

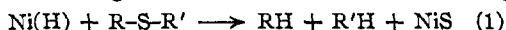
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The Source of Hydrogen in Reductive Desulfuration

BY WILLIAM A. BONNER

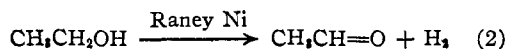
The literature records conflicting postulates as to the source of hydrogen in reductive desulfuration reactions. One suggestion maintains that surface-bound hydrogen on the nickel catalyst is the source; the other maintains that the hydrogen is furnished by the nickel catalyzed conversion of the ethanol solvent to acetaldehyde. Several critical experiments, involving the action of Raney nickel on β -thionaphthol under varying conditions, have been conducted to determine which hypothesis is correct. The results leave little doubt that the hydrogen for reductive desulfuration is provided by that bound to the catalyst.

For the commonly employed process of Raney nickel desulfuration (1) there have been several suggestions as to the source of the hydrogen producing hydrogenolysis. In one of the earliest general investigations of this reaction Mozingo



and co-workers suggested¹ that surface-bound hydrogen acted as the hydrogen source. This was a logical deduction from the finding¹ that one gram of Raney nickel catalyst prepared in the ordinary way held around 40–120 ml. of hydrogen bound to it in some unspecified fashion. Later workers have held² to this view and, indeed, Hauptmann has recently provided³ evidence suggesting that Reaction (1) is followed only if surface hydrogen is present. Thus with catalyst samples partially or completely free of hydrogen by heating *in vacuo*, diaryls, diaryl sulfides and stilbenes, rather than simple aromatics, were obtained when nickel acted on aromatic mercaptals, mercaptols, disulfides and thioesters in xylene solution.

An alternative suggestion as to the source of the hydrogen in reductive desulfuration was advanced by Wolfrom and Karabinos,⁴ who noted the production of acetaldehyde as a by-product when Raney nickel in dilute ethanol converted heptanal diethyl mercaptal to heptane and ethane. Basing their reasoning on the known fact⁵ that Raney nickel converts alcohols to aldehydes or ketones in the presence of a hydrogen acceptor (such as an olefin), they suggested that the ethanol solvent might provide hydrogen for the desulfuration, the net Reaction (2) presumably applying.



In connection with another problem it became necessary for us to know accurately the source of hydrogen in reductive desulfuration and to decide experimentally between these conflicting hypotheses.

When β -thionaphthol was refluxed in ethanol with Raney nickel, and an air current passed through the apparatus and into a solution of 2,4-dinitrophenylhydrazine (I) naphthalene was formed

(1) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *THIS JOURNAL*, **65**, 1013 (1948).

(2) G. W. Kenner, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 957 (1948).

(3) H. Hauptmann, B. Wladislaw and P. F. Camargo, *Experientia*, **4**, 385 (1948); H. Hauptmann and B. Wladislaw, *THIS JOURNAL*, **72**, 707, 711 (1950).

(4) M. L. Wolfrom and J. V. Karabinos, *ibid.*, **66**, 909 (1944); H. G. Fletcher, Jr., and N. K. Richtmyer, "Advances in Carbohydrate Chemistry," Vol. V, Academic Press, Inc., New York, N. Y., 1950, p. 2.

(5) W. Reeves and H. Adkins, *THIS JOURNAL*, **62**, 2874 (1940); E. C. Kleiderer and E. C. Kornfeld, *J. Org. Chem.*, **13**, 465 (1948).

quantitatively. The quantity of acetaldehyde 2,4-dinitrophenylhydrazone (II) isolated, however, amounted to only about 11% of that theoretically required by Reaction (2). Approximately identical quantities of II were obtained in blank runs lacking the β -thionaphthol. Thus Raney nickel apparently slowly catalyzes Reaction (2) at reflux temperature whether a sulfur compound or other hydrogen acceptor is present or not.

Similarly, when β -thionaphthol was refluxed with Raney nickel in benzene solution, naphthalene was produced in a yield identical with that obtained using alcohol. Here Reaction (2) could not possibly provide a source of hydrogen, yet the product and yield were not altered.

While the above results leave little doubt that surface-bound hydrogen is the source available for reductive desulfuration, the following confirmatory evidence was obtained. When β -thionaphthol was refluxed in ethanol containing "hydrogen-free" Raney nickel⁶ it was converted to β -naphthyl disulfide. The quantity of II formed on sweeping air through the system again corresponded only to the blank. It is interesting to note here that, while surface-bound hydrogen is essential for the normal Reaction (1), Reaction (2) proceeds independently of its initial presence or absence. When benzene was used as solvent with "hydrogen-free" nickel, β -naphthyl disulfide was again obtained, a result in general agreement with those of Hauptmann and Wladislaw.

