The Stereochemistry of the 1,2 Elimination of β-Hydroxy Sulfinamides to Form Olefins

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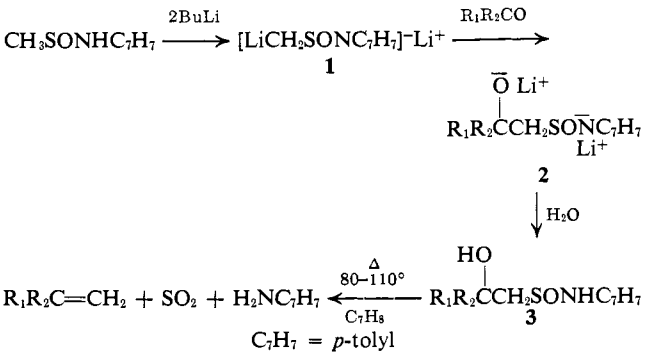
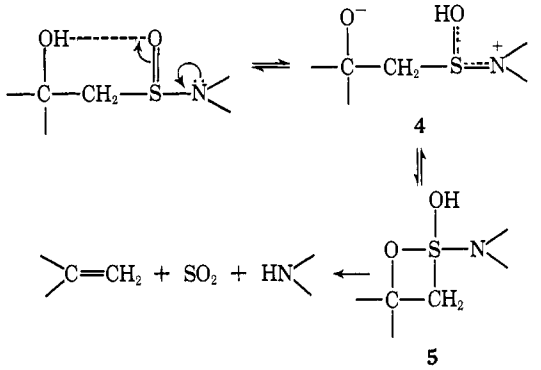
Abstract: The thermal decomposition of β-hydroxy sulfinamides to produce olefins has been shown to occur stereospecifically by a *cis*-elimination pathway.

We have recently reported a new synthesis of olefins starting from aldehydes or ketones and carbanions derived by α deprotonation of sulfinamides by the two-step sequence illustrated by the following equations.[1]

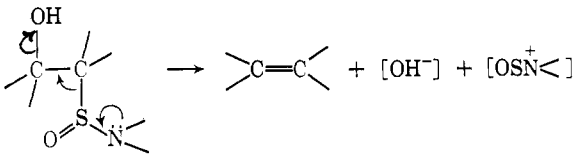


The intermediate anionic adducts (**2** or the corresponding O-monoanions in the case of monolithio reagents such as $LiCH_2SON(CH_3)_2$) are stable and do not tend to undergo olefin-forming elimination. In contrast the neutral β-hydroxy sulfinamides **3** are readily decomposed by heating to 80–110° in dry benzene or toluene to give olefin, amine, and sulfur dioxide. Our working hypothesis[1] in regard to the mechanism of this new route to olefins has been that the elimination of amine and sulfur dioxide from a β-hydroxy sulfinamide occurs *via* a dipolar ion **4** which can cyclize to form an intermediate **5** capable of 1,2 cycloelimination to give



olefin. The dipolar ion **4**, whose formation ought to be relatively favorable because of the enhancement of basicity of the sulfinyl function by nitrogen, is in certain respects analogous to the familiar phosphonium-alkoxide dipolar ion intermediate of the Wittig reaction.

This cycloelimination mechanism implies that there should be *cis* elimination in the olefin-forming step. Reasonable alternative mechanisms can be devised, however, which deserve serious consideration; for example, the elimination might proceed by a process in which there is *no* bonding between oxygen and sulfur in the transition state for olefin formation with the two leaving groups *trans* to one another.



This paper reports some experimental results which are relevant to the mechanistic problem and which, in particular, argue against the *trans*-elimination pathways.

In order to determine the preferred stereochemistry of olefin formation from β-hydroxy sulfinamides, a case was chosen in which *cis*- and *trans*-elimination routes would be structurally possible and also distinguishable given a knowledge of the geometries of the starting β-hydroxy sulfinamide and the olefinic product. *trans*-2-Hydroxycyclododecanesulfinanilide, the actual test substrate, might in principle afford *cis*-cyclododecene by a *trans* pathway or *trans*-cyclododecene by a *cis* elimination. These olefins are both known, are readily distinguishable by standard procedures and are not interconvertible under the conditions required for decomposition of β-hydroxy sulfinamides. In addition they are of comparable thermodynamic stability ($\Delta\Delta F$ at 373.6°K = 0.49 kcal/mol).[2] The stereospecific synthesis of *trans*-2-hydroxycyclododecanesulfinanilide (**11**) was accomplished starting from *cis*-cyclododecene by the route outlined in Figure 1, which leaves no doubt as to stereochemistry.

