TABLE IV
HOMOGENEITY OF DISULFIDES 3 AND 4

RC(O)SSR′	R_f* [a]	[RC(O)S]$_2$ or R′SSR′
	0.93	$[CH_3C(O)S]_2$
$CH_3C(O)SS(CH_2)_2NHAc$ (3)	0.72	
	0.30	$[AcNH(CH_2)_2S]_2$
$C_6H_5C(O)SS(CH_2)_2NHAc$ (4)	0.91	
	1.00	$[C_6H_5C(O)S]_2$

[a] Reference 11.

iodine resulted in indecisive end points and consumption in excess of 100% of theory.

B. Hydrolysis.—A solution of 0.758 g of 2-acetamidoethyl benzoyl disulfide (4) and 0.37 g of potassium hydroxide in 10 ml of water was heated on a steam bath for 30 min. The basic solution was acidified to pH 2 and extracted with benzene. The benzene was evaporated and the residue washed with boiling water. Chilling of the aqueous washes gave 0.161 g of benzoic acid (44%): infrared spectrum identical with that of authentic material; mp and mmp 120–121°.

Homogeneity of Unsymmetrical Carbonyl Disulfides.—Column chromatography of 0.25 g of phenyl benzoyl disulfide (6) on 7.0 g of Woelm Silica Gel G (activity I) with hexane–ether (50:1) resulted in elution of only one material, disulfide 6 with unchanged physical properties (100% recovery). Glpc analysis of 2 μl of phenyl acetyl disulfide (5) with an oven temperature of 185°, and attenuation of 16 demonstrated disulfide 5 to be a single component with a retention time of 176 sec; phenyl disulfide and acetyl disulfide had retention times of 565 and 60 sec, respectively. Tlc was used to demonstrate the homogeneity of disulfides 3 and 4 with the results shown in Table IV.

Disproportionation of Carbonyl Disulfides.—Thermal stabilities of disulfides 3–6 were determined by the general procedure below, the % disproportionation being determined either by large-scale isolation (3, 4, and 6) or by glpc analysis of the reaction products (5).

A. By Large-Scale Isolation.—The disulfide (1.00 mmole) was dissolved in 10 ml of dioxane[16] in a glass ampoule. The solution was frozen (0°), and the tube was purged with nitrogen and sealed. The tube then was wrapped with aluminum foil and heated at 100° for the period stated (Table II), after which the contents were freeze dried to constant weight (24–48 hr).[17]

Disproportionation products were separated as described below for the various disulfides and were dried to constant weight. The results of these experiments are given in Table II. Materials for which values are given in Table II were identified by infrared spectra, melting points and mixture melting points, and/or tlc R_f (*vs.* an authentic sample).

With 2-acetamidoethyl acetyl disulfide (3), the dried product was washed with 5 ml of anhydrous ether at 0° to separate 3 from the insoluble N,N′-diacetylcystamine; acetyl disulfide was assumed to be the weight lost in the original evaporation and was not characterized. With 2-acetamidoethyl benzoyl disulfide (4), the product was washed with 10 ml of methanol–water (3:7) to separate disulfide 4 and N,N′-diacetylcystamine from the insoluble benzoyl disulfide; the residue from evaporation of the filtrate was washed with 2 ml of water at 0° to separate the N,N′-diacetylcystamine from the disulfide 4; all three products then were identified by their spectra and tlc R_f. With phenyl benzoyl disulfide (6), the product was chromatographed on a 0.5 × 10 cm column of 7.0 g of Woelm Silica Gel G (activity 1) with 25 ml of hexane–ether (10:1); disulfide 6 was recovered (100%) unchanged from the hexane–ether effluent, less than 0.5% of the original weight being eluted by hexane alone (which would have displaced any phenyl disulfide).

B. Disproportionation of 5 by Gas–Liquid Partition Chromatography.—Glpc was performed as usual (oven temperature, 175°).[11] Retention times for the various components were as follows: dioxane, 11–20 sec; 1,2,4-trichlorobenzene, 55 sec; phenyl acetyl disulfide (5), 190 sec.

Disulfide 5 (0.1838 g) and 0.1678 g of trichlorobenzene were dissolved to volume in 10 ml of dioxane and a 3-ml aliquot was heated in a sealed tube at 100° as usual. The contents of this tube were chromatographed. The per cent disproportionation was taken as the ratio of the change in area[18] of the peak for disulfide 5 from its area in a sample of the original solution (which had been kept frozen) to the original area, times 100.

