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Prostanoids: LXXXVII.* Synthesis of 3-Hydroxy-2-phenylsulfonyl-2-cyclopentenone and Its Ethylene Acetal

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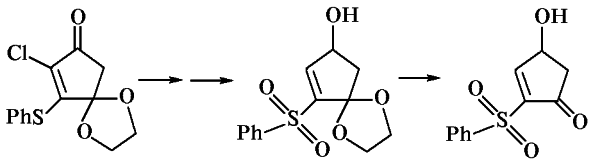
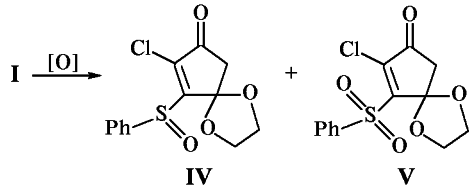
Abstract—By oxidation of 3-phenylmercapto-2-chloro-4,4-ethylenedioxycyclopet-2-en-1-one with H_2O_2 in AcOH (or with m-$ClC_6H_4CO_3H$ in CH_2Cl_2) was obtained 2-chloro-3-phenylsulfonyl-4,4-ethylenedioxycyclopent-2-en-1-one which on reduction with $NaBH_4$ or $LiAlH_4$ afforded respectively 3-hydroxy-2-phenylsulfonylcyclopent-2-en-1-one and its ethyleneketal.

We described formerly a convenient preparation of phenylmercaptocyclopentenone (**I**) from hexachlorocyclopentadiene [1]. The present paper reports on conversion of compound **I** into sulfones **II** and **III**. The latter are aimed to be used as the central cyclopentenone building blocks in designing prostaglandine structures along the scheme of the triple convergent coupling [2, 3]. This approach based on a one-pot addition of the α- and ω-chains of prostaglandine to appropriate cyclopentenone derivatives is among the well-known and efficient procedures of prostaglandine syntheses [4, 5].



I **II** **III**

The first approach suggested to convert **I** into the target compounds **II, III** by reduction of enone **I** oxo function with $LiAlH_4$ or $NaBH_4$ did not result in the desired products [1]. Therefore it was decided to start with oxidation of the phenylmercapto group into phenylsulfonic group hoping that in sulfone **V** the elimination of the vinyl chlorine atom activated by SO_2Ph group should be achieved by reduction with common reagents.



IV **V**

Several common reagents were tested in oxidation of sulfide **I**. Sulfoxide **IV** formed selectively when heating at reflux with 10 equiv of H_2O_2, but conversion of the initial compound **I** did not exceed here 25%. Only traces of sulfoxide were obtained with $Na_2WO_4 \cdot 2H_2O$ (TLC). We succeeded in selective preparation both of the desired sulfone **V** and the product of compound **I** incomplete oxidation, sulfoxide **IV**, applying an oxidative system H_2O_2–HOAc and varying the substrate to oxidant ratio and the reaction time. Sulfoxide **IV** is also fit for the use in syntheses because such sulfoxides can be brought into conjugate addition reaction with organometallic compounds [6, 7]. The structure of compounds **IV** and **V** was proved by IR and ^{13}C NMR spectra and on comparison of their R_f on Silufol plates (sulfoxides are known to be more polar than sulfones). The most characteristic signals in the ^{13}C NMR spectra of sulfoxide **IV** and sulfone **V** are those of C^3 at 165.2 and 156.8 ppm respectively.

The oxidation of sulfide **I** with *m*-$ClC_6H_4CO_3H$ afforded sulfone **V** in high yield.

In acetone solution dimethyldioxirane [8] under mild conditions oxidized sulfide **I** to the corresponding sulfone **V** in an almost quantitative yield (95%) (see table).

After development of an optimum procedure of sulfone **V** preparation we started looking for the method of its conversion into the target sulfones **II** and **III**. The reduction of sulfone **V** with $NaBH_4$ depending on reaction temperature and workup

* For preceding communication see [1].