Thermal decomposition of the *trans*-β-hydroxy sulfinanilide **11**, either in benzene at 80–85° or neat at 150°, afforded stereospecifically *trans*-cyclododecene in high yield. It is clear, therefore, that the *cis-elimination pathway dominates.*

Consonant with this finding is the observation that *trans*-2-hydroxycyclohexylsulfinanilide (**12**) which was synthesized from *trans*-2-mercaptocyclohexanol by a route analogous to that used for **11** (Figure 1), is quite stable thermally under conditions which cause the complete decomposition of **11** and other β-hydroxy sulfinanilides to olefins. In this instance *cis* elimination is unfavorable because it would necessitate the

(1) (a) E. J. Corey and T. Durst, *J. Am. Chem. Soc.*, **88**, 5656 (1966); (b) E. J. Corey and T. Durst, *ibid.*, **90**, 5548 (1968); (c) E. J. Corey, *Pure Appl. Chem.*, **14**, 19 (1967).

(2) A. C. Cope, P. T. Moore, and W. R. Moore, *J. Am. Chem. Soc.*, **81**, 3153 (1959).

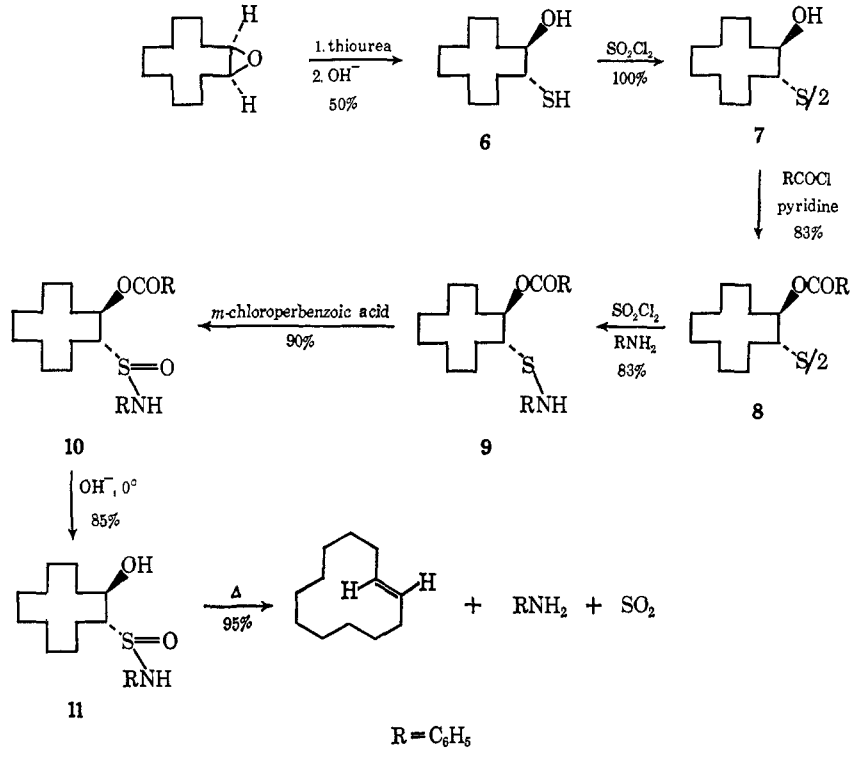
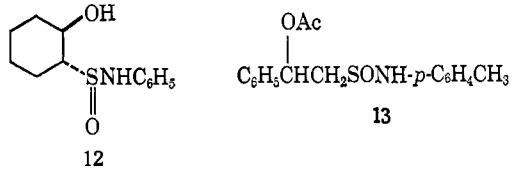


Figure 1.

formation of *trans*-cyclohexene, presently unknown and doubtless extremely unstable. The thermal stability of **12** indicates that the *trans*-elimination pathway is unfavorable even though it would lead to the stable *cis*-cyclohexene.

