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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY, LAFAYETTE, IND.]

The Stereochemistry of the Nucleophilic Addition of *p*-Toluenethiol to 1-*p*-Tolylsulfonyl-cyclohexene[1]

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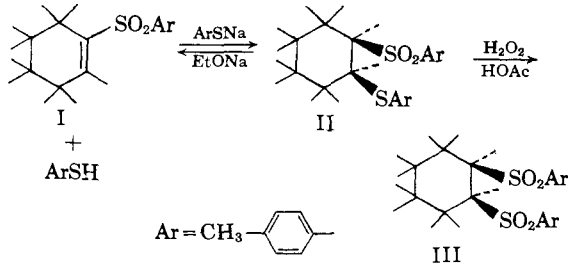
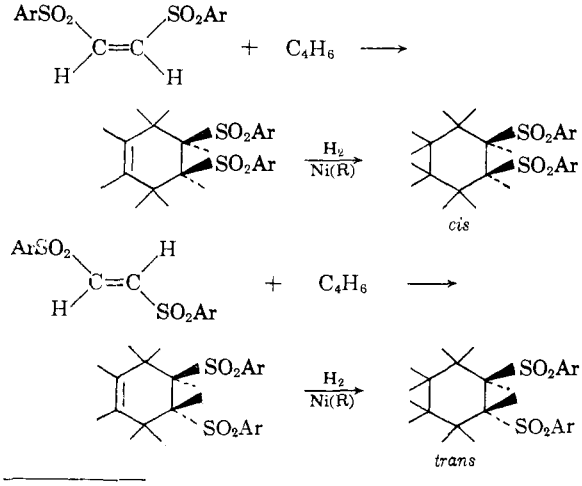
p-Toluenethiol adds to 1-*p*-tolylsulfonyl-cyclohexene, under mildly basic conditions, in a *trans* manner giving *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane. The stereochemistry of the adduct was confirmed by independent synthesis and supported by n.m.r. spectra. A mechanism for the addition is proposed and evidence presented to support it.

Having demonstrated[2-4] that thiols under basic conditions add to acetylenes in a *trans* manner, we undertook the study of the stereochemistry of like additions to olefins. 1-*p*-Tolylsulfonyl-cyclohexene (I)[5] was selected for initial study because the double bond is activated and the system lends itself to a facile structure proof. The adduct II from the addition of alcoholic sodium *p*-toluenethiolate to the olefin I was oxidized to its disulfone III. Both the *cis* and *trans* isomers of 1,2-bis-(*p*-tolylsulfonyl)-cyclohexane (III) were independently synthesized from the known[6,7] *cis*- and *trans*-1,2-*bis*-*p*-tolylsulfonylethenes.

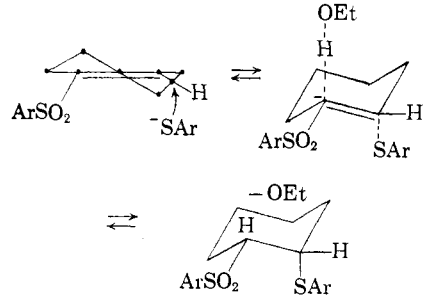




The independently prepared *trans*-disulfone was different from III, while the independently prepared *cis*-disulfone was shown to be identical with III, thus establishing that the nucleophilic addition had proceeded in a *trans* manner. The assignment of a *cis* configuration to II is further supported by n.m.r. spectra; *vide infra*.

Under the conditions of the reaction (0.1 molar equivalent of base) the addition of the nucleophile to the olefin was found to be reversible; with a full equivalent of base the adduct dissociates almost completely to olefin and thiolate. However, regardless of the reaction time, only the *cis* isomer was found.

It is well established[8,9] that for cyclohexane compounds substituted in the 1,2-positions the *trans* isomer is thermodynamically more stable. Therefore, the stereoselective addition leading *exclusively* to the less stable isomer can best be explained by a reaction mechanism involving a virtually concerted process.



Nucleophilic attack *via* the least hindered path corresponds to the axial direction[10a-c] in the transition state. If it is assumed that the bonds about the carbon atom developing a partial negative charge become tetrahedral,[11a-c] and that

(1) Presented at the 17th National Organic Chemistry Symposium of the American Chemical Society, June 29, 1961, Bloomington, Ind.