Registry No.—3, 10048-01-8; 4, 10048-03-0; 5, 5813-74-1; 6, 5718-98-9.

(16) Purified according to the procedure of K. Hess and H. Frahm, as described by L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1955, p 285.

(17) If not analyzed immediately, the mixture was kept (frozen) at −5°.

(18) Area was the average of three determinations with a planimeter, corrected for slight differences reflected by the trichlorobenzene standard.

Variations in the Stereochemistry of Sulfone Desulfuration[1]

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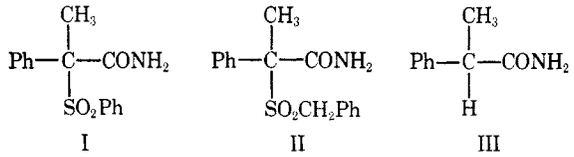
2-Phenyl-2-phenylsulfonylpropanoamide (I) is desulfurated by Raney nickel with predominant inversion of configuration in ethanol solvent and with predominant retention in acetone solvent. Variable ratios of inversion to retention are noted after pretreating the Raney nickel catalyst with different solvents. 2-Phenyl-2-benzylsulfonylpropanoamide (II) is desulfurated with predominant retention of configuration in both ethanol and acetone solvent, but the extent of retention again varies with the pretreatment of the nickel catalyst. Benzyl sulfones (such as II and dibenzyl sulfone) undergo Raney nickel desulfuration markedly more rapidly than phenyl sulfones (such as I and diphenyl sulfone) in ethanol and react more slowly in benzene solvent than in ethanol. Tentative explanations of these results are suggested.

In 1952, initiating studies on the stereochemical consequences of Raney nickel catalyzed hydrogenolyses of various functional groups, we undertook experiments involving the desulfuration of the enantiomers of 2-phenyl-2-phenylsulfonylpropanoamide (I).[2] When (−)-I was heated with W-2 Raney nickel[3] in refluxing ethanol, *R*-(−)-hydratropamide (*R*-(−)-III)[4] was produced of about 50% optical homogeneity. Similarly (+)-I yielded *S*-(+)-III with analogous stereoselectivity. On the basis of the application of Freudenberg's "displacement rule"[5] to a limited series of derivatives related to (−)-I and *R*-(−)-III, it was tentatively



(1) (a) This constitutes communication XVII in the series "The Stereochemistry of Raney Nickel Action;" (b) for XVI, see W. A. Bonner and R. A. Grimm, *J. Org. Chem.*, **32**, (1967).

(2) W. A. Bonner, *J. Am. Chem. Soc.*, **74**, 1034 (1952).

(3) R. Mozingo, *Org. Syn.*, **21**, 15 (1941).

(4) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York, 1962, pp 89, 93.

(5) K. Freudenberg, "Stereochemie," F. Deuticke, Leipzig, 1933, p 695 ff.