Finally, it has been observed that the acetylation of β-hydroxy sulfinamides stabilizes these substances against thermal decomposition to olefins. For example, the β-acetoxy sulfinamide **13**, resists decomposition under conditions which convert the corresponding β-hydroxy sulfinamide to styrene in good yield.



From the present study it would appear that the decomposition of β-hydroxy sulfinamides to olefins is strictly a *cis*-elimination process and that structures such as **4** and **5** are reasonable reaction intermediates. A similar mechanism may obtain for the elimination of β-hydroxy phosphonamides to form olefins stereospecifically.[3]

Experimental Section

Melting points were determined using a Büchi apparatus with capillary tubes and are corrected. Infrared spectra were taken using a Perkin-Elmer Model 137 Infracord and nmr data were obtained using a Varian Associates Model A-60 spectrometer. Nmr shifts are expressed in parts per million downfield from internal tetramethylsilane. Microanalyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark, and A. Bernhardt, Mulheim, Germany.

Tetrahydrofuran was purified just prior to use by distillation from lithium aluminum hydride. Alkyllithium reagents were commercial products of the Foote Mineral Co.

trans-**2-Mercaptocyclododecanol (6).** *cis*-Cyclododecene, prepared by diimide reduction of *trans,trans,cis*-1,5,9-cyclododecatriene,[4] was converted to the corresponding epoxide by reaction with a 1.3-fold excess of peracetic acid (40% solution in acetic acid buffered with sodium acetate) in methylene chloride. The solid epoxide (8.0 g), purified by distillation at 76–81° (0.9 mm), was treated with thiourea (4.0 g) in water (17 ml)–ethanol (10 ml)–dioxane (20 ml)–sulfuric acid (1.5 ml, 36 *N*) mixture for 3 hr at 25°. The precipitate of colorless thiouronium sulfate salt (9.8 g) was washed thoroughly with ether and then acetone. The hydrolysis of this salt to **6** was carried out on an 11.2-g scale by addition over a 10-min period to a solution of 20 g of sodium hydroxide in 30 ml of water and subsequent stirring for 1 hr. The reaction mixture was poured into a solution of 40 ml of 12 *N* hydrochloric acid, 200 ml of water, and 100 ml of ether. The ether layer was separated and the aqueous phase extracted once more with ether. The combined ether extracts were dried, and the solvent was evaporated. The oily solid (6.12 g) was recrystallized from cold pentane to give 5.72 g (73%) of *trans*-2-mercaptocyclododecanol (**6**) as colorless granules, mp 60–62°. The infrared spectrum showed $\lambda_{max}^{CCl_4}$ at 2.82 (m), 9.30 (m), and 9.92 (m) μ. The nmr spectrum (CCl_4) showed a singlet at 1.22 ppm (S*H*, 1 H) and multiplets at 1.2–2.1 (methylene and methine protons, 20 H), 2.6–3.1 (C*H*SH and O*H*, 2 H), and 3.4–3.8 ppm (C*H*OH, 1 H).

Anal. Calcd for $C_{12}H_{24}OS$: C, 66.63; H, 11.18; S, 14.80. Found: C, 66.97; H, 10.87; S, 14.99.

trans-**2-Hydroxycyclododecyl Disulfide (7).** A solution of 1.28 g (9.5 mmol) of sulfuryl chloride in 10 ml of methylene chloride was added dropwise to 4.11 g (19 mmol) of 2-mercaptocyclododecanol in 40 ml of methylene chloride. Evolution of sulfur dioxide occurred immediately. The reaction mixture was stirred for 10 min at room temperature then filtered from a small amount of solid. Evaporation of the solvent yielded 4.08 g (99%) of a colorless solid which was recrystallized from acetone to give the disulfide **7** as colorless needles, mp 136–138°. The infrared spectrum showed $\lambda_{max}^{CCl_4}$ at 2.80 (m) and 9.30 (m) μ. The nmr spectrum ($CDCl_3$) showed multiplets at 1.2–2.0 (20 H), 2.3–2.6 (O*H* 1 H), 2.8–3.2 (C*H*S, 1 H), and 3.7–4.0 ppm (C*H*OH).