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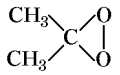
Oxidation of 3-phenylmercapto-2-chloro-4-ethylenedioxycyclopent-2-en-1-one (**I**) with various oxidants

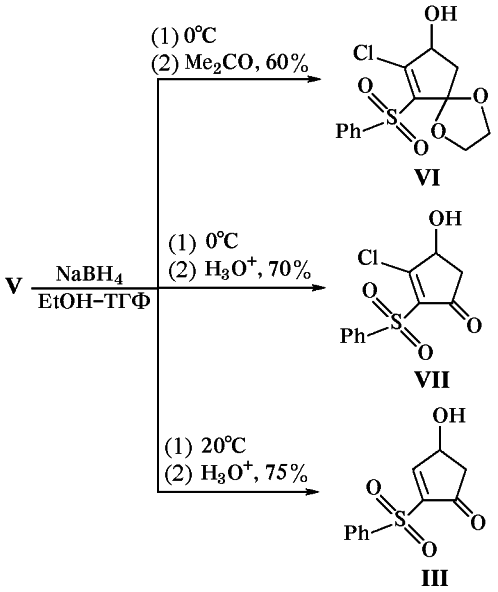
Oxidant–solvent	Substrate/oxidant, mol	Temperature, °C	Time, min (h)	Yield, % (compounds ratio[a] **IV : V**)
H_2O_2[b]–AcOH[c]	1 : 3	118	10	55 (1 : 0)
H_2O_2–AcOH	1 : 3	118	40	55 (9 : 1)
H_2O_2–AcOH	1 : 5	118	10	70 (3 : 2)
H_2O_2–AcOH	1 : 5	118	80	65 (2 : 3)
H_2O_2–AcOH	1 : 10	118	40	30 (0 : 1)
H_2O_2–AcOH	1 : 15	118	40	82 (0 : 1)
H_2O_2–Me_2CO	1 : 10	56	(6)	10[d] (1 : 0)
 (Me_2CO)	11 : 2	20	30	95 (0 : 1)
H_2O_2–THF, $Na_2WO_4.2H_2O$	1 : 4 : 0.1	65	(10)	20[d] (1 : 0)
$ClC_6H_4CO_3H$	1 : 3.3	20	90	90 (5 : 95)

[a] RSO/RSO_2 ratio was estimated from ^{13}C NMR spectra.
[b] 50% solution of H_2O_2.
[c] Glacial acetic acid.
[d] Substrate conversion 25%.

procedure provided three different sulfones **III, VI**, and **VII**. The reduction at 0°C followed by quenching of the reaction mixture with water or acetone afforded expected alcohol **VI**, and workup under acid conditions furnished ketoalcohol **VII**. Sulfone **III**, the product of simultaneous reduction, dechlorination, and removal of the dioxolane protection was obtained in 75% yield when the reaction was carried out at room temperature, and the excess of reductant was quenched with acid. Sulfone **V** did not undergo reduction with $LiAlH_4$ at 0°C, and at 20°C a mixture of alcohol **VI** and sulfone **II** was obtained in 2 : 3 ratio.

The structure of obtained sulfones **II, III, VI,** and **VII** is well confirmed by spectral data. Their IR spectra contain absorption bands of SO_2 (1300 cm^{-1}) and OH groups (3400 cm^{-1}), of C=C–C=O moiety (1720 cm^{-1}) (**III**), of a monosubstituted aromatic fragment (700, 760, 1500, 1590, 3080 cm^{-1}). The presence of a vinyl proton in sulfones **II** and **III** is evidenced by downfield signals in their ^1H NMR spectra at 6.2 and 6.11 ppm respectively, and also by doublets at 158.45 and 163.93 ppm in the corresponding ^{13}C NMR spectra.

Thus we developed convenient procedures for preparation of phenyl cyclopentenyl sulfones **II** and **III**, the key synthons for the planned approach to prostaglandine synthesis.



EXPERIMENTAL

IR spectra were recorded on spectrophotometeres UR-20 and Specord M-80 from samples as film or mull in mineral oil. ^1H and ^{13}C NMR spectra were registered on spectrometer Bruker AM-300 at operating frequencies 300.13 and 75.47 MHz respectively from solutions in $CDCl_3$. The solvent signals were

used as internal references (δ 7.27, δ_C 77.00 ppm). The mass spectra were measured on MKh-1306 device, ionizing electrons energy 20 and 70 eV, ionizing chamber temperature 75–100°C. The reaction progress was monitored by TLC on Silufol plates, eluent hexane–ethyl acetate. The spots were visualized with the use of anisaldehyde or alkaline solution of $KMnO_4$ [9].