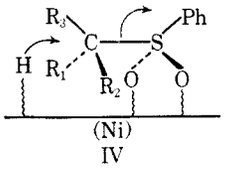
TABLE I

DESULFURATIONS OF 2-PHENYL-2-PHENYLSULFONYL (I) AND 2-PHENYL-2-BENZYLSULFONYLPROPANOAMIDE (II) UNDER VARIOUS CONDITIONS

Sulfone			Raney nickel catalyst			Reaction conditions			Hydratropamide product			Configurational result	
No.	Isomer	Wt, mg	Amt, tsp	Pretreatment solvent	Time, days	Solvent	Vol, ml	Time, hr	Wt, mg	Yield, %	$[\alpha]^{23-28}D$	Inversion, %	Retention, %
1	*S*-(+)-I[a]	209	0.5	EtOH	184	EtOH	35	5	104	96	+16.4	73	27
2	*R*-(−)-I[b]	100	0.25	EtOH	1	EtOH	25	5	...	...	−11.9	69	31
3	*R*-(−)-I[b]	101	0.25	H_2O, EtOH	32, then 11	EtOH	25	5	54	103	−14.3	72	28
4	*S*-(+)-I[a]	150	0.5	H_2O	9	EtOH	20	5	78	100	+11.5	66	34
5	*R*-(−)-I[b]	102	0.25	H_2O	45	EtOH	25	5	53	100	−6.9	61	39
6	*R*-(−)-I[b]	150	0.25	H_2O	42	2-PrOH	25	5	50	65	−8.2	63	37
7	*S*-(+)-I[a]	150	0.25	H_2O	24	Me_2CO	25	5	75	97	−16.9	26	74
8	*R*-(−)-I[b]	150	0.25	H_2O	32	EtOH	20	5	79	102	+7.4	39	61
				Me_2CO (25 ml)	2 hr[c]								
9	*S*-(+)-I[a]	150	0.25	H_2O	36	EtOH	25	5	85	109	+2.7	54	46
				Me_2CO (25 ml)	2 hr[c]								
				EtOH (25 ml)	1 hr[c]								
10	*S*-(+)-I[a]	100	0.25	EtOH	6	Me_2CO	25	5[d]	35	68	+2.6	54	46
			0.25	EtOH	6	Me_2CO	25	1					
11	*R*-(−)-I[b]	150	0.25	EtOH	5	Me_2CO–EtOH[e]	25	5[d]	61	79	−7.9	67	38
			0.25	EtOH	5	Me_2CO–EtOH[e]	25	1					
12	*R*-(−)-II	150	0.5	H_2O	11	EtOH	25	0.25	77	104	+9.6	39	61
13	*S*-(+)-II	150	0.5	H_2O	2	EtOH	25	0.25	40	54	−5.4	43	57
14	*S*-(+)-II	150	0.5	H_2O	2	Me_2CO	25	0.83	54	73	−9.3	39	61
				Me_2CO (25 ml)	0.5 hr[c]								
15	*S*-(+)-II	154	0.5	H_2O[f])	2	EtOH	25	0.25	74	100	−3.6	46	54
				EtOH (25 ml)	0.5 hr[c]								

[a] 83.7% optically pure. [b] 75.9% optically pure. [c] Heat under reflux. [d] Thin layer chromatography showed incomplete reaction; fresh catalyst added. [e] Weight ratio, 1:1.2. [f] Similar results obtained with catalyst stored under ethanol for 6 months.

concluded that these two compounds had opposite configurations and that Walden inversion had attended the desulfuration of the sulfones (+)- and (−)-I. A mechanism (IV), involving adsorption of the sulfone through its sulfonyl oxygen atoms, followed by SN2 displacement by hydrogen adsorbed on the catalyst

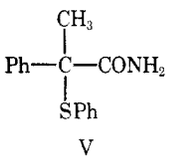


IV

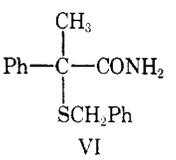
surface, was provisionally proposed[2] to rationalize these tentative stereochemical conclusions. The unanticipated results described below have recently prompted us[1b] to place the configurational assignments of (−)-I, as well as the benzyl analog (−)-II, on a more definitive basis by optical rotatory dispersion measurements.[6] The latter have demonstrated unequivocally that both (−)-I and (−)-II possess the *R* configuration[1b] and that Walden inversion did in fact attend the Raney nickel catalyzed desulfuration of *R*-(−)-I to *R*-(−)-III.

In the hope of testing further the tentative mechanistic hypothesis symbolized by IV, we have now undertaken to study the Raney nickel catalyzed desulfuration of optically active I under a wider variety of conditions and have also extended such studies to the structurally related enantiomers of 2-phenyl-2-benzylsulfonylpropanoamide (II). The unexpected results of these experiments are recorded herein.

At the outset we attempted to assess the possible effects of solvent, as well as pretreatment of the Raney nickel catalyst, on the stereochemical consequences of the conversion of I into III. As indicated in detail in Table I, samples of Raney nickel catalyst, pretreated in various ways and used in either ethanol or acetone as the reaction solvent, led to widely different stereochemical results in the hydrogenolysis of I into III. These results are summarized in abridged form in Table II. The stereochemical results of several similar experiments involving desulfuration of the enantiomers of the analogous benzyl sulfone II are likewise summarized in Table II, along with results obtained with the sulfide precursors of I and II, V and VI, respectively.



V



VI

As seen in Tables I and II, the variable having the most striking effect on the stereochemical course of the desulfuration of the phenyl sulfone I is the solvent with which the Raney nickel catalyst is pretreated and/or in which the reaction is conducted. When the catalyst storage solvent is ethanol or water and the desulfuration is conducted in refluxing ethanol, the reaction is attended, as previously reported,[2] by inversion of configuration (No. 1–5). When the catalyst is conditioned by pretreatment with refluxing acetone or the reaction is conducted in acetone solvent, however, desulfuration proceeds with significant and predominant *retention* of configuration (No. 7), a result which persists to a lesser extent even if ethanol is subsequently used as the reaction solvent (No. 8). The conflicting optical course dictated by the use of ethanol or acetone as pretreatment and reaction solvents is also attested by low degree of inversion found in No. 9 and 10, where,

(6) C. Djerassi, K. Undheim, and A. Weidler, *Ann. Chem. Scand.*, **16**, 1147 (1962).