(2) W. E. Truce, J. A. Simms and M. M. Boudakian, *J. Am. Chem. Soc.*, **78**, 695 (1956).

(3) W. E. Truce and J. A. Simms, *ibid.*, **78**, 2756 (1956).

(4) W. E. Truce and R. F. Heine, *ibid.*, **81**, 592 (1959).

(5) F. G. Bordwell and R. J. Kern, *ibid.*, **77**, 1141 (1955).

(6) W. E. Truce and R. J. McManimie, *ibid.*, **76**, 5745 (1954).

(7) W. E. Truce, *et al.*, *ibid.*, **78**, 2743 (1956).

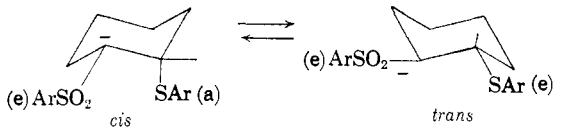
(8) W. G. Dauben and K. S. Pitzer in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 19.

(9) *cis*-2-(Phenylsulfonyl)-methylcyclohexane was completely isomerized to its *trans* isomer by heating in a basic medium; F. G. Bordwell and W. A. Hewitt, *J. Am. Chem. Soc.*, **79**, 3493 (1957).

(10) This is analogous to the proposed direction of attack on cyclohexenyl systems by free radicals: (a) H. L. Goering, P. I. Abell and B. F. Aycock, *ibid.*, **74**, 3588 (1952); (b) H. L. Goering and L. L. Sims, *ibid.*, **77**, 3465 (1955); (c) J. C. D. Brand and I. D. R. Stevens, *J. Chem. Soc.*, 629 (1958).

(11) (a) G. Cilento, *Chem. Revs.*, **60**, 147 (1960); (b) E. J. Corey and E. T. Kaiser, *J. Am. Chem. Soc.*, **83**, 490 (1961); (c) H. E. Zimmerman and B. S. Thyagarajan, *ibid.*, **82**, 2505 (1960).

the bulky arylsulfonyl group will occupy the equatorial position, then only an axial position is open to protonation by the solvent. Thus the *cis* adduct should be preferentially formed. This stereochemical argument requires the anion to have at most a fleeting existence (*i.e.*, the process is essentially concerted), for protonation must occur before the anion has an opportunity to isomerize to the thermodynamically more stable *trans* configuration.[9]



This hypothesis can be tested by effecting the addition in the presence of only a limited proton source. Under these conditions the mechanistic path may change from an essentially concerted process to a two-step process in which the intermediate anion has an extended lifetime and an opportunity to isomerize to the thermodynamically more stable *trans* anion before protonation. When the reaction was run in dioxane with a limited amount of water and ethanol present as proton source, a mixture of isomers was isolated with the *trans* isomer greatly predominating. That the *trans* isomer isolated arose from the initially formed anion and not from reversal of *cis* adduct to this anion was demonstrated by the fact that pure *cis* isomer did not isomerize to the *trans* form under these conditions.

The unlikely possibility of the *trans* isomer being initially formed and then isomerizing to the *cis* isomer, when the addition was effected in ethanol, was definitely excluded by showing that the *trans* isomer was recovered unchanged after refluxing in ethanol in the presence of base.

The possibility of the addition reaction proceeding *via* a free radical process was also considered. When the addition was attempted in dioxane solvent with benzoyl peroxide as a catalyst[12] in the absence of base, or in ethanol with benzoyl peroxide as a catalyst and a trace of base, no reaction occurred. Since these conditions are favorable to the formation of radicals, it is highly unlikely that a free radical reaction occurred under so-called "ionic conditions."