Oxidation of sulfide I. (a) With H_2O_2 in AcOH. To a solution of 1.1 g (3.85 mmol) of sulfide **I** in 15 ml of AcOH was added 3.3 ml (58.4 mmol) of 50% solution of H_2O_2, and the reaction mixture was heated at reflux (the reaction conditions and products yield see table). The reaction mixture was evaporated, diluted with 15 ml of a saturated Na_2SO_3 solution, the products were extracted into $CHCl_3$ (3 × 30 ml). The combined organic extracts were washed in succession with saturated solutions of Na_2SO_3, $NaHCO_3$, and NaCl, dried over $MgSO_4$, and evaporated. Sulfone **V** was obtained by recrystallization of the residue from ethyl acetate. Sulfoxide **IV** was isolated by column chromatography on silica gel (eluent petroleum ether–ethyl acetate, 9 : 1) of the residue after evaporation of the mother liquor.

(b) With *m*-chloroperbenzoic acid. To a solution of 3.92 g (11.33 mmol) of 50% *m*-chloroperbenzoic acid in 15 ml of CH_2Cl_2 at 20°C was added dropwise 1.0 g (3.54 mmol) of sulfide **I** in 15 ml of CH_2Cl_2. After stirring for 6 h the reaction mixture was filtered, diluted with 15 ml of CH_2Cl_2, and washed with H_2O. The organic products from the water layer were extracted with 30 ml of CH_2Cl_2, and the combined organic solutions were washed with $NaHCO_3$ till neutral washings, dried over $MgSO_4$, and evaporated. The recrystallization from ethyl acetate afforded 0.8 g (72%) of sulfone **V**.

3-Phenylsulfinyl-2-chloro-4,4-ethylenedioxycyclopent-2-en-1-one (IV), mp 185–187°C (from ethylacetate). IR spectrum, cm^{-1}: 1728, 1584, 1216, 1148, 1024. ^1H NMR spectrum, δ, ppm: 2.89 s (2H, $2H^5$), 4.08 s (2H, CH_2O), 4.36 d (2H, CH_2O, *J* 6.98 Hz), 7.55 m (3H arom), 7.86 m (2H arom). ^{13}C NMR spectrum, δ, ppm: 48.15 (C^5), 66.78 (CH_2O), 66.95 (CH_2O), 110.89 (C^4), 125.68 (C_o), 129.43 (C_p), 131.91 (C_m), 137.84 (C^2), 141.91 (C^3), 163.43 (C_i), 192.31 (C^1). Found, %: C 52.41; H 3.83; Cl 12.08; O 20.74; S 10.94. $C_{13}H_{11}ClO_4S$. Calcd., %: C 52.27; H 3.71; Cl 11.87; O 21.42; S 10.73.

3-Phenylsulfonyl-2-chloro-4,4-ethylenedioxycyclopent-2-en-1-one (V), mp 165–166°C (from ethyl acetate). IR spectrum, cm^{-1}: 1012, 1084, 1192, 1320, 1600, 1736. ^1H NMR spectrum, δ, ppm: 2.86 s (2H, $2C^5H$), 4.09 t (2H, CH_2O, *J* 8.5 Hz), 4.44 t (2H, CH_2O, *J* 8.5 Hz), 7.71 t (2H, *J* 7.6 Hz, $2H_m$), 7.82 t (1H Hz, H_n, *J* 7.6), 8.02 t (2H, $2H_o$, *J* 7.6 Hz). ^{13}C NMR spectrum, δ, ppm: 47.68 (C^5), 66.35 ($2CH_2O$), 110.45 (C^4), 128.41 (C_o), 129.16 (C_m), 134.58 (C_p), 140.03 (C^2), 143.27 (C^3), 156.37 (C_i), 192.37 (C^1). Found, %: C 49.32; H 3.78; Cl 11.33; O 25.33; S 10.24. $C_{13}H_{11}ClO_5S$. Calculated, %: C 49.61; H 3.52; Cl 11.26; O 25.42; S 10.19.