TABLE II
EFFECTS OF SOLVENT AND STRUCTURE ON THE STEREOCHEMISTRY OF SULFONE DESULFURATION

No.	Substrate	Pretreatment solvent	Solvent	Hydratropamide III	Optical course	Stereoselectivity,[a] %
1	*S*-(+)-I	EtOH	EtOH	*S*-(+)	Inversion	46
2	*R*-(−)-I	EtOH	EtOH	*R*-(−)	Inversion	38
3	*R*-(−)-I	EtOH–H_2O	EtOH	*R*-(−)	Inversion	44
4	*S*-(+)-I	H_2O	EtOH	*S*-(+)	Inversion	32
5	*R*-(−)-I	H_2O	EtOH	*R*-(−)	Inversion	22
6	*R*-(−)-I	H_2O	2-PrOH	*R*-(−)	Inversion	26
7	*S*-(+)-I	H_2O	Me_2CO	*R*-(−)	Retention	48
8	*R*-(−)-I	H_2O–Me_2CO	EtOH	*S*-(+)	Retention	22
9	*S*-(+)-I	H_2O–Me_2CO–EtOH	EtOH	*S*-(+)	Inversion	8
10	*S*-(+)-I	EtOH	Me_2CO	*S*-(+)	Inversion	8
11	*R*-(−)-I	EtOH	Me_2CO–EtOH	*R*-(−)	Inversion	24
12	*R*-(−)-II	H_2O	EtOH	*S*-(+)	Retention	22
13	*S*-(+)-II	H_2O	EtOH	*R*-(−)	Retention	14
14	*S*-(+)-II	H_2O–Me_2CO	Me_2CO	*R*-(−)	Retention	22
15	*S*-(+)-II	H_2O–EtOH	EtOH	*R*-(−)	Retention	8
16	*R*-(−)-V	EtOH	EtOH, Me_2CO or C_6H_6	(±)	Racemization	...
17	*S*-(+)-VI	EtOH	EtOH, Me_2CO or C_6H_6	(±)	Racemization	...

[a] Per cent excess of the predominant enantiomer, *i.e.*, 100 minus % racemate = ([α]D(obsd) of product)/([α]D(max) of product).

TABLE III
COMPLETION TIMES FOR DESULFURATION OF SEVERAL SULFONES UNDER VARIOUS CONDITIONS

	Sulfone		Raney nickel catalyst			Reaction conditions			Time for completion of reaction, min
No.	Compd	Wt, mg	Amt, tsp	Storage solvent	Time, days	Solvent	Vol, ml	Eluent[a]	
1	Dibenzyl	150	0.25	H_2O	49	EtOH	20	A	<11
2	Diphenyl	133	0.25	H_2O	49	EtOH	20	A	>450[b]
3	(±)-II	150	0.25	EtOH	7	EtOH	25	B	<2
4	(±)-I	143	0.5	EtOH	72	EtOH	25	B	~58
5	Dibenzyl	150	0.25	H_2O, EtOH	32, then 21	C_6H_6	30[c]	A	>135
6	(±)-II	204	0.5	H_2O	4	C_6H_6	50[c]	B	>795
7	Dibenzyl	150	0.25	EtOH	89	EtOH–C_6H_6[d]	25	A	<10

[a] For thin layer chromatography: A = C_6H_6–Et_2O (4:1); B = C_6H_6–Me_2CO (2:3). [b] Starting material (20 mg) isolated from reaction mixture filtrate. [c] Reaction mixture distilled (*ca.* 10 ml) for azeotropic topping before adding sulfone. [d] Volume ratio 1.5:1.

respectively, pretreatment involved refluxing acetone, then refluxing ethanol, followed by ethanol as the reaction solvent, or catalyst storage under ethanol, followed simply by the use of acetone solvent. These data indicate clearly that catalyst storage under ethanol or water followed by reaction in ethanol solvent strongly promotes configurational inversion during desulfuration of the phenyl sulfone I, while acetone pretreatment and acetone solvent strongly promotes configurational retention. Other data in Tables I and II suggest that the age of the catalyst, the quantity used, and the storage solvents have an effect also on the *extent* of inversion or retention during the desulfuration of I, but that these effects are rather secondary to the above major effect seen in the differences due to ethanol or acetone as reaction solvent. That the latter appear attributable to the functionality of the reaction solvent and not its skeletal structure is shown by No. 6 where 2-propanol, like ethanol, led to predominant configurational inversion.