(3) E. J. Corey and G. T. Kwiatkowski, *J. Amer. Chem. Soc.*, 88, 5652, 5653 (1966).

(4) M. Ohno and M. Okamoto, *Tetrahedron Letters*, 2423 (1964). We thank these authors for a detailed experimental procedure and for spectra of *cis*-cyclododecene.

Anal. Calcd for $C_{24}H_{46}O_2S_2$: C, 66.94; H, 10.77; S, 14.86. Found: C, 67.19; H, 10.79; S, 15.04.

trans-**2-Benzoyloxycyclododecyl Disulfide (8).** Benzoyl chloride (750 mg, 5.35 mmol) in 10 ml of dry pyridine was added in one portion to a −20° solution of 1.035 g (2.47 mmol) of disulfide **7** in 20 ml of pyridine. The reaction mixture was kept at 0° for 24 hr, diluted with water, and set aside for a further 30 min. Extraction with ether followed by drying of the ether extracts and evaporation of the solvent yielded a yellow oil which when dissolved in 10 ml of 1:1 ether–pentane and cooled to −20° deposited 1.27 g (83%) of *trans*-2-benzoyloxycyclododecyl disulfide. Recrystallization from methylene–chloride pentane gave a colorless solid, mp 146–150°. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ at 5.83 (s), 7.86 (vs), and 8.96 (s) μ. The nmr spectrum showed multiplets at 1.1–2.5 (20 H), 2.9–3.4 (C*H*S), 5.3–5.7 (C*H*O, 1 H), 7.2–7.6 (*para* and *meta* aromatic, 3 H), and 7.9–8.2 ppm (*ortho* aromatic, 2 H).

Anal. Calcd for $C_{38}H_{54}O_4S_2$: C, 71.44; H, 8.52; S, 10.02. Found: C, 70.64; H, 8.45; S, 10.61.

trans-**2-Benzoyloxycyclododecanesulfinanilide (10).** To a solution of 614 mg (1.0 mmol) of *trans*-2-benzoyloxycyclododecyl disulfide (**8**) in 10 ml of methylene chloride was added dropwise 150 mg (1.1 mmol) of sulfuryl chloride. The yellow reaction mixture was allowed to stand at −20° for 2 hr after which time the solvent was evaporated at 20° (1 mm). The yellow oil which was obtained was immediately redissolved in 5 ml of methylene chloride and added quickly to a solution of 465 mg (5.0 mmol) of aniline in 10 ml of methylene chloride. A colorless precipitate formed immediately after the two solutions were mixed. The reaction mixture was stirred for 30 min, diluted with water, and extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated yielding a yellow gum. Purification by preparative thin layer chromatography using 4:3 ligroin–chloroform as eluent gave 685 mg (83%) of *trans*-2-benzoyloxycyclododecanesulfenanilide (**9**) as a pale yellow oil. No attempt was made to induce crystallization since the compound was immediately oxidized to the corresponding sulfinamide **10**. The infrared spectrum of the sulfenamide **9** showed $\lambda_{max}^{CHCl_3}$ at 2.95 (w), 5.83 (s), 7.85 (vs), and 8.96 (s) μ. Nmr absorption occurred at 1.1–2.2 (20 H), 2.6–3.0 (C*H*S, 1 H), 4.93 (N*H*, singlet, 1 H), 5.2–5.6 (C*H*O, 1H), and 6.5–8.2 ppm (aromatic, 10 H).

