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REGIOSELECTIVE ALKYLATION AND THE RAMBERG-BÄCKLUND TYPE REACTION OF α-(p-TOLYLSULFONYL)THIANE S,S-DIOXIDE. A NEW ROUTE TO THE SYNTHESIS OF 3-ALKYL-3-CYCLOPENTENONES

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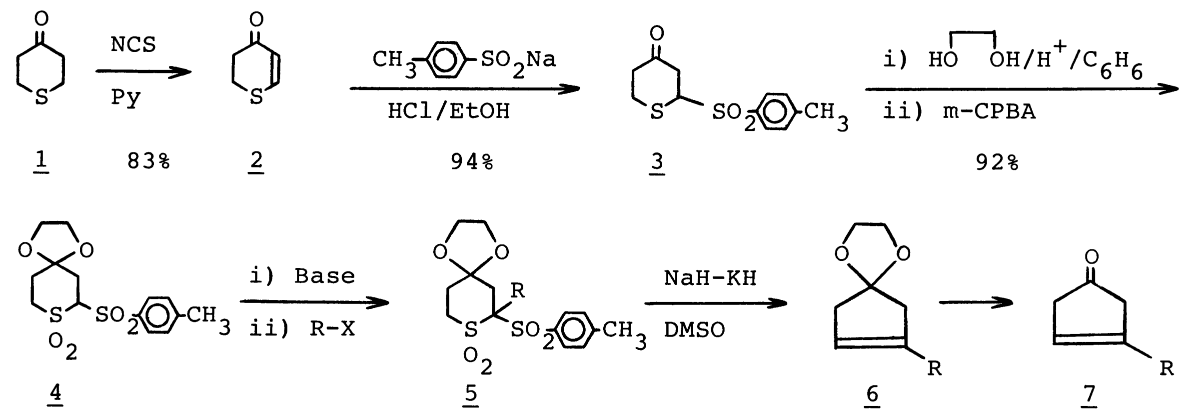
A new general olefin synthesis, via regioselective alkylation of α-(p-tolylsulfonyl)thiane S,S-dioxide, 1,4-dioxa-7-p-tolylsulfonyl-8-thiaspiro[4.5]decane 8,8-dioxide, and subsequent Ramberg-Bäcklund type elimination of p-toluenesulfinate and SO_2, is here applied to the synthesis of 3-alkyl-3-cyclopentenones.

The Ramberg-Bäcklund reaction represented one of the first alkene syntheses in which the position of double bond was clearly defined.[1] Recently, we reported a general synthesis of 2-alkyl-3-cyclopentenones via the Ramberg-Bäcklund reaction starting from thian-4-one (1) as a 5 C synthon.[2] In recent years, there are a few reports on the synthesis of 3-cyclopentenones,[3] although much work has been devoted to preparation of 2-cyclopentenones. In connection with our search of new fragrant compounds, we wish to describe the synthesis of some 3-alkyl-3-cyclopentenones in this paper.

We found that α-alkyl-α-(p-tolylsulfonyl)thiane S,S-dioxides (5) were successfully converted into the corresponding cyclopentenes (6) by the action of NaH-KH in dimethyl sulfoxide (DMSO) in good yields. The key compound 4 was readily prepared according to Scheme 1. 2,3-Dihydrothiin-4-one (2)[4] was converted into 1,4-dioxa-7-p-tolylsulfonyl-8-thiaspiro[4.5]decane 8,8-dioxide (4)[5] by 1,4-addition of p-toluenesulfinic acid (sodium p-toluenesulfinate, HCl, EtOH; 0 °C → room temperature), protection of carbonyl group of 3[6] (ethylene glycol, p-TsOH (cat.),



Scheme 1.

C_6H_6-reflux), followed by oxidation (m-chloroperbenzoic acid (3 equiv.), CH_2Cl_2; 0 °C → room temperature). For the regioselective alkylation of 4 with alkyl halides (R-X), two types of procedure were employed: (a) with K_2CO_3 in dry acetone (reflux; "Method A"), and (b) with NaH in N,N-dimethylformamide (DMF) (70 °C; "Method B"). The results are summarized in Table 1, showing that both Method A and Method B gave monoalkylated sulfones 5 in good yields.[7)]

Table 1. Reaction Conditions and Yields in the Conversion of 4 to 5

Entry	Alkyl halides	Method[a)]	5	Mp θ_m/°C	Yield/%
1	CH_3-I	A	5a	175.0-175.5	96
2	$C_6H_5CH_2$-Br	A	5b	164.0-164.4	88
3	CH_2=CH-CH_2-Br	A	5c	150.2-151.4	97
4	C_5H_{11}-I	B	5d	106.2-108.2	86
5	$CH_3OC(=O)(CH_2)_4CH_2$-I	B	5e	132.9-134.3	93
6	$C_6H_5CH_2CH_2$-Br	B	5f	168.5-169.5	80

