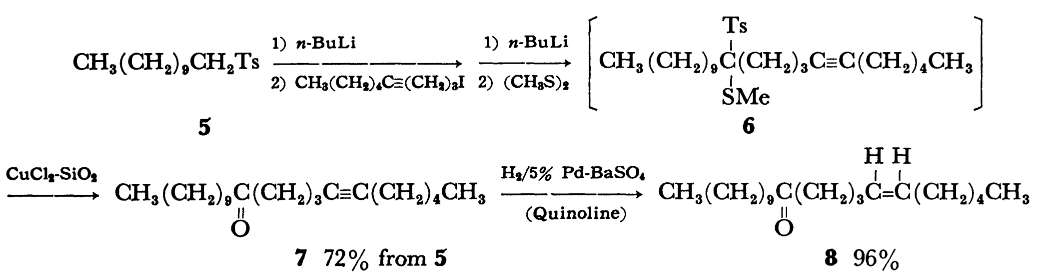
Next, this method was applied to the synthesis of Douglas Fir Tussock Moth Pheromone[3)] starting from *p*-tolyl undecyl sulfone (**5**) according to the following scheme. The reaction proceeded smoothly, and acetylenic ketone (**7**) was obtained in high yield in a similar manner above mentioned. A catalytic hydrogenation of **7** over 5% Pd–$BaSO_4$ (deactivated by quinoline) gave the desired pheromone (**8**) in an excellent yield.

Experimental

All the melting points are uncorrected. The NMR and IR spectra were recorded on JEOL/PMX-60 and JASCO IRA-1 spectrometers, respectively.

Materials. Freshly distilled THF from potassium under nitrogen was used. Thin-layer chromatography (TLC) was performed on Merck's silica gel 60 PF_{254} (Art. 7749).

A Typical Experimental Procedure for the Preparation of the Ketones. To a solution of phenethyl *p*-tolyl sulfone (123 mg, 0.5 mmol) in dry THF (5 ml) was added *n*-BuLi (0.55 mmol, hexane solution) dropwise at −20 °C under N_2. The reaction mixture was allowed to warm to room temperature in a period of 20 min and then a solution of phenethyl bromide



Scheme 2. Synthesis of Douglas Fir Tussock Moth Pheromone.

Table 1. The synthesis of acyclic ketones from alkyl *p*-tolyl sulfones (**1**)

No.	R	R′X	$CuCl_2 \cdot SiO_2$	Reaction conditions	Yield of $4^{a)}$/%
1	$CH_3(CH_2)_9$	$C_6H_5CH_2Br$	2 equiv.	r.t., 20 min	62 (**4a**)
2	$CH_3(CH_2)_9$	$C_6H_5(CH_2)_2Br$	2 equiv.	r.t., 40 min	58 (**4b**)
3	C_6H_5	$CH_3(CH_2)_4C{\equiv}C(CH_2)_3I$	2 equiv.	r.t., 1 h	69 (**4c**)
4	C_6H_5	$C_6H_5(CH_2)_2Br$	2 equiv.	r.t., 30 min	80 (**4d**)
5	$C_6H_5CH_2$	$CH_3(CH_2)_4C{\equiv}C(CH_2)_3I$	2 equiv.	r.t., 2.5 h	67 (**4e**)
6	$C_6H_5CH_2$	$C_6H_5(CH_2)_2Br$	2 equiv.	r.t., 1 h	59 (**4f**)

a) Based on **1**.

(102 mg, 0.55 mmol) in dry THF (2 ml) was added slowly at −78 °C. The temperature of the solution was raised to room temperature, cooled down again at −20 °C, and treated with *n*-BuLi (0.55 mmol) followed by the addition of a solution of $(CH_3S)_2$ (52 mg, 0.55 mmol) in dry THF (2 ml) at −78 °C. The reaction temperature was gradually raised to room temperature, quenched with buffer solution of pH=7 ($NaOH+KH_2PO_4$) (5 ml) and HCl, extracted with AcOEt, dried over Na_2SO_4 and concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (5 ml) and treated with $CuCl_2$–SiO_2 (752 mg) for 1 h at room temperature. After filtration and concentration, the residue was subjected to preparative TLC (solvent : benzene) to give the desired ketone in 59% yield (66 mg) based on phenethyl *p*-tolyl sulfone (**1**).

