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REACTION OF THIOPHENOL WITH SOME ALIPHATIC EPOXYKETONES

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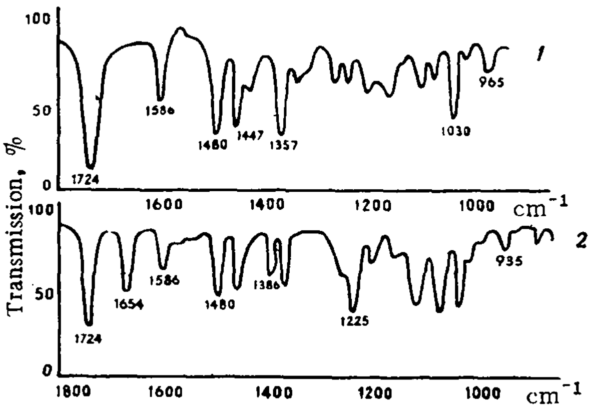
The reaction of thiophenol with 3, 4-epoxybutan-2-one, 3-methyl-3, 4-epoxybutan-2-one, and 3-methyl-3, 4-epoxy-pentan-2-one is investigated. It is found that when these epoxyketones react with thiophenol, oxygen ring opening occurs at the α carbon atom, to give α-phenylmercapto-β-hydroxyketones. Some reactions of the resultant compounds are investigated.

A previous paper [1] described reaction of benzylmercaptan with oxides derived from methylvinyl-, methylisopropenyl-, and methylisobutenyl ketones. It was shown that in the presence of active carbon and sodium thiophenate, benzylmercaptan smoothly adds to these epoxyketones, to give α-benzylmercapto-β-hydroxyketones, which can split off formaldehyde or acetaldehyde to give 3-benzylmercaptobutan-2-one.



IR spectra (0.1M solution in CCl_4, layer thickness 0.225 mm): 1) 3, 4-di(phenylmercapto) butan-2-one; 2) 3-phenylmercaptobut-3-en-2-one.

Reaction of epoxyketones with thiol compounds is a simple method of synthesizing difficultly accessible or wholly unknown organic sulfur compounds, containing several functional groups. Hence it was appropriate to investigate reaction of the above-mentioned epoxyketones with thiophenol.

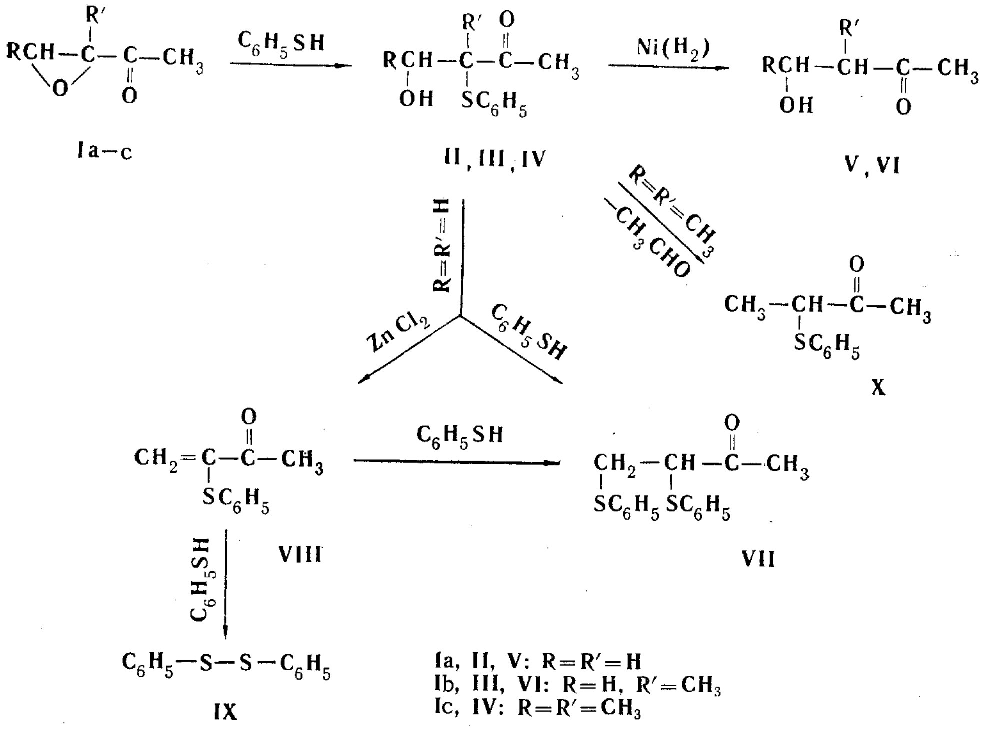
It was found that reaction of thiophenol with excess 3, 4-epoxybutan-2-one (Ia) gives a quantitative yield of 3-phenylmercapto-4-hydroxy-butan-2-one (II), the position of its thiol and hydroxyl groups being shown by its being desulfurized with Raney nickel to 4-hydroxybutan-2-one (V) [2]. The resultant phenylmercaptohydroxybutanone II gives 3, 4-di (phenylmercapto) butan-2-one (VII) when heated with thiophenol, while on dehydration using zinc chloride, it gives 3-phenylmercaptobut-3-en-2-one (VIII), identified by its IR spectrum, and by conversion back to VII by treatment with thiophenol.