Reaction of sulfone V with $NaBH_4$. (a) To a solution of 0.2 g (0.64 mmol) of sulfone **V** in ethanol–THF mixture (1 : 1 by volume) was added at 0°C 0.024 g (0.64 mmol) of $NaBH_4$. The reaction mixture was stirred for 20 min, and then treated as follows.

(1) To the reaction mixture was added 3 ml of acetone, the reaction products were extracted into $CHCl_3$ (3 × 10 ml), the combined organic solutions were washed with H_2O, dried with $MgSO_4$, evaporated, the residue was subjected to chromatography on SiO_2 (eluent petroleum ether–ethyl acetate, 7 : 3). We obtained 0.12 g (60%) of alcohol **VI**.

(2) To the reaction mixture was added 5 ml of 5% hydrochloric acid. The mixture was evaporated, the residue was diluted with 10 ml of H_2O, the reaction product was extracted into $CHCl_3$ (3 × 10 ml), the combined extracts were washed with H_2O, dried with $MgSO_4$, evaporated, and subjected to chromatography (eluent petroleum ether–ethyl acetate, 7 : 3). We obtained 0.12 g (70%) of ketoalcohol **VII**.

(b) To a solution of 0.2 g (0.64 mmol) of sulfone **V** in ethanol–THF mixture (1 : 1 by volume) was added at 20°C 0.024 g (0.64 mmol) of $NaBH_4$. The reaction mixture was stirred for 20 min, and then 10 ml of 5% hydrochloric acid was added, and the mixture was evaporated. The residue was diluted with 10 ml of H_2O, the reaction product was extracted into $CHCl_3$ (3 × 10 ml), the combined extracts were washed with H_2O, dried with $MgSO_4$, evaporated, and subjected to chromatography (eluent petroleum ether–ethyl acetate, 7 : 3). We obtained 0.12 g (75%) of alcohol **III**.

3-Phenylsulfonyl-2-chloro-4,4-ethylenedioxycyclopent-2-en-1-ol (VI). Colorless oily substance. IR spectrum, cm^{-1}: 1342, 1615, 3400. ^1H NMR spectrum, δ, ppm: 2.11 d.d (1H, H^{5A}, *J* 4 and 16 Hz), 2.6 d.d (1H, H^{5B}, *J* 4 and 16 Hz), 3.70–3.90 m (4H, $2CH_2O$), 4.60 br.s (1H, H^4), 7.10–7.3 m (5H arom). ^{13}C NMR spectrum, δ, ppm: 45.22 (C^5), 66.13 and 65.76 ($2CH_2O$), 70.96 (C^1), 115.20 (C^4), 146.88 (C^2), 130.14 (C^3), 128.01 (C_p), 129.09 (C_o), 129.95 (C_m), 132.19 (C_i). Found, %: C 49.74; H 4.53;

Cl 11.28; O 25.12; S 9.33. $C_{13}H_{13}ClO_5S$. Calculated, %: C 49.29; H 4.14; Cl 11.19; O 25.25; S 10.12.

4-Hydroxy-2-phenylsulfonyl-3-chlorocyclopent-2-en-1-ol (VII). mp 111–113°C. IR spectrum, cm^{-1}: 1344, 1584, 1733, 3400. ^1H NMR spectrum, δ, ppm: 2.23 m (2H, H^5), 4.39 m (1H, H^4), 7.50 m ($2H_o$), 7.57 m ($1H_p$), 7.96 ($2H_m$). ^{13}C NMR spectrum, δ, ppm: 45.22 (C^5), 78.59 (C^4), 129.10 (C_p), 130.39 (C_o), 133.92 (C_i), 134.82 (C_m), 148.02 (C^2), 176.95 (C^3), 195.92 (C^1). Found, %: C 48.22; H 3.17; Cl 12.95; O 24.18; S 11.48. $C_{11}H_9ClO_4S$. Calculated, %: C 48.45; H 3.33; Cl 13.00; S 11.76.