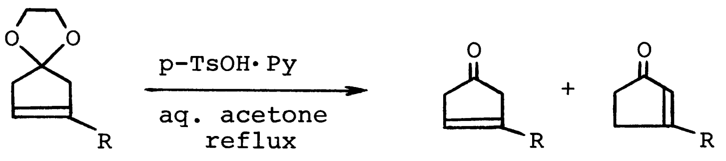
a) Method A: sulfone 4 (2 mmol), alkyl halide (4 mmol), K_2CO_3 (6 mmol), dry acetone (40 ml), reflux 6-10 h. Method B: sulfone 4 (2 mmol), alkyl halide (4 mmol), NaH (2.5 mmol), dry DMF (20 ml), 70 °C, 20-24 h.

6-Membered sulfones (5) were transformed into cyclopentenes (6)[8)] by the Ramberg-Bäcklund type reaction (NaH (2.5-3 equiv.) -KH (0.1 equiv.), DMSO, 20-30 °C, 24 h) under nitrogen (Table 2). After cleavage of 1,3-dioxolane of 6 by acid catalyzed de-dioxolanation[9)] (p-TsOH•Py (cat.), aq. acetone-reflux), the expected 3-cyclopentenones (7)[10)] were formed as major component ($>$ 80%) along with minor amount of 2-cyclopentenone isomer (8)[11)] (by a GLC analysis) (Table 3). The ratio of 3-cyclopentenone/2-cyclopentenone decreased with the increase of the reaction time.

Table 2. Cyclopentene 6 Obtained by the Ramberg-Bäcklund Type Reaction of 5

Entry	Sulfone (5)	Yield of 6/%
1	R= CH_3	60
2	C_5H_{11}	87
3	$C_6H_5CH_2CH_2$	70

Table 3. 3-Cyclopentenone 7 Obtained by Acid-catalyzed De-dioxolanation of 6



6 7 8

Entry	Cyclopentene (6)	Reaction time/ h	Yield of (7 + 8)/%	Isomer ratio[a) 7 : 8
1	R= CH_3	10	50	100 : 0
2	C_5H_{11}	10	94	82 : 18
3	C_5H_{11}	22	92	75 : 25
4	$C_6H_5CH_2CH_2$	10	82	85 : 15

a) Determined by GLC.

In a typical experiment, sodium hydride (12.5 mmol; 2.5 equiv.) and potassium hydride (0.5 mmol; 0.1 equiv.) were added to a stirred solution (DMSO, 20 ml) of sulfone 5d (R= C_5H_{11}; 5.0 mmol) at room temperature. The reaction mixture was stirred for 24 h at room temperature under nitrogen. The reaction mixture was quenched with ice and water and the product was extracted with pentane (100 ml x 2). The pentane extracts were combined, washed successively with water (50 ml x 5) and brine (50 ml), and dried over sodium sulfate. Filtration and solvent evaporation gave an oil (87%) which was mostly pure cyclopentene 6d (R= C_5H_{11}; >94% pure; checked by a GLC analysis). The minor by-product was 3-pentyl-3-cyclopentenone 7d (6% yield). A solution of an oily 6d (1.5 mmol) and catalytic pyridinium p-toluenesulfonate (p-TsOH·Py, 38 mg; 0.1 equiv.) in aqueous acetone (10 ml; water : acetone = 1 : 4) was refluxed for 10 h and extracted with pentane gave 3-cyclopentenone 7d (R= C_5H_{11}) and 2-cyclopentenone 8d (R= C_5H_{11}) (isomer ratio; 7d : 8d = 82 : 18) in 94% yield. Pure 7d was obtained by preparative TLC on silica gel and /or preparative GLC.

In conclusion, this synthetic approach from 1 to 7 offers several advantages. (i) The starting material 1 and reagents used are readily available; (ii) all operations in the reaction steps (4 → 5 → 6) are simple; (iii) the yields are moderate to good.

References

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2) H. Matsuyama, Y. Miyazawa, Y. Takei, and M. Kobayashi, Chem. Lett., 1984, 833.
3) Typical procedures for the synthesis of 3-cyclopentenones;
a) Cyclization of cis-1,4-dichloro-2-butene with methyl methylthiomethyl sulfoxide; K. Ogura, M. Yamashita, M. Suzuki, S. Furukawa, and G. Tsuchihashi, Bull. Chem. Soc. Jpn., 57, 1637 (1984);

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c) Jones oxidation of cyclopentenol; P. A. Grieco, J. Org. Chem., 37, 2363 (1972);

d) Thermolysis of vinyl cyclopropane; E. J. Corey and S. W. Walinsky, J. Am. Chem. Soc., 94, 8932 (1972).