In view of this latter reaction, it can be assumed that formation of 3, 4-di (phenylmercapto) butan-2-one (VII) by reaction of 3-phenylmercapto-4-hydroxybutan-2-one (II) with thiophenol involves dehydration of II to VIII, thiophenol then adding to the double bond of the latter, though direct reaction of thiophenol with the hydroxyl group of phenylmercaptohydroxybutanone is not excluded. 3-Phenylmercaptobut-3-en-2-one (VIII) unexpectedly reacts with thiophenol in the presence of sodium thiophenate. Diphenyldisulfide (IX) was isolated and identified as the main reaction product. No other products could be isolated, and close investigation was impossible due to considerable resin formation.

Reaction of 3-methyl-3, 4-epoxybutan-2-one (Ib) with thiophenol gives a high yield of 3-phenylmercapto-3-methyl-4-hydroxybutan-2-one (III) whose structure was proved by hydrogenolysis over Raney nickel to 4-hydroxy-3-methylbutan-2-one (VI), previously described in the literature [3].

Thiophenol adds quite vigorously to 3-methyl-3, 4-epoxypentan-2-one (Ic) in the presence of sulfuric acid, and from the products of this condensation under mild conditions, a high yield of 3-phenylmercapto-4-hydroxy-3-methylpentan-2-one (IV) was isolated. Its structure was established by scission to acetaldehyde and the previously reported [4] 3-phenylmercaptobutan-2-one (X). When the same reactants were brought together in the presence of sodium thiophenate, at 130° C, acetaldehyde and 3-phenylmercaptobutan-2-one (X) were isolated from among the products.

The IR spectrum of VIII (Fig., plot 2) has a medium intensity band with a maximum at 1654 cm^{-1}, due to C=C valence vibrations, and a weak band frequency 935 cm^{-1}. Evidently they arise through out-of-plane deformation vibrations of =CH which are shown by unsymmetrically disubstituted ethylenes [5]. In the spectra of compounds VII and VIII, bands at 1724 cm^{-1} belong to carbonyl group vibrations, while bands in the 1600–1450 cm^{-1} region belong to benzene ring vibrations.



Experimental

The starting epoxyketones were obtained by alkaline hydrogen peroxide oxidation of α, β unsaturated ketones: 3, 4-epoxybutan-2-one bp 44° C (27 mm), n_D^{20} 1.4226; 3-methyl-3, 4-epoxybutan-2-one bp 37.5° C (15 mm), n_D^{18} 1.4180: 3-methyl-3, 4-epoxypentap-2-one bp 92–93° C (120 mm), n_D^{20} 1.4192 [6–8]. CP thiophenol was used bp 168–169° C, n_D^{20} 1.5907.