In the conversion of β -thionaphthol to either naphthalene or β -naphthyl disulfide, hydrogen must be eliminated from the -SH group. It is conceivable that our failure to isolate acetaldehyde in the theoretically predicted quantity from reactions in ethanol might be the result of catalytic recombination with hydrogen by reversal of Equation (2). That this explanation is groundless, however, is shown by the fact that the quantity of II produced when ethyl sulfide was desulfurated again corresponded only to that obtained in blank experiments.

Experimental

Raney Nickel and Ethanol.—To see if Reaction (2) occurred in the absence of a hydrogen acceptor Raney nickel⁶ (20 g.) and ethanol (50 ml.) were refluxed for 45 minutes. During this period an air stream was passed through the vessel and conducted through a sintered glass bubbler into a tower containing a solution of I. This solution was prepared by dissolving 5 g. of I in sulfuric acid (25 ml.), diluting with methanol (100 ml.) and then water (100 ml.). The entire solution was used. During the specified time 0.25 g. of II precipitated, m.p. 137–138°. Since oxygen of the air might have been the hydrogen acceptor in this blank, the

(6) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).

process was continued for two hours sweeping with a stream of nitrogen. Here 0.45 g. of II resulted, m.p. 137°. The solid samples were combined and recrystallized from a mixture of ethyl acetate and ethanol, m.p. 147.5–148°, mixed m.p. with an authentic sample of II (m.p. 148.5°) 148–148.5°. In another blank run on a second batch of Raney nickel, bubbling the air stream through (rather than blowing over) the catalyst bed, 1.35 g. of II, m.p. 145° resulted after four hours. No. II was formed on adding a solution of I to the supernatant ethanol over Raney nickel at room temperature even when the catalyst had been standing for over a year.

Raney Nickel, β -Thionaphthol and Ethanol.— β -Thionaphthol (3.2 g.), Raney nickel (30 g.) and ethanol (60 ml.) were refluxed in an air stream as above. A precipitate of II began forming in the I solution after forty minutes. At the outset of precipitation of II a sample of the reaction mixture was withdrawn, filtered of catalyst and evaporated dry. The residue smelled of naphthalene and gave a negligible qualitative test for sulfur, suggesting completion of the reaction. After 3.5 hours 0.50 g. of II was collected. The catalyst was filtered, rinsed with hot ethanol and the filtrate evaporated to dryness, leaving 2.0 g. (78%) of naphthalene, m.p. after recrystallization from dilute ethanol 78–80°, no mixed m.p. depression with an authentic sample. The theoretical quantity of II in the above reaction would be 4.5 g. if the hydrogen of Equation (2) were involved in the reductive desulfurization.

When 2.5 g. of naphthalene was dissolved in a comparable quantity of ethanol and distilled to dryness 2.0 g. (80%) remained. This suggests that the actual production of naphthalene in the above experiment was quantitative.

One ml. of acetaldehyde, spent Raney nickel (30 g.) and ethanol (60 ml.) were refluxed in the usual apparatus, sweeping with an air stream. The formation of II in the bubbler was instantaneous. After 90 minutes 3.95 g. (99%) of II was collected, m.p. and mixed m.p. 145–146°. This result indicates that any acetaldehyde produced by Reaction (2) would be quantitatively accounted for.

Raney Nickel, β -Thionaphthol and Benzene.—Raney nickel (30 g.) under absolute ethanol was filtered, rinsed with benzene and transferred to a flask under 70 ml. of benzene. The mixture was distilled (ca. 20 ml.) to remove remaining ethanol azeotropically, then treated with β -thionaphthol (3.2 g.). After four hours of reflux the catalyst was filtered and rinsed with hot benzene. It was still strongly pyro-

phoric, indicating the presence of adsorbed hydrogen. The filtrate was evaporated leaving 2.0 g. (78%) of naphthalene, m.p. 78–80° after recrystallization from dilute ethanol.

"Hydrogen-free" Raney Nickel.—This was made by heating Raney nickel at 200° at oil-pump pressure, after the general method of Hauptmann and Wladislaw.³ Benzene was admitted over the nickel after completion of the heating without first breaking the vacuum.