Nuclear magnetic resonance studies support the structural assignments. The bands used for structure determination were those of the tertiary protons which fall in the range of 6.30 to 6.92 p.p.m. Since both tertiary protons in *trans*-1,2-bis-(*p*-tolylsulfonyl)-cyclohexane are axial, the singlet at 6.30 p.p.m. fixes the position of a tertiary axial hydrogen α to a *p*-tolylsulfonyl group. *trans*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane absorbs at both 6.28 and 6.92 p.p.m. Again both tertiary hydrogens are in axial positions, therefore the band at 6.92 must be due to the axial hydrogen α to the *p*-tolylmercapto group. *cis*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane has a sharp band at 6.20 p.p.m. and a somewhat broader band at 6.64 p.p.m. Because an arylsulfonyl group has a much larger steric requirement than an arylmercapto group, the former should tend to occupy an equatorial position and the latter an axial position in this compound. Therefore the band at 6.20 p.p.m. results from the axial hydrogen α to the *p*-tolylsulfonyl group and the band at 6.64 p.p.m. from the equatorial hydrogen α to the *p*-tolylmercapto group. An axial proton absorbs at higher frequencies than its equatorial counterpart[13]; thus since the proton α to the arylmercapto group in the *trans*-sulfone-sulfide (an axial proton) appears at a higher field than the proton α to the arylmercapto group in the *cis*-sulfone-sulfide (an equatorial proton), the n.m.r. spectra support the original configurational assignments.

The generality of the reaction mechanism discussed is currently being studied with five-membered (and other) carbocyclic systems in order to extend the scope of our proposals to olefins whose stereochemistry differs from that of cyclohexane.

Experimental[14,15]

Addition of *p*-Toluenethiol to 1-*p*-Tolylsulfonyl-cyclohexene in Ethanol.—A solution of 4.72 g. (0.02 mole) of 1-*p*-tolylsulfonyl-cyclohexene in 40 ml. of ethanol was placed in a 200-ml. three-neck flask equipped with mechanical stirrer, reflux condenser and a by-pass addition funnel. To this was slowly added a mixture prepared from 2.48 g. (0.02 mole) of *p*-toluenethiol, 0.06 g. (0.002 g. atom) of sodium and 60 ml. of ethanol; the resulting solution was refluxed under nitrogen for 16 hours.

The cooled solution was evaporated to dryness, the residue was added to 200 ml. of a chilled 10% NaOH solution and the mixture was extracted with chloroform. After drying the chloroform layer over anhydrous magnesium sulfate, the chloroform was removed under reduced pressure. The residue was crystallized from hot methanol to yield a white solid, m.p. 117–133°; recrystallization from 95% ethanol gave 4.10 g. (57%) of a white solid, m.p. 132–133°.

From the methanolic filtrate 1.62 g. (34.3%) of 1-*p*-tolylsulfonyl-cyclohexene was recovered; 0.44 g. (17.7%) of *p*-toluenethiol was recovered from the NaOH layer.

An extended reaction time (44 hours) resulted in no appreciable change in either nature or quantity of the products.

Preparation of *cis*-1,2-Bis-(*p*-tolylsulfonyl)-cyclohexane.—To a solution of 1.80 g. (0.005 mole) of *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane in 20 ml. of glacial acetic acid, 33 ml. of 30% hydrogen peroxide was slowly added and the solution refluxed for 1 hour. The mixture was poured into cold water and a white solid precipitated. The solid was filtered, and recrystallized from methanol and then twice from 95% ethanol to give an essentially quantitative yield of a white crystalline solid, m.p. 197–198°. A mixed melting point with independently synthesized *cis*-disulfone showed no depression.

Anal. Calcd. for $C_{20}H_{24}O_4S_2$: C, 61.19; H, 6.16. Found: C, 61.13; H, 6.33.

Preparation of *cis*-4,5-Bis-(*p*-tolylsulfonyl)-cyclohexene.—A mixture of 5.0 g. (0.015 mole) of *cis*-1,2-bis-*p*-tolylsulfonylethene and 70 ml. of benzene was placed in a 200-ml. autoclave and cooled to −78°. Butadiene (55 ml., 34.1 g., 0.44 mole) was condensed in a Dry Ice-bath and added to the autoclave which was then sealed and heated at 100° for 24 hours. The autoclave was cooled to room temperature, excess diene was permitted to escape and solvent was removed under reduced pressure. Several recrystallizations of the residue gave 2.38 g. (48.4%) of a white solid, m.p. 158–160° dec., lit.[16] m.p. 164–165° dec.