3-Phenylmercapto-4-hydroxybutan-2-one (II). 60 g (0.7 mole) 3, 4-epoxybutan-2-one (Ia) and 12 g (0.11 mole) thiophenol were heated together at 50° C in a sealed tube for 40 hr. Excess oxide was distilled off at 15 mm. As the reaction product decomposed to ketosulfide VIII and water when vacuum-distilled, the remaining oxide was removed by subjecting the reaction products to a vacuum of 0.5 mm at 20°. Thin-layer chromatography on silica gel gave one spot, and it was analyzed crude. Yield of II 20,3 g (94.8% calculated on the thiophenol), straw-colored liquid with a characteristic odor, d_4^{20} 1.1760, n_D^{20} 1.5750. Found: C 61.12, 61.02; H 6.29, 6.34; S 16.55, 16.31; OH 8.66, 8.72%. MR_D 55.14. Calculated for $C_{10}H_{12}O_2S$: C 61.19; H 6.17; S 16.33; OH 8.98%. MR_D 54.38. Semicarbazone, white needles mp 121.5° (ex H_2O). Found: N 16.45, 16.40% . Calculated for $C_{11}H_{15}N_3O_2S$: N 16.59%.

Hydrogenolysis of 3-phenylmercapto-4-hydroxybutan-2-one (II). 4.5 g (0.023 mole) ketosulfide II, 50 ml dry dioxane, and 15 g type W-5 Raney Ni were placed together in a long-necked hydrogenation flask, and H_2 passed in until 350 ml/NTP has been absorbed. The catalyst was then filtered off, the solvent distilled off, and the residue vacuum-distilled, to give 1 g 4-hydroxybutan-2-one (V), bp 76–78° C (13 mm); phenylhydrazone mp 85° C (ex EtOH) (the literature [2] gives bp 73° C (11 mm), phenylhydrazone mp 86–87° C).

3, 4-Di(phenylmercapto) butan-2-one (VII). 2 g (0.01 mole) adduct II and 2 g (0.018 mole) thiophenol were heated together in a sealed tube at 170° C for 9 hr. On cooling, the contents of the tube crystallized. Yield 2.4 g 3, 4-di(phenylmercapto) butan-2-one (VII), white plates mp 82° C (ex MeOH-H_2O). Found: C 66.73, 66.51; H 5.85, 5.62; S 22.10, 22.40%. Calculated for $C_{16}H_{16}OS_2$: C 66.63; H 5.59; S 22.23%. The 2, 4-dinitrophenylhydrazone formed yellow crystals, mp 117° C (ex $CHCl_3$-MeOH). Found: N 11.73, 11.78%. Calculated for $C_{22}H_{20}N_4O_4S_2$: N 11.96%.

3-Phenylmercaptobut-3-ene-2-one (VIII). 2 g (0.01 mole) ketohydroxysulfide II and 0.02 g fused $ZnCl_2$ were heated together in a sealed tube at 130° C for 8 hr, the products extracted with ether, the ether extracts thrice washed with water, dried over $MgSO_4$, the ether evaporated off, and the residue recrystallized from MeOH to give 1.2 g VIII, white crystals mp 77.5° C. Found: C 67.26, 67.14; H 9.51, 9.50; S 17.99, 17.80%, Calculated for $C_{10}H_{10}OS$: C 67.38; H 9.43; S 17.98%.

Action of thiophenol on the unsaturated sulfide VIII

a) 1.16 g (6.5 mmole) ketosulfide VIII and 0.72 g (6.5 mmole) thiophenol were heated together at 150° for 6 hr. Recrystallization from MeOH gave 0.87 g (47.3%) 3, 4-di (phenylmercapto) butan-2-one (VII), mp 82°. Found: S 22.13, 21.87%. Calculated for $C_{16}H_{16}OS_2$: S 22.23%.

b) 0.01 g sodium metal was first dissolved in 1.3 g (12 mmole) thiophenol, 2 g (11 mmole) thiophenol, 2 g (11 mmole) ketosulfide VIII added, and the whole heated at 160° C for 6 hr. On cooling the products crystallized almost completely. Recrystallization from MeOH gave 0.73 g (29.8%) diphenyl disulfide XI, mp 61°C. The literature [9] gives mp 61° C. Found: S 29.45, 29.52%. Calculated for $C_{12}H_{10}S_2$: S 29.37%.