The Active $CuCl_2$–SiO_2. After a mixture of $CuCl_2\cdot 2H_2O$ (0.85 g), SiO_2 (3.5 g), and water (8 ml) was air-dried for 1 h, it was heated up at 110—130 °C for 3 h and allowed to cool to room temperature. The mixture thus obtained must be used immediately.

Preparation of 1-Iodo-4-decyne. *Preparation of 1-Chloro-4-decyne*: To a solution of 1-heptyne (15.8 mmol) in dry THF (15 ml) was added a solution of *n*-BuLi (15.8 mmol) in hexane (10 ml) at −78 °C under N_2. After the reaction temperature was raised to room temperature, a solution of 1-bromo-3-chloropropane (17.4 mmol) in dry THF (12 ml) was added to the reaction mixture and refluxed for 21 h. After the solvent was removed *in vacuo*, quenched with buffer solution ($NaOH+KH_2PO_4$) (20 ml) and HCl followed by extraction with AcOEt. The AcOEt extract was distilled under reduced pressure. Bp 83 °C/6 Torr, (61% yield).

Conversion of the Chloride to the Corresponding Iodide: A solution of 1-chloro-4-decyne (7.4 mmol) and NaI (7.4×4.5 mmol) in dry acetone (20 ml) was refluxed for 15 h. After the solvent was removed, AcOEt was added and the AcOEt extract was distilled under reduced pressure to give 1-iodo-4-decyne in 86% yield. Bp 73 °C/0.03 Torr; IR (neat) 2930, 1450, 1220 cm^{-1}; NMR ($CDCl_3$) δ 0.63—1.08 (distored t, 3H), 1.08—1.73 (m, 6H), 1.73—2.63 (m, 6H), 3.23 (t, 2H, $J=6$ Hz).

Preparation of p-*Tolyl Undecyl Sulfone*: A suspension of 1-bromoundecane (2.35 g, 10 mmol) and sodium *p*-toluenesulfinate tetrahydrate (3.75 g, 15 mmol) in EtOH (20 ml) was refluxed for 8.5 h. Then, the reaction mixture was poured into a lot of ice–water to result in precipitation of the crude product, which was collected and dried. Recrystallization from MeOH gave a pure compound. Yield 2.68 g (87%). Mp 70—71 °C. Found: C, 69.49; H, 9.98%. Calcd for $C_{18}H_{30}O_2S$: C, 69.63; H, 9.74%.

Identification of Products (4a—f). **4a**: Oil, *m/e*: 260 (M^+), IR (neat) 2930, 1710, 1600, 1495, 1450 cm^{-1}. NMR ($CDCl_3$) δ 0.73—1.04 (distored t, 3H), 1.04—1.76 (m, 16H), 2.35 (t, 2H, $J=7.0$ Hz), 3.55 (s, 2H), 7.08 (s, 5H).

4b: Oil, *m/e* 274 (M^+), IR (neat) 2930, 1710, 1600, 1495, 1450 cm^{-1}; NMR ($CDCl_3$) δ 0.6—1.02 (distored t, 3H), 1.02—1.73 (m, 16H), 2.33 (t, 2H, $J=7$ Hz), 2.50—3.07 (m, 4H), 7.10 (s, 5H).

4c: Oil, *m/e* 242 (M^+), IR (neat) 2940, 1680, 1600, 1580, 1450 cm^{-1}; NMR ($CDCl_3$) δ 0.70—1.05 (distored t, 3H), 1.05—1.68 (m, 6H), 1.68—2.48 (m, 6H), 3.05 (t, 2H, $J=7.0$ Hz), 7.15—7.50 (m, 3H), 7.68—7.95 (m, 2H).