To a solution of 680 mg (1.65 mmol) of *trans*-2-benzoyloxycyclododecanesulfenanilide in 15 ml of methylene chloride at 0° was added dropwise a solution of 300 mg (1.8 mmol) of *m*-chloroperbenzoic acid. After stirring for 10 min at 0° the brown reaction mixture was poured into a 5% sodium hydroxide solution. The aqueous phase was extracted two times with 25 ml of methylene chloride. The combined organic extracts were dried, and the solvent was evaporated yielding a reddish gum. Addition of 10 ml of 1:1 ether–pentane resulted in the formation of 636 mg (90%) of *trans*-2-benzoyloxycyclododecanesulfinanilide as a tan solid. Recrystallization from methylene chloride–pentane gave colorless granules, mp 132–139° dec. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ at 2.98 (m), 5.80 (s), 7.86 (vs), 9.00 (s), 9.35 (s), and 10.6 (m) μ. The nmr spectrum showed multiplets at 1.1–2.6 (20 H), 3.2–3.7 (C*H*S, 1 H), 5.5–5.9 (C*H*O, 1 H), and 6.6–8.2 ppm (10 H).

Anal. Calcd for $C_{25}H_{33}O_3NS$: C, 70.23; H, 7.78; S, 7.45. Found: C, 70.22; H, 7.61; S, 7.40.

trans-**2-Hydroxycyclododecanesulfinanilide (11).** A solution of 245 mg (0.57 mmol) of *trans*-2-benzoyloxycyclododecanesulfinanilide (**10**) in 20 ml of 1:1 ethanol–dioxane was cooled to 0° and treated with 3 ml of *N* sodium hydroxide and kept at 0° for 15 hr. The reaction mixture was diluted with 50 ml of water and extracted with three portions of 25 ml of methylene chloride. The combined organic extracts were dried, and the solvent was evaporated. The crude product was triturated with pentane to yield 157 mg (85%) of a tan solid. Recrystallization from methylene chloride–pentane gave *trans*-2-hydroxycyclododecanesulfinanilide as colorless needles, mp 133–139°. The infrared spectrum ($CHCl_3$) showed broad absorption at 3.0, 9.6, and 11.5 μ. The nmr spectrum ($CDCl_3$) showed multiplets at 1.2–1.9 (20 H), 2.9–3.2 (C*H*S, 1 H), 4.2–4.5 (C*H*O, 1 H), and 6.9–7.3 ppm (5 H).

Anal. Calcd for $C_{18}H_{29}NO_2S$: C, 66.84; H, 9.04; S, 9.89. Found: C, 66.56; H, 9.07; S, 10.02.

Pyrolysis of *trans*-2-Hydroxycyclododecanesulfinanilide. A. In Benzene. A benzene solution of 10.7 mg of *trans*-2-hydroxycyclododecanesulfinanilide (**11**) was heated in a sealed tube at 80–85° for 12 hr. Analysis of the reaction mixture by vapor phase chromatography (vpc) (10 ft, 25% TCEP on Chromosorb, 100°, 30 psi) showed the presence of only one product whose retention time (25.1 min) was identical with that of *trans*-cyclododecene (the retention time of *cis*-cyclododecene under identical conditions was 30.1 min). The analytical yield of *trans*-cyclododecene was greater than 95%.

B. Neat at 150°. *trans*-2-Hydroxycyclododecanesulfinanilide (33.2 mg) was heated neat under nitrogen at 150° for 10 min. The dark oil which had formed was dissolved in ether and washed twice with 10 ml of 1 *N* hydrochloric acid. The ether layer was dried and the solvent evaporated yielding 12.6 mg (74%) of *trans*-cyclododecene. The infrared spectrum (CCl_4) was identical with that of an authentic sample.

trans-**2-Benzoyloxycyclohexyl Disulfide.** To a solution of 1.05 g (8.0 mmol) of *trans*-2-mercaptocyclohexanol[5] in 20 ml of methylene chloride was added dropwise 540 mg (4.0 mmol) of sulfuryl chloride. The reaction mixture was allowed to stand at room temperature for 5 min. Evaporation of the solvent yielded *trans*-2-hydroxycyclohexyl disulfide as a colorless viscous oil which was sufficiently pure for the next reaction.

The crude disulfide was dissolved in 10 ml of dry pyridine, cooled to 0°, and allowed to react with 1.12 g (8.0 mmol) of benzoyl chloride for 12 hr. The reaction mixture was diluted with water and allowed to stand at room temperature for 30 min. The usual work-up gave a yellowish oil which upon addition of 10 ml of 1:1 ether–pentane yielded 655 mg (51%) of *trans*-2-benzoyloxycyclohexyl disulfide as colorless needles, mp 144–146°. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ at 5.83 (s) and 7.85 (s) μ. The nmr spectrum ($CDCl_3$) showed multiplets at 1.2–2.5 (8 H), 2.7–3.1 (1 H), 4.8–5.2 (1 H), 7.2–7.6 (3 H), and 7.9–8.2 ppm (2 H).