Another unexpected variable whose effect on stereochemistry is apparent in Table II is the *structure* of the sulfone undergoing desulfuration. In No. 12–15 we find that the *benzyl* sulfone II undergoes reductive desulfuration with predominant *retention* of configuration, regardless of the catalyst pretreatment or the reaction solvent employed. The above-mentioned solvent effects are still apparent in these experiments, however, in that ethanol catalyst storage and ethanol solvent (No. 15) still promoted more inversion (*i.e.*, lower retention stereoselectivity), whereas refluxing acetone pretreatment and acetone solvent (No. 14) again led to greater configurational retention. The effect of catalyst age is likewise suggested in Table I, where we note that a fresher catalyst (No. 13) promoted less configurational retention during desulfuration of the benzyl sulfone II than did an older catalyst similarly pretreated (No. 12).

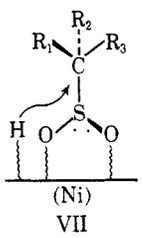
Table II also indicates that desulfurations of the analogous phenyl (V, No. 16) or benzyl (VI, No. 17) sulfides in either ethanol, acetone, or benzene solvents were accompanied, as previously reported,[2] by complete racemization and loss of optical activity in their hydratropamide products. Hydratropamide itself was found to racemize only slowly under the action of Raney nickel in ethanol (2–4% in 5 hr) but to racemize more rapidly in acetone solvent (45% in 5 hr). The optical results shown in Tables I and II have not been corrected for such racemization of the hydratropamide products and would, of course, show greater stereoselectivity in all cases were such corrections possible.

In order to assess further in a preliminary way the above structural effect on the stereochemistry of sulfone desulfuration, crude rate experiments were undertaken on desulfurations involving diphenyl and dibenzyl sulfones, as well as the analogs I and II. In these experiments the disappearance of starting sulfone was followed roughly by thin layer chromatography of aliquots of the reaction mixture collected at various time intervals, after which the approximate time for completion of reaction was noted (Table III and Experimental Section). Here we found that dibenzyl sulfone de-

sulfurated in ethanol over 40 times as fast as did diphenyl sulfone (No. 1, 2) and that the benzyl sulfone II reacted around 30 times as rapidly as did the phenyl sulfone I (No. 3, 4). Furthermore, both dibenzyl sulfone (No. 5) and the benzyl sulfone II (No. 6) desulfurated vastly more slowly in benzene solvent than in ethanol. That benzene was not a simple catalyst poison, however, was suggested by the fact that dibenzyl sulfone desulfurated as rapidly in 1:1.5 benzene–ethanol solvent (No. 7) as it did in pure ethanol (No. 1). These experiments indicate that benzyl sulfones desulfurate far more readily in ethanol than do phenyl sulfones and that the rate of desulfuration of benzyl sulfones is greatly enhanced in a polar solvent such as ethanol as compared to a nonpolar solvent such as benzene.

Any explanation of the above effects of solvent and structural factors on the stereochemistry of sulfone desulfuration must at this stage necessarily be only tentative and suggestive. In regard to the solvent effect, we should note that acetone is a solvent which, because of its reducible carbonyl function, is capable of depleting the supply of surface-bound hydrogen on a sample of Raney nickel catalyst. Ethanol, on the other hand, is a solvent capable of dehydrogenation when heated under reflux in the presence of Raney nickel.[7] Thus, in principle, ethanol might be able to maintain a roughly uniform, or at least less depleted supply, of surface-bound hydrogen on the catalyst. It seems therefore possible that the stereochemical course of sulfone desulfuration may in some way be dependent on the availability of surface-bound hydrogen on the nickel catalyst, such that the greater the hydrogen availability, the greater is the tendency for intervention of an inversion mechanism. Experiments designed to test this hypothesis are currently in preparation.