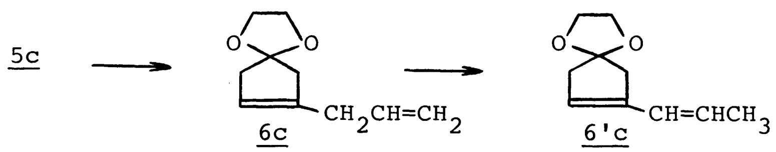
4) 2: bp 65.3-67.0 °C (4 mmHg); IR (neat) 1650 (C=O), 1550 cm^{-1}; ^1H-NMR ($CDCl_3$) δ2.33-2.97 (2H, m), 3.10-3.47 (2H, m), 6.17 (1H, d, J= 10.5 Hz), 7.45 (1H, d, J= 10.5 Hz); R. J. Batten, J. D. Coyle, and R. J. K. Taylor, Synthesis, 1980, 910.

5) 4: mp 216.5-218.2 °C (dec.); IR (KBr) 1335,1300 (SO_2, as) and 1145, 1110 cm^{-1} (SO_2, s); ^1H-NMR ($CDCl_3$) δ2.00-2.70 (7H, m containing s at 2.47), 3.00-3.40 (2H, m), 4.03 (4H, s), 4.57 (1H, dd, J= 10 and 6 Hz), 7.37 and 7.88 (4H, A_2B_2 m, J= 8 Hz); MS, m/e 346 (M^+), 347 (M^++ 1).

6) 3: mp 113.0 °C (dec.); IR (KBr) 1710 (C=O), 1310, 1140 cm^{-1} (SO_2); ^1H-NMR ($CDCl_3$) δ2.47 (3H, s), 2.70-3.10 (5H, m), 3.20-4.00 (1H, m), 4.34 (1H, br t, J= 5.0 Hz), 7.33 and 7.77 (4H, A_2B_2 m, J= 8 Hz); MS, m/e 270 (M^+), 271 (M^++ 1).

7) 5: ^1H-NMR ($CDCl_3$) of 5 (7-alkyl-1,4-dioxa-7-p-tolylsulfonyl-8-thiaspiro[4.5]-decane 8,8-dioxide) shows no peak at δ4.57 ppm (doublet of doublet; $-SO_2-C\underline{H}-SO_2-C_6H_4-CH_3$-p) corresponding to compound 4.

8) ^1H-NMR ($CDCl_3$) of cyclopentene 6 (7-alkyl-1,4-dioxaspiro[4.4]non-7-ene) shows a new peak at δ5.20-5.40 ppm (-C<u>H</u>=C-, multiplet); In the case of 5c (R= $CH_2-CH=CH_2$), allylic olefin isomerization of the resulting cyclopentene 6c was observed under these conditions to give isomer 6'c:



9) R. Sterzycki, Synthesis, 1977, 724.

10) 3-cyclopentenones (7): 7a (R= CH_3): IR (pentane) 1745 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$) δ1.80 (3H, br s), 2.70-3.00 (4H, m), 5.60-5.80 (1H, m); MS, m/e 96 (M^+). 7d (R= C_5H_{11}): IR (neat) 1745 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$) δ0.96 (3H, br t), 1.00-1.80 (6H, m), 2.00-2.30 (2H, m), 5.50-5.80 (1H, m); MS, m/e 152 (M^+). 7f (R= $C_6H_5CH_2CH_2$): IR (pentane) 1745 cm^{-1} (C=O); ^1H-NMR ($CDCl_3$) δ2.20-3.10 (8H, m), 5.70 (1H, m), 7.20 (5H, s); MS, m/e 186 (M^+).

11) 2-cyclopentenones (8): 8a (R= CH_3): Hendrickson et al. reported the synthesis of 3-methyl-2-cyclopentenone (8a); J. B. Hendrickson and P. S. Palumbo, J. Org. Chem., 50, 2110 (1985). 8d (R= C_5H_{11}): IR (neat) 1705 (C=O), 1615 cm^{-1}; ^1H-NMR ($CDCl_3$) δ0.90 (3H, br t, J= 7 Hz), 1.10-1.90 (6H, m), 2.20-2.70 (6H, m), 5.80-6.00 (1H, m); MS, m/e 152 (M^+). 8f (R= $C_6H_5CH_2CH_2$): IR ($CDCl_3$) 1700 (C=O), 1670 cm^{-1}; ^1H-NMR ($CDCl_3$) δ2.20-3.10 (8H, m), 5.93 (1H, m), 7.17 (5H, s); MS, m/e 186 (M^+).

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