(12) F. G. Bordwell, R. D. Chapman and W. H. McKellin, *J. Am. Chem. Soc.*, **76**, 3637 (1954).

(13) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 116.

(14) All melting points are uncorrected.

(15) Microanalyses were performed by C. S. Yeh, I. Groten and V. Keblys.

(16) H. R. Snyder and D. P. Hallada, *J. Am. Chem. Soc.*, **74**, 5595 (1952).

Anal. Calcd. for $C_{20}H_{22}O_4S_2$: C, 61.51; H, 5.68. Found: C, 61.51; H, 5.99.

Independent Synthesis of *cis*-1,2-Bis-(*p*-tolylsulfonyl)-cyclohexane.—A solution of 1.4 g. (0.0036 mole) of *cis*-4,5-bis-*p*-tolylsulfonylcyclohexene in a 1:1 mixture of ethanol–benzene was placed in a Parr pressure bottle. A catalytic amount of Raney nickel was added and a pressure of 55 pounds of hydrogen applied. After shaking overnight the solution was filtered through a sintered glass funnel and solvent was removed under reduced pressure. The residue was decolorized with activated charcoal and recrystallized several times from methanol to yield 1.00 g. (72.2%) of a crystalline white solid, m.p. 197–198°.

Preparation of *trans*-4,5-Bis-(*p*-tolylsulfonyl)-cyclohexene.—Starting with *trans*-1,2-*bis*-*p*-tolylsulfonylethene the procedure previously described for the *cis* isomer gave a white solid, m.p. 178.5–180°, lit.[17] m.p. 174–178°.

Independent Synthesis of *trans*-1,2-Bis-(*p*-tolylsulfonyl)-cyclohexane.—Starting with *trans*-4,5-bis-(*p*-tolylsulfonyl)-cyclohexene the procedure previously described for the *cis* isomer gave a white solid, m.p. 143–145°.

Elimination of *p*-Toluenethiol from *cis*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane.—A solution of 1.09 g. (0.003 mole) of *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane in 30 ml. of ethanol was placed in a 100-ml. three-neck flask equipped with reflux condenser, mechanical stirrer and a by-pass addition funnel. A solution of 0.0069 g. (0.0003 g. atom) of sodium in 25 ml. of ethanol was slowly added and the solution refluxed under nitrogen for 16 hours. The cooled solution was neutralized with concentrated hydrochloric acid; further work-up involved the same procedure previously described for the addition reaction. *cis*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane (0.8 g.) was recovered, along with approximately 0.1 g. of 1-*p*-tolylsulfonyl-cyclohexene and a trace amount of *p*-toluenethiol.

When this same reaction was run using a molar equivalent of base, 1-*p*-tolylsulfonyl-cyclohexene and *p*-toluenethiol were obtained in greater than 90% yield. No *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane was recovered.

Attempted Isomerization of *trans*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane in Ethanol.—In a 100-ml. three-neck flask equipped with mechanical stirrer, reflux condenser and a by-pass addition funnel was placed a solution of 3.0 g. (0.008 mole) of *trans*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane in 30 ml. of ethanol. A solution of 0.02 g. (0.0008 g. atom) of sodium in 20 ml. of ethanol was added. The mixture was refluxed under nitrogen for 16 hours and then worked up in the previously described manner. The sole product isolated was the starting *trans*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane; none of the *cis* isomer was found.

Addition of *p*-Toluenethiol to 1-*p*-Tolylsulfonyl-cyclohexene in Dioxane.—To a 500-ml. three-neck flask equipped with reflux condenser, mechanical stirrer and by-pass addition funnel was added 9.44 g. (0.04 mole) of I and 0.216 g. (0.004 mole) of sodium methoxide in 80 ml. of pure dioxane. *p*-Toluenethiol (4.96 g., 0.04 mole), ethanol (1.2 g., 0.026 mole) and water (2 g., 0.11 mole) in 120 ml. of pure dioxane was slowly added with stirring. The solution was then refluxed under nitrogen for 14 hours, allowed to cool and neutralized with concentrated hydrochloric acid. The solution was poured into cold water; the milky mixture that formed was extracted with ethyl ether, and the ether layer extracted with 400 ml. of chilled 5% NaOH. The alkaline layer was neutralized with concentrated hydrochloric acid, extracted with ether, dried, and the ether removed under reduced pressure. The residue was crystallized from ethanol to give 0.87 g. (17.5%) of recovered *p*-toluenethiol.