Regarding the effect of structure on sulfone desulfuration stereochemistry, it is tempting to speculate that the above observed enhanced rate of benzyl sulfone hydrogenolysis must somehow be intimately connected with a mechanism favoring configurational retention. If the $PhCH_2$–SO_2 bond of II is vastly more readily cleaved than the Ph–SO_2 bond of I, it might be possible, for example, for an intermediate to be preferentially produced from II, whose adsorption geometry

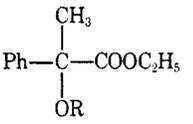


VII

(*e.g.*, VII) renders it far more subject to subsequent hydrogenolysis from the front side than from the rear side. With the more slowly cleaving Ph–SO_2 bond of I, on the other hand, the intervention of a mechanism such as VII might be less important, so that the S_N2 mechanism IV could competitively predominate. Furthermore, the above vastly more rapid desulfuration of benzyl sulfones in ethanol, as opposed to benzene solvent, suggests the possible intervention of ionic species during such desulfurations in polar solvents.

(7) W. A. Bonner, *J. Am. Chem. Soc.*, **74**, 1033 (1952).

Mitsui, Imaizumi, and their co-workers have noted a number of structural factors influencing the steric course of Raney nickel catalyzed hydrogenolyses of esters (VIII) derived from atrolactic acid. With ethyl atrolactate itself,[8] as well as with its O-alkyl and O-benzyl ethers (VIIIa), configurational retention attended



VIIIa, R = H, R, $PhCH_2$
b, R = Ar
c, R = RCO, ArCO
d, R = *o*- or *p*-$MeOC_6H_4$

hydrogenolysis to ethyl hydratropate.[9] With O-phenyl and other O-aryl ethers (VIIIb), on the other hand, as well as with O-acyl derivatives (VIIIc), predominant inversion was observed during hydrogenolysis.[9] More recently these investigators have extended their experiments to include other catalysts,[10] with the finding that the nature of the catalyst also influences the steric course of hydrogenolysis. Thus, while Raney nickel engendered inversion during hydrogenolysis of aryl ethers (VIIIb), palladium on charcoal led to retention of configuration with such ethers (except in the cases of the methoxyphenyl derivatives VIIId). Later studies with other series of compounds have confirmed these striking stereochemical differences dependent on the nature of the catalyst and the structure of the substrate,[11–17] the inclusion of various additives during hydrogenolysis,[18–22] and the type of solvent employed.[23] In the above papers Mitsui and Imaizumi have endeavored to explain their divergent stereochemical results in terms of the adsorptions of specific groups of the substrate onto the catalyst surface prior to hydrogenolysis, probable steric hindrance to such adsorption when other substituents are present on the substrate, and the possibility that substrate adsorption may occur at either a single site, or simultaneously at two sites, on the catalyst surface. These hypotheses provide logical rationalizations after the facts. In view of our preliminary observations above as to the effects

(8) W. A. Bonner, J. A. Zderic, and G. A. Casaletto, *J. Am. Chem. Soc.*, **74**, 5086 (1952).

(9) S. Mitsui and S. Imaizumi, *Bull. Chem. Soc. Japan*, **34**, 744 (1961), and earlier references contained herein.

(10) S. Mitsui and S. Imaizumi, *ibid.*, **36**, 855 (1963).

(11) S. Mitsui, Y. Senda, and K. Konno, *Chem. Ind.* (London), 1354 (1963).

(12) S. Mitsui, K. Iijima, and T. Masuko, *Nippon Kagaku Zasshi*, **84**, 833 (1963); *Chem. Abstr.*, **60**, 5369*b* (1964).

(13) S. Mitsui, S. Imaizumi, I. Takamura, and M. Takamura, *ibid.*, **84**, 838 (1963); *Chem. Abstr*, **60**, 5369*f* (1964).

(14) S. Mitsui, S. Imaizumi, and Y. Takahashi, *ibid.*, **84**, 842 (1963); *Chem. Abstr.*, **60**, 5370*a* (1964).

(15) K. Konno and S. Mitsui, *ibid.*, **85**, 497 (1964); *Chem. Abstr.*, **62**, 11728*g* (1965).

(16) S. Mitsui and K. Iijima, *ibid.*, **85**, 682 (1964); *Chem. Abstr.*, **62**, 16010*f* (1965).

(17) S. Mitsui and Y. Kudo, *Chem. Ind.* (London), 381 (1965).

(18) S. Mitsui and S. Imaizumi, *Nippon Kagaku Zasshi*, **86**, 219 (1965); *Chem. Abstr.*, **63**, 4133*f* (1965).

(19) Y. Senda and S. Mitsui, *ibid.*, **86**, 229 (1965); *Chem. Abstr.*, **63**, 4134*e* (1965).

(20) S. Mitsui and S. Imaizumi, *ibid.*, **86**, 232 (1965); *Chem. Abstr.*, **63**, 4134*h* (1965).