4-Hydroxy-2-phenylsulfonylcyclopent-2-en-1-ol (III). Yellow oily substance. IR spectrum, cm^{-1}: 1344, 1696, 1712, 3400. ^1H NMR spectrum, δ, ppm: 3.0 br.s (1H, OH), 3.15 m (2H, $2H^5$), 4.32 m (1H, H^4), 6.11 m (1H, H^3), 7.7 m ($2H_o$), 7.77 m ($1H_p$), 7.88 m ($2H_m$). ^{13}C NMR spectrum, δ, ppm: 30.73 (C^5), 65.35 (C^4), 128.91, 133.1, 134.23, 136.32 (C arom), 138.32 (C^2), 163.92 (C^3), 197.25 (C^1). Found, %: C 55.02; H 3.92; O 26.53; S 13.41. $C_{11}H_{10}O_4S$. Calculated, %: C 55.45; H 4.23; O 26.86; S 13.46.

Reaction of sulfone V with $LiAlH_4$. To a dispersion of 0.03 g (0.78 mmol) of $LiAlH_4$ in 3 ml of anhydrous ether at room temperature was added in argon flow dropwise 0.2 g (0.64 mmol) of sulfone **V** solution in 6 ml of anhydrous THF. The reaction mixture was stirred for 6 h at 60°C, cooled to 0°C, 3 ml of water was added, the reaction product was extracted into chloroform (3 × 10 ml). The combined organic solutions were washed with saturated solution of NaCl, dried over $MgSO_4$, and evaporated. The residue was subjected to chromatography (eluent petroleum ether–ethyl acetate, 7 : 3). We obtained 0.08 g (45%) of sulfone **VI** and 0.06 g (30%) of sulfone **II**.

3-Phenylsulfonyl-4,4-ethylenedioxycyclopent-2-en-1-ol (II). Yellow oily substance. IR spectrum, cm^{-1}: 1340, 1590, 3390. ^1H NMR spectrum, δ, ppm: 2.20 d.d (1H, $2H^{5A}$, *J* 15.4 and 6.3 Hz) and 2.72 d.d (1H, $2H^{5B}$, *J* 15.4 and 6.3 Hz), 3.91–4.32 m (5H, $2CH_2O$, OH), 4.60 m (1H, H^1), 6.17 m (1H, H^3) 7.01–7.23 m (5H arom). ^{13}C NMR spectrum, δ, ppm: 46.59 (C^5), 65.78 (CH_2O), 66.32 (CH_2O), 71.15 (C^1), 114.74 (C^4), 125.26, 127.37, 128.67, 135.46 (C arom), 142.01 (C^2), 158.45 (C^3). Found, %: C 55.42; H 5.25; O 27.84; S 11.49. $C_{13}H_{14}O_5S$. Calculated, %: C 55.31; H 5.00; O 28.34; S 11.36.

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REFERENCES

1. Ivanova, N.A., Khusainova, A.A., Shangiraeva, F.G., Akhmetvaleev, R.R., and Miftakhov, M.M., *Zh. Org. Khim.*, 2003, vol. 39, no. 10.
2. Donaldson R.E. and Fuchs P., *J. Am. Chem. Soc.*, 1981, vol. 103, p. 2108.
3. Saddler, J.C. and Fuchs, P.L., *J. Am. Chem. Soc.*, 1981, vol. 103, p. 2112.
4. Loots, M.J. and Schwartz, J., *Tetrahedron Lett.*, 1978, p. 4381.
5. Tsujiyama, H. and Yoshino, T., Okamoto, S., and Sato, F., *Tetrahedron Lett.*, 1990, p. vol. 31, p. 4481.
6. Mase, N., Watanabe, Y., and Toru, T., *J. Org. Chem.*, 1998, p. 3899.
7. Pozner, G. and Miura, K., Khal'ts, M., and Kogan, T., *Sovremennye napravleniya v organicheskom sinteze* (Modern Trends in Organic Chemistry), Moscow: Mir, 1986, p. 251.
8. Abdrakhmanova, A.R., Kabal'nova, N.N., Rol'nik, L.Z., and Yagofarova, G.G., *Bashk. Khim. Zh.*, 2000, p. 27.
9. Kirchner, J.G., *Thin-Layer Chromatography,* Perry, E.S., Ed., New York: Wiley, 1978, 2nd ed. Translated under the title *Tonkosloinaya khromatografiya*, Moscow: Mir, 1981, vol. 1, p. 616.