(17) W. E. Truce and R. J. McManimie, *J. Am. Chem. Soc.*, **75**, 1672 (1953).

The initial ether layer was dried and the solvent removed under reduced pressure. The residue after several recrystallizations from methanol gave 2.0 g. of white crystals, m.p. 58–59°. The mother liquor was evaporated to dryness. Part of the residue was dissolved in hot hexane, and the fraction which was insoluble in hexane was dissolved in hot methanol. Upon cooling, the latter gave 0.70 g. of II, m.p. 125–132°. The hexane fraction upon cooling gave 3.19 g. of recovered I, m.p. 77–82°.

When the hexane mother liquor was evaporated an oil remained which could not be crystallized. The oil was chromatographed on a column of activated alumina using hexane as the solvent. The column was eluted with hexane–benzene mixtures. Evaporation and crystallization gave 2.75 g. of a white solid, m.p. 50–59°; 0.27 g. of II; and 1.04 g. of I, m.p. 68–82°.

In a 50-ml. flask there was placed 0.90 g. of the compound m.p. 58–59°, 10 ml. of glacial acetic acid and 16 ml. of 30% hydrogen peroxide. The solution was refluxed for 2 hours and worked up in the manner previously described for oxidations to yield 0.89 g. (90.1%) of a white solid, m.p. 143–145°. This solid was admixed with a sample of independently prepared *trans*-1,2-bis-(*p*-tolylsulfonyl)-cyclohexane and no melting point depression resulted. Thus the solid, m.p. 58–59°, is *trans*-2-*p*-tolylmercapto-1-*p*-tolylsulfonyl-cyclohexane. Therefore from the addition reaction, 4.23 g. (44.8%) of the starting olefin was recovered along with 4.75 g. (60.0% yield) of *trans*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane and 0.97 g. (12.2% yield) of the *cis* adduct.

Attempted Isomerization of *cis*-2-*p*-Tolylmercapto-1-*p*-tolylsulfonylcyclohexane in Dioxane.—A solution of 3.60 g. (0.01 mole) of *cis*-2-*p*-tolylmercapto-1-*p*-tolylsulfonylcyclohexane, 0.054 g. (0.001 mole) of sodium methoxide, 50 ml. of pure dioxane, 0.4 g. (0.009 mole) of ethanol and 0.5 g. (0.0027 mole) of water was refluxed under nitrogen for 44 hours and then worked up in the manner previously described. Virtually all of the starting *cis* isomer was recovered. No *trans* isomer could be detected.

Attempted Free Radical Addition of *p*-Toluenethiol to 1-*p*-Tolylsulfonyl-cyclohexene. (A) Dioxane Solvent.—A solution of 2.36 g. (0.01 mole) of 1-*p*-tolylsulfonyl-cyclohexene, 1.36 g. (0.011 mole) of *p*-toluenethiol and 0.12 g. (0.0005 mole) of benzoyl peroxide in 50 ml. of pure dioxane was refluxed under nitrogen for 18 hours with stirring. No addition products were found, and 2.04 g. (86.4%) of the starting olefin was recovered.

(B) Ethanol Solvent with a Trace of Base.—A solution of 2.36 g. (0.01 mole) of 1-*p*-tolylsulfonyl-cyclohexane, 1.24 g. (0.01 mole) of *p*-toluenethiol, 0.12 g. (0.0005 mole) of benzoyl peroxide and three drops of morpholine in 50 ml. of ethanol was refluxed under nitrogen for 17 hours with stirring. No addition products were found, and 2.05 g. (87%) of the starting olefin was recovered.

N.m.r. Apparatus and Procedure.—The equipment consisted of a Varian V4311 spectrometer operating at a frequency of 60 mc./sec. Samples were run in deuteriochloroform and the spectra were calibrated by the usual side-band technique. Tetramethylsilane was used as an internal standard and all values are referred to the proton signal of this compound.

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