(21) S. Mitsui and S. Imaizumi, *Kogyo Kagaku Zasshi*, **65**, 816 (1965); *Chem. Abstr.*, **63**, 9777*c* (1965).

(22) S. Mitsui and Y. Nagahisa, *Chem. Ind.* (London), 1975 (1965).

(23) S. Mitsui and K. Iijima, *Nippon Kagaku Zasshi*, **85**, 687 (1964); *Chem. Abstr.*, **62**, 16010*h* (1965).

of solvent and structure on the stereochemistry and rate of hydrogenolysis of a *single type* of functionally substituted substrate, however, we feel[24] that many additional critical experimental data will be required before definitive conclusions as to the mechanisms of stereoselective catalytic hydrogenolyses are possible.

Experimental Section

***S*-(+)- and *R*-(−)-2-Phenyl-2-phenylsulfonylpropanoamides.**—*S*-(+)-2-phenyl-2-phenylmercaptopropanoic acid (mp 85–87°, $[\alpha]^{25}D$ +163° (*c* 2.66, EtOH)) was prepared as previously described.[2] This was converted as before[2] into *S*-(+)-2-phenyl-2-phenylmercaptopropanoamide: mp 102–103°; $[\alpha]^{27}D$ +106° (*c* 2.07, EtOH). The latter was oxidized with 30% hydrogen peroxide in acetic acid[2] to yield *S*-(+)-2-phenyl-2-phenylsulfonylpropanoamide (*S*-(+)-I): mp 180–181°; $[\alpha]^{29}D$ +60.7° (*c* 0.61, EtOH). The corresponding enantiomers were similarly prepared: *R*-(−)-2-phenyl-2-phenylmercaptopropanoic acid, mp 85–87°, $[\alpha]^{25}D$ −163° (*c* 2.69, EtOH); *R*-(−)-2-phenyl-2-phenylmercaptopropanoamide, mp 102–103°, $[\alpha]^{27}D$ −106° (*c* 1.63, EtOH); *R*-(−)-2-phenyl-2-phenylsulfonylpropanoamide (*R*)-(−)-I), mp 181–182°, $[\alpha]^{29}D$ −55.1° (*c* 0.58, EtOH).

***S*-(+)- and *R*-(−)-2-Phenyl-2-benzylsulfonylpropanoamides.**—The previously described[1b] *S*-(+)-2-phenyl-2-benzylmercaptopropanoamide (mp 107.5–108°, $[\alpha]^{28}D$ +14.5° (*c* 0.79, EtOH), 1.00 g) was dissolved in acetic acid (8 ml) and treated with 30% hydrogen peroxide (4 ml). The mixture was heated on the steam bath for 30 min, treated with additional 30% hydrogen peroxide (4 ml), heated again for 30 min, then cooled, and diluted with water. The crude product (1.15 g, 99%) was filtered and recrystallized from acetone (10 ml) containing sufficient ligroin (bp 60–68°) to cause incipient turbidity. The 0.94 g of *S*-(+)-II product had mp 176–177°, $[\alpha]^{27}D$ +91.6° (*c* 0.62, EtOH).

Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.46; H, 5.65; N, 4.62; S, 10.55. Found: C, 63.46; H, 5.35; N, 4.50; S, 10.77.

The enantiomeric *R*-(−)-sulfone (*R*-(−)-II), prepared analogously from *R*-(−)-2-phenyl-2-benzylmercaptopropanoamide,[1b] had mp 175.5–176.5°, $[\alpha]^{27}D$ −90.7° (*c* 0.93, EtOH).

Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.46; H, 5.65; N, 4.62; S, 10.55. Found: C, 63.17; H, 5.39; N, 4.52; S, 10.60.

Action of Raney Nickel on *R*-(−)-Hydratropamide. A. In Ethanol.—W-2 Raney nickel[3] (0.25 tsp of damp paste, 3 days old, stored under water) was rinsed thrice with ethanol (sintered-glass funnel) and then suspended in ethanol (20 ml). *R*-(−)-hydratropamide (100 mg, $[\alpha]^{24}D$ −29.2° (*c* 10.6, 75% EtOH)) was added and the mixture was stirred under reflux for 5 hr, whereupon the catalyst was filtered and rinsed with ethanol. Solvent evaporation and recrystallization of the residue from benzene–ligroin provided a product having $[\alpha]^{28}D$ −28.6° (*c* 5.93, 75% EtOH). In similar experiments with other batches of catalyst, the loss of optical activity was 0.5–1.1°/5 hr, corresponding to 2–4% racemization of the starting amide.