4d: Mp 70.5—71.5 °C; IR (neat) 3032, 1708, 1600, 1172, 750 cm^{-1}; NMR ($CDCl_3$) δ 2.62—2.87 (m, 4H), 3.53 (s, 2H), 6.38—7.50 (m, 10H), Found: C, 85.40; H, 6.77%. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71%.

4e: Oil, *m/e* 256 (M^+), IR (neat) 2920, 1710, 1600, 1495, 1450 cm^{-1}; NMR ($CDCl_3$) δ 0.70—1.05 (distored t, 3H), 1.05—1.67 (m, 8H), 1.67—2.35 (m, 4H), 2.55 (t, 2H, $J=7.0$ Hz), 3.67 (s, 2H), 7.22 (s, 5H).

4f: Oil, *m/e* 224 (M^+), IR (neat) 2930, 1710, 1600, 1490, 1450 cm^{-1}; NMR ($CDCl_3$) δ 2.43—3.08 (m, 4H), 3.60 (s, 2H), 6.87—7.67 (m, 10H).

The Reaction Condition for the Synthesis of Pheromone (8). Preparation of 6-Heneicosyn-11-one (7) from 5: A synthetic procedure was the same manner above mentioned. *p*-Tolyl undecyl sulfone (**5**) (310 mg, 1 mmol), 1-iodo-4-decyne (264 mg, 1 mmol), and dimethyl disulfide (94 mg, 1 mmol) were used for the formation of **6** (479 mg). The procedure for the conversion of **6** to **7** is as follows: To a solution of **6** (96 mg, 0.2 mmol) in CH_2Cl_2 (6 ml) was added $CuCl_2$–SiO_2 (820 mg, 1 mmol), and the suspension was stirred for 2 d at room temperature. The usual work-up gave 44 mg of **7**. Total yield of **7** was 72% based on **5**.
IR (neat) 2910, 2850, 1705, 1460, 1370, 1090 cm^{-1}; NMR ($CDCl_3$) δ 0.62—1.05 (distored t, 6H), 1.05—2.23 (m, 28H), 2.37 (t, 2H, $J=7$ Hz), 2.47 (t, 2H, $J=7$ Hz).

IR and NMR spectra of **7** were identical with those of literature.[3]

Preparation of Pheromone (8) from 7. A methanol solution (15 ml) of **7** (116 mg, 0.38 mmol) containing one drop of quinoline was hydrogenated over 5% Pd–$BaSO_4$ (20 mg) under atmospheric pressure for about 5 h. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to give a residue which was taken up into AcOEt. The AcOEt solution was washed with dil-HCl, brine, dried over Na_2SO_4, and concentrated *in vacuo* to give the desired material as a single product in 96% yield (112 mg). Its IR and NMR data were identical with the reported values.[4] IR (neat) 3000, 2920, 2850, 1715, 1455, 1370, 1125, 1080 cm^{-1}; NMR ($CDCl_3$) δ 0.75—1.05 (distored t, 6H), 1.05—1.75 (m, 24H), 1.95 (m, 4H), 2.34 (t, 4H, $J=7$ Hz), 5.27 (m, 2H).

References

1) H. Kotake, K. Inomata, H. Kinoshita, Y. Sakamoto, and Y. Kaneto, *Bull. Chem. Soc. Jpn.*, **53**, 3027 (1980).

2) K. Ogura, M. Suzuki, J. Watanabe, M. Yamashita, H. Iida, and G. Tsuchihashi, *Chem. Lett.*, **1982**, 813.

3) R. G. Smith, G. E. Daterman, and G. D. Daves, Jr., *Science*, **1975**, 63; K. Kondo and S. Murahashi, *Tetrahedron Lett.*, **1979**, 1237; K. Mori, M. Uchida, and M. Matsui, *Tetrahedron*, **33**, 385 (1977); L. H. Smith, R. G. Smith, T. M. Loehr, G. D. Daves, Jr., G. E. Daterman, and R. H. Wohleb, *J. Org. Chem.*, **43**, 2361 (1978).

4) B. Akermark and L. Vist, *J. Org. Chem.*, **43**, 4387 (1978).