Anal. Calcd for $C_{26}H_{30}O_4S_2$: C, 66.37; H, 6.43; S, 13.61. Found: C, 66.22; H, 6.45; S, 13.83.

trans-**2-Benzoyloxycyclohexanesulfinamide.** To a solution of 400 mg (0.85 mmol) of *trans*-2-benzoyloxycyclohexyl disulfide and 102 mg (1.7 mmol) of glacial acetic acid in 10 ml of methylene chloride at −10° was added dropwise 270 mg (1.7 mmol) of sulfuryl chloride. The pale yellow reaction mixture was allowed to stand at room temperature for 1 hr. The solvent was evaporated yielding a yellowish oil which was not further purified but dissolved in 5 ml of methylene chloride and added directly to a solution of 318 mg (3.40 mmol) of aniline in 10 ml of methylene chloride. The reaction mixture was stirred for 30 min and then washed with water. The methylene chloride layer was dried, and the solvent was evaporated yielding a yellow oil. Addition of 5 ml of 1:1 ether–pentane gave 183 mg (33%) of *trans*-2-benzoyloxycyclohexanesulfinamide as colorless needles, mp 110–125°. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ at 3.0 (m), 5.80 (s), and 7.88 (vs) μ. The nmr spectrum ($CDCl_3$) showed broad absorption at 1.2–2.5 (8 H), 2.9–3.4 (1 H), 5.2–5.6 (1 H), and 6.9–8.2 ppm (10 H).

Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.46; H, 6.16; S, 9.32. Found: C, 66.01; H, 6.05; S, 9.11.

trans-**2-Hydroxycyclohexanesulfinamide.** *trans*-2-Benzoyloxycyclohexanesulfinamide (70 mg, 0.21 mmol) and 0.1 g of potassium hydroxide were dissolved in 2 ml of methanol. The solution was refluxed for 30 min. Upon cooling 31 mg (67%) of *trans*-2-hydroxycyclohexanesulfinamide precipitated. Recrystallization from chloroform–ligroin (bp 66–75°) gave colorless granules, mp 147–151°. The infrared spectrum showed λ_{max}^{Kaydol} at 3.15 (m), 9.6–9.8 (s), and 11.3 (m) μ.

Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.24; H, 7.16; S, 13.38. Found: C, 59.68; H, 6.93; S, 13.38.

Pyrolysis of *trans*-2-Hydroxycyclohexanesulfinamide. A solution of 75.2 mg of *trans*-2-hydroxycyclohexanesulfinamide in 10 ml of benzene was refluxed overnight. Vpc analysis of the product showed the absence of cyclohexene. On cooling of the reaction mixture *trans*-2-hydroxycyclohexanesulfinamide crystallized and was recovered (yield 67 mg, 90%). When *trans*-2-hydroxycyclohexanesulfinamide was heated neat to 175° the melt became black but no gas evolution was observed.

Acetylation of β-Hydroxy-β-phenylethanesulfin-*p*-toluidide. To a solution of 0.04 ml (0.37 mmol) of acetic anhydride in 5 ml of pyridine at 0° was added 102 mg of β-hydroxy-β-phenylethanesulfin-*p*-toluidide. The reaction mixture was kept at 0° for 24 hr. Dilution with water caused precipitation of 78 mg (70%) of the β-acetoxy sulfinamide **13** as colorless plates, mp 159–164°. The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ at 3.10 (m), 5.70 (s), and 8.6 (s) μ.

Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 66.34; H, 6.04; S, 10.08. Found: C, 63.75; H, 6.05; S, 9.89.

Pyrolysis of the β-acetoxy sulfinamide **13** in refluxing dry toluene for 5 hr gave no styrene as determined by vpc analysis of the reaction mixture.

(5) F. G. Bordwell and H. M. Andersen, *J. Am. Chem. Soc.*, 75, 4959 (1953).