B. In Acetone.—The above Raney nickel sample (0.5 tsp) was rinsed with acetone and suspended in acetone (20 ml) and the mixture was heated under reflux for 30 min. At this point the above *R*-(−)-hydratropamide (75 mg) in acetone (5 ml) was added and the mixture was stirred under reflux for 5 hr. The product was isolated and recrystallized as before. It showed $[\alpha]^{25}D$ −16° (*c* 2.64, 75% EtOH), corresponding to a rotation loss of 13.5°, or 46% racemization per 5 hr.

An optically impure sample of *S*-(+)-hydratropamide (74 mg, $[\alpha]^{27}D$ +16.4° (*c* 4.53, 75% EtOH)) was recrystallized from benzene (1 ml) and 4 ml of ligroin (bp 60–68°). The recrystallized product (47 mg) had the same specific rotation, indicating that no optical enrichment occurred during crystallization.

Desulfurations of 2-Phenyl-2-phenylmercaptopropanoamide and 2-Phenyl-2-benzylmercaptopropanoamide in Various Solvents.—*R*-(−)-2-Phenyl-2-phenylmercaptopropanoamide (*R*-(−)-V) and *S*-(+)-2-phenyl-2-benzylmercaptopropanoamide (*S*-(+)-VI) were desulfurated with W-2 Raney nickel in refluxing ethanol in the manner previously described.[2] In each case, as before, the hydratropamide product was optically inactive. The two amides were then similarly desulfurated using Raney nickel in refluxing acteone and in refluxing benzene, with 5-hr reaction times. Customary processing again afforded racemic samples of hydratropamide as the product of each reaction.

Desulfurations of 2-Phenyl-2-phenylsulfonylpropanoamide and 2-Phenyl-2-benzylsulfonylpropanoamide in Various Solvents.—Samples of W-2 Raney nickel were "pretreated" by allowing them to stand in various solvents for varying periods of time following their preparation. The samples were then collected on sintered-glass funnels, rinsed several times with the reaction solvent, and then suspended in the reaction solvent. In some cases the suspension was heated under reflux, filtered, and treated with additional reaction solvent prior to the desulfuration reaction. The appropriate sulfone was then added to the mixture, stirring and refluxing were continued for 5 hr, and the catalyst was filtered and rinsed. The hydratropamide products from each experiment were isolated and recrystallized (benzene–ligroin) in the usual way and examined for optical activity (*c* 1.5–5, 75% EtOH). They generally melted over a 1° range in the interval 90–94° and in those cases tested were homogeneous on thin layer chromatography. The results of these experiments are summarized in Table I. Pettersson[25] has reported $[\alpha]^{25}D$ ±46.5° (absolute EtOH) as the specific rotation of optically pure hydratropamide, in contrast to $[\alpha]^{25}D$ ±28.5° (75% EtOH) previously reported[26] by Levene and co-workers. We have recently found[1b] a ratio of 1.10 for the rotations of hydratropamide measured in absolute ethanol and in 75% ethanol. The configurational results in Table I are based on Pettersson's rotation for hydratropamide and are corrected for both the solvent change and the optical purity of the starting sulfones.

Sulfone Desulfuration Rate Experiments.—The indicated quantity of W-2 Raney nickel catalyst, stored as described in Table III, was rinsed several times with the reaction solvent, then suspended in the latter. The stirred suspension was heated to reflux temperature and the indicated amount of the appropriate sulfone was added. Stirring under reflux was continued, whereupon 1-ml aliquots of the mixture were removed at various time intervals. The catalyst was allowed to settle and a sample of the supernatant was placed on a thin layer chromatogaphic plate coated with silica gel, then eluted with the indicated eluent. The plate was then examined for the presence or absence of starting sulfone by spraying with ceric sulfate solution and baking.[27] The times indicated in Table III are those at which the starting sulfone was found absent on such thin layer chromatography.

Registry No.—*S*-(+)-I, 14182-52-6; *R*-(−)-I, 14182-53-7; *R*-(−)-II, 14182-54-8; *S*-(+)-II, 14182-55-9; *S*-(+)-III, 13490-74-9; *R*-(−)-III, 14182-57-1; (±)-III, 2328-25-8; *R*-(−)-V, 14182-59-3; *S*-(+)-VI, 13448-68-5; dibenzyl sulfone, 620-32-6; diphenyl sulfone, 127-63-9; *R*-(−)-2-phenyl-2-phenylmercaptopropanoic acid, 14182-43-5.

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