3-Phenylmercapto-4-hydroxy-3-methylbutan-2-one (III). 14 g (0.14 mole) 3-methyl-3, 4-epoxybutan-2-one (Ib) and 17 g (0.15 mole) thiophenol were heated together at 120° C for 16 hr, then the reaction products vacuum-distilled to give 25 g (81%) ketohydrosulfide III, a colorless viscous liquid with a characteristic odor. Bp 104° (0.025 mm), d_4^{20} 1.1500, n_D^{20} 1.5630. Found: C 62.74, 62.57; H 6.69, 6.63; S 15.35, 15.41; OH 8.10, 8.03%; MR_D 59.39. Calculated for $C_{11}H_{14}O_2S$: C 62.82; H 6.71; S 15.24; OH 8.08%; OH 8.10, 8.03%; MR_D 59.39. Calculated for $C_{11}H_{14}O_2S$: C 62.82; H 6.71; S 15.24; OH 8.08%; MR_D 59.00. Semicarbazone mp 149° (ex H_2O). Found: N 15.51, 15.56%. Calculated for $C_{12}H_{17}N_3O_3S$: N 15.72%

Hydrogenolysis of ketohydroxysulfide (III). 4 g (0.19 mole) III, 20 g Raney Ni, and 40 g dry dioxane were placed together in a long-necked hydrogenation flask and shaken at 50° in H_2 until 330 ml of the latter was absorbed. The products were worked up in the usual way to give 1.4 g 4-hydroxy-3-methylbutan-2-one (VI), bp 90–92° C (15 mm), n^{20} 1.4352; the literature [3] gives: bp 80° C (10 mm), n^{20} 1.4340.

3-Phenylmercapto-4-hydroxy-3-methylpentan-2-one (IV). A mixture of 5 g (0.044 mole) epoxyketone Ic and 5 g (0.045 mole) thiophenol, cooled by circulating water, was vigorously stirred and conc. H_2SO_4 dropped in, when the temperature rapidly rose to 70° C, after which it was held at 30–32° C. To bring the reaction to completion, the mixture was heated for 30 min at 32–34° C, shaken with K_2CO_3 solution, and extracted with ether. The ether extracts were washed with water, the ether distilled off under a slight vacuum, the pressure then reduced to 0.5 mm, and the residue held for 4 hr at 30° C to remove traces of starting materials. Yield 8.3 g (84.4%) of adduct IV, as a very viscous yellowish liquid with a characteristic odor. On vacuum-distillation the adduct decomposed with separation of acetaldehyde. d_4^{20} 1.1257, n_D^{20} 1.5593. Found: C 64.18, 64.14; H 7.39, 7.33; S 14.47, 14.35; OH 7.52, 7.79%; MR_D 64.36. Calculated for $C_{12}H_{16}O_2S$: C 64.28; H 7.14; S 14.29; OH 7.58%; MR_D 63.62.

Scission of ketohydroxysulfide IV. 4.06 g (0.018 mole) IV was heated at 160° C for 40 min. The acetaldehyde formed was trapped in a saturated solution of 2, 4-dinitrophenylhydrazine hydrochloride in MeOH, to give 3.7 g (90%) of the 2, 4-dinitrophenylhydrazone of acetaldehyde, indicating the clear-cut nature of the addition reaction. After distilling off the acetaldehyde, the residue was vacuum-distilled, to give 2.51 g (77%) 3-phenylmercaptobutan-2-one (X), bp 130–133° C (13 mm), n_D^{20} 1.5559; the literature [4] gives bp 132–133° C (13 mm), n_D^{20} 1.556

3-Phenylmercaptobutan-2-one (X). 0.02 g Na metal was first dissolved in 13 g (0.12 mole) thiophenol, then mixed with 13 g (0.11 mole) epoxyketone Ic, and the whole heated in a sealed tube at 130° C for 70 hr. 4.3 g acetaldehyde was distilled off from the mixture, and it was identified as the 2, 4-dinitrophenylhydrazone mp 168° C [10]. After vacuum-distilling off the acetaldehyde, 19 g (89.6% on the ketohydroxide) IX was isolated as described in the previous experiment, in the form of a pale yellow liquid with a characteristic odor. Bp. 133° C (13 mm), d_4^{20} 1.0870; n_D^{20} 1.5559. Found: S 17.63, 17.61%; MR_D 53.30. Calculated for $C_{10}H_{12}OS$: S 17.79%; MR_D 52.86.

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