3β-Diethylaminocholestane.—A mixture of 0.99 g. (0.0025 mole) of cholestanone, 0.75 ml. of formic acid (0.02 mole) and 1.0 ml. (0.01 mole) of diethylamine was heated at 134° for 5 hours. The basic product was chromatographed on alumina. Elution with 700 ml. of low-boiling petroleum ether gave 0.18 g. of an oil which could not be induced to crystallize. This isomer may be assigned the 3α-configuration since it is the less polar of the two isomers (*vide infra*). The picrate crystallized as needles from ethanol, m.p. 176–179°.

Anal. Calcd. for $C_{37}H_{60}N_4O_7 \cdot {}^1/_2C_2H_5OH$: C, 65.58; H, 9.12; N, 8.05. Found: C, 65.37, 65.44; H, 8.78, 8.83; N, 7.98, 8.55.

Further elution with low-boiling petroleum ether containing benzene gave 0.52 g. of a solid which on crystallization from acetone gave 0.45 g. (41%) of 3β-diethylaminocholestane as colorless plates, m.p. 101.5–103.5°, $[\alpha]_D$ +20°.

Anal. Calcd. for $C_{31}H_{57}N$: C, 83.90; H, 12.94; N, 3.16. Found: C, 83.92; H, 13.24; N, 3.24.

The picrate crystallized as plates from ethanol, m.p. 137–139° (solidified) and 147–148°.

Anal. Calcd. for $C_{37}H_{60}N_4O_7$: C, 66.04; H, 8.99; N, 8.33. Found: C, 66.32; H, 9.19; N, 8.52.

3β- and 3α-Benzylaminocholestane.—Cholestanone (0.99 g., 0.0025 mole), benzylamine (1.07 g., 0.01 mole) and formic acid (0.75 ml., 0.02 mole) were heated at 174–179° for 9.5 hours. Hydrolysis of the formamide was effected directly by adding 4 ml. of concentrated hydrochloric acid and 30 ml. of absolute ethanol. Heating at reflux for 18 hours was followed by addition of 100 ml. of water. The precipitated hydrochloride salts were collected and washed with water and ether. Basification of the salts with potassium hydroxide solution followed by ether extraction gave a mixture of the two amines. Crystallization from acetone gave 0.465 g. (39%) of **3β-benzylaminocholestane** as colorless plates, m.p. 113–115°, $[\alpha]_D$ +16° (lit.[3] m.p. 114–115°, $[\alpha]_D$ +19°).

Chromatography of the residual basic material on alumina gave 0.15 g. of a solid on elution with 1:1 low-boiling petroleum ether–benzene. Crystallization from acetone gave 0.10 g. (8%) of **3α-benzylaminocholestane** as colorless plates, m.p. 74–76°, $[\alpha]_D$ +27° (lit.[3] m.p. 75–77°, $[\alpha]_D$ +27°).

3α- and 3β-Cyclohexylaminocholestane.—A mixture of 0.99 g. (0.0025 mole) of cholestanone, 0.99 g. (0.01 mole) of cyclohexylamine and 0.75 ml. of formic acid was heated at 176° for 8 hours. Hydrolysis of the amide under the conditions used for the benzylaminocholestanes gave a mixture of cyclohexylaminocholestanes which could not be separated by crystallization from acetone. Chromatography on alumina gave two fractions. Elution with 2:1 low-boiling petroleum ether–benzene gave 0.095 g. (8%) of **3α-cyclohexylaminocholestane**, m.p. 103.5–105.5°, $[\alpha]_D$ +21°.

Anal. Calcd. for $C_{33}H_{59}N$: C, 84.36; H, 12.66; N, 2.98. Found: C, 84.00; H, 12.31; N, 3.25.

Elution with benzene–ether mixtures gave 0.105 g. (9%) of **3β-cyclohexylaminocholestane**, m.p. 142–144.5° (colorless needles from acetone), $[\alpha]_D$ +18° (lit.[4] m.p. 140–141°, $[\alpha]_D$ +17°).

NEW BRUNSWICK, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

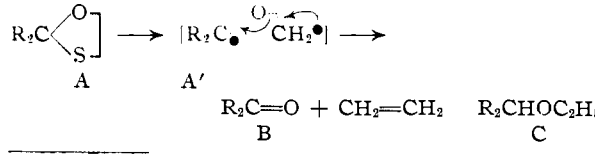
Studies in Organic Sulfur Compounds. X.[1] The Scope of the Raney Nickel Desulfurization of Cyclic Hemithioketals (1,3-Oxathiolanes and 1,3-Oxathianes)[2]

BY CARL DJERASSI, M. SHAMMA[3a] AND T. Y. KAN[3b]

RECEIVED JANUARY 20, 1958

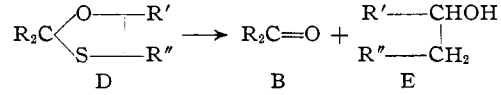
The synthesis of 1,1-diphenyl-4-mercapto-2-butanol and thence of substituted 1,3-oxathianes has been described. A detailed parallel study of the desulfurization of 1,3-oxathiolanes and 1,3-oxathianes has led to the following results. In ketonic solvents, desulfurization of 1,3-oxathiolanes and 1,3-oxathianes proceeds in the same manner by "oxygen introduction" leading to the corresponding ketone and alcohol fragments in good yield. Modifications in the structure of the hemithioketal can alter the product composition to an appreciable extent and furnish a certain proportion of the corresponding substituted ethyl or propyl ether. The isolation of 3α-ethoxycholestane (XXIa) from several desulfurizations of spiro-(1,3-oxathiolane-2,3′-cholestane) (XX) has a bearing on the mode of formation and stereochemistry of this hemithioketal. A mechanism is proposed for the "oxygen introduction" step involving an intermediate hemiketal and this is based on the facile cleavage of hemithioketals under mild alkaline conditions. This observation greatly increases the utility of such derivatives as protecting groups for carbonyl functions. In benzene solution under anhydrous conditions, the desulfurization proceeds by different paths depending upon ring size. 1,3-Oxathiolanes yield almost exclusively the ketone and corresponding hydrocarbon, each in high yield and it is suggested that this reaction proceeds *via* a 1,4-diradical. On the other hand, the desulfurization of 1,3-oxathianes in benzene solution is more complex and leads to variable amounts of ketone, alcohol, ether and hydrocarbons.

The desulfurization of 5-membered hemithioketals (1,3-oxathiolanes) (A) with Raney nickel catalyst in acetone solution was found[4] to yield the corresponding ketone B rather than ethyl ether C and the following mechanism was suggested initially



A A′ B C

Subsequently,[5] it was observed in work with appropriately substituted hemithioketals[6] (D) that the course of this Raney nickel desulfurization was more complex and that in addition to the ketone B an alcohol E corresponding to the other fragment was formed. In fact, the yield of B and E each exceeded 50% which meant that oxygen had to be introduced from an outside source.



D B E

We have now examined in more detail the structural and experimental scope of this reaction and have discovered that depending upon the circum-

(1) Paper IX, C. Djerassi and J. Grossman, THIS JOURNAL, **79**, 2553 (1957).

(2) This work was carried out in part under contract No. DA-20-018-ORD-13474 with the Office of Ordnance Research, U. S. Army.

(3) (a) Postdoctorate Research Fellow (1955–1956); (b) Monsanto Predoctorate Research Fellow (1956–1957).

(4) J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4961 (1951).

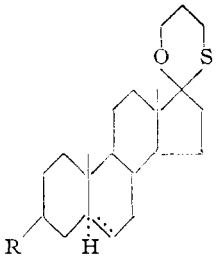
(5) C. Djerassi, M. Gorman and J. A. Henry, *ibid.*, **77**, 4647 (1955).

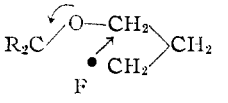
(6) C. Djerassi, M. Gorman, F. X. Markley and E. B. Oldenburg, *ibid.*, **77**, 568 (1955).

stances its direction could be modified appreciably. Furthermore, certain observations were made which point toward the probable mechanism of the "oxygen introduction" step in the desulfurization D → B + E.

Synthesis of Starting Materials.—As pointed out in an earlier communication,[5] proper identification of both fragments in the desulfurization of hemithioketals requires substitution of the β-mercaptoethanol moiety in order to facilitate the isolation of products such as E. This approach already has been used with considerable success[5] with 5-membered hemithioketals (1,3-oxathiolanes) (D) and it was felt that this work ought to be extended to the 6-membered homologs—the 1,3-oxathianes—since this might offer a means of testing the 1,4-diradical mechanism proposed originally[4] (see A → B). Indeed, such *un*substituted trimethylene hemithioketals derived from γ-mercaptopropanol already have been described[7] and two of them, spiro-(1,3-oxathiane-2,17′-androstane) (I) and the corresponding Δ^5-3β-alcohol (II), already have been treated[8] in acetone or benzene solution with Raney nickel catalyst whereupon the appropriate 17-ketone was isolated in good yield.

A priori, this would definitely rule out a 1,4-diradical mechanism of the type outlined above (A′) but the possibility could not be excluded—in the absence of isolation of the corresponding three carbon fragment—that a cyclopropane intermediate F might be involved. In order to examine this 1,5-diradical alternative as well as the product composition under different desulfurization conditions, it was necessary to prepare certain substituted 1,3-oxathianes and this in turn required a supply of the requisite substituted γ-mercaptopropanol.



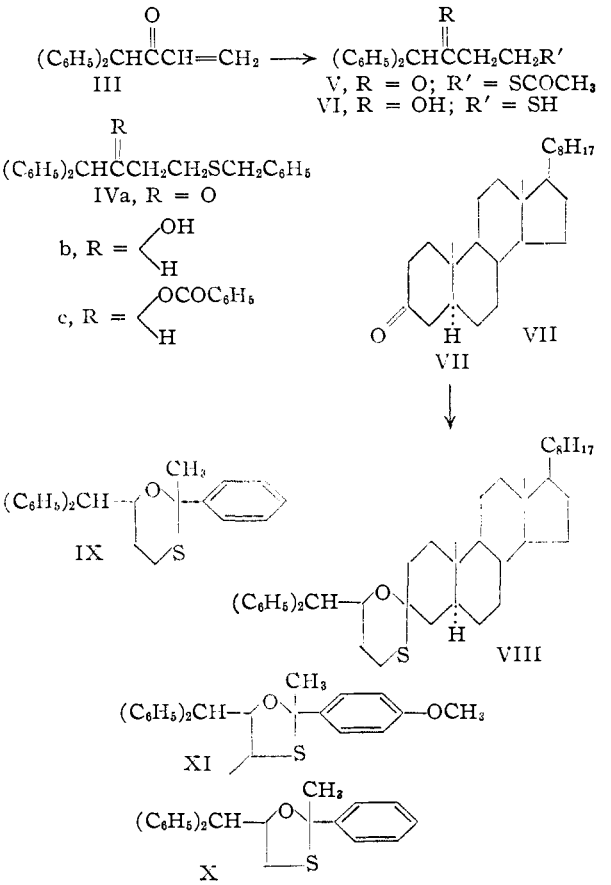


I, R = H
II, R = OH; double bond at 5-6

Our original work[5] in the 1,3-oxathiane series indicated that a benzhydryl substituent was sufficiently bulky so as to lead to easily recognizable fragments and our immediate attention was directed toward the synthesis of 1,1