"Hydrogen-free" Raney Nickel, β -Thionaphthol and Ethanol.—About 12 g. of "hydrogen-free" Raney nickel was decanted of benzene and washed into the usual apparatus with 80 ml. of ethanol. Approximately 15 ml. of solvent was distilled to remove residual benzene. β -Thionaphthol (1.5 g.) was added, and the mixture refluxed in an air stream for 3.5 hours. Before the first hour the white reaction product was noticeable in the flask containing the catalyst. During this period 0.18 g. of II was formed in the bubbling tower. The catalyst was filtered, rinsed thoroughly with boiling acetone and the filtrate stripped of solvent to give 0.75 g. (50%) of β -naphthyl disulfide, m.p. after recrystallization from a mixture of acetone and ethanol 141.5–142°. A mixed m.p. with an authentic sample prepared below was undepressed. Similar results were obtained with "hydrogen-free" Raney nickel when benzene replaced ethanol as the solvent.

β -Naphthyl Disulfide.— β -Thionaphthol (3.2 g.) was dissolved in acetic acid (50 ml.) and treated with 30% hydrogen peroxide (1.2 g., 6% excess) at 25°. On standing overnight the flask filled with tan crystals, 2.15 g. (68%), m.p. 139–140°. After two recrystallizations from a mixture of acetone and ethanol the m.p. was constant at 141–141.5°. Cleve⁷ gives the m.p. of β -naphthyl disulfide as 139°.

Raney Nickel, Ethyl Sulfide and Ethanol.—Ethyl sulfide (1.3 g.), Raney nickel (20 g.) and ethanol (40 ml.) were refluxed in the usual apparatus. After 90 minutes II began to precipitate in the bubbler and 0.97 g. was filtered after three hours. Hydrogen sulfide was noted on adding hydrochloric acid to the spent catalyst. The theoretical quantity of acetaldehyde from Reaction (2) would here give 3.4 g. of II. About one gram would be predicted from the previous runs. The amount produced is thus only equivalent to the blank.

(7) P. T. Cleve, *Ber.*, **21**, 1099 (1888).

STANFORD, CALIFORNIA

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Stereochemical Paths of Reductive Desulfuration

BY WILLIAM A. BONNER

To determine the stereochemical fate of an asymmetric center adjacent to a sulfur atom during reductive desulfuration with Raney nickel, 2-phenyl-2-phenylmercaptopropionic acid has been synthesized and resolved into both enantiomorphs. The resolved acids were converted into their amides, and the latter subjected to reductive desulfuration. The products obtained were completely racemic, a result which accords with a previously proposed free radical mechanism. When the enantiomorphous 2-phenyl-2-phenylmercaptopropionamides were oxidized to the corresponding sulfones, however, and the sulfones desulfurated with Raney nickel, the products were optically active, enantiomorphous, and about 90% optically homogeneous. Hydrogen bonding between the sulfone and amide groups has been eliminated as a possible explanation for the differing stereochemical paths followed by sulfides and sulfones on desulfuration. The results indicate that sulfones are not desulfurated *via* intermediate sulfides, and that mechanistically the two desulfuration paths are distinct. An alternative mechanism involving direct displacement and inversion is postulated for sulfone desulfuration, and optical evidence is presented suggesting that inversion indeed occurs.

Despite a rapidly growing literature concerning practical applications of the Raney nickel catalyzed reductive desulfuration process, very little is known regarding the essential nature of this useful reaction. While, as considered later, several mechanistic proposals have been advanced little actual experimental work has been undertaken to provide mechanistic information. In particular, the stereochemical course of reductive desulfuration has not been elucidated. While it is known from work with

carbohydrates,¹ biotin² and amino acids³ that the conditions of reductive desulfuration do not engender change in an asymmetric center situated at a

(1) H. G. Fletcher, Jr., and N. K. Richtmyer, "Advances in Carbohydrate Chemistry," Vol. V, Academic Press, Inc., New York, N. Y., 1950, chap. I; W. A. Bonner and J. E. Kahn, *THIS JOURNAL*, **73**, 2241 (1951); W. A. Bonner, *ibid.*, **73**, 2659 (1951).

(2) V. du Vigneaud, D. B. Melville, K. Folkers, D. E. Wolf, R. Mozingo, J. C. Keresztesy and S. A. Harris, *J. Biol. Chem.*, **146**, 475 (1942).

(3) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *THIS JOURNAL*, **65**, 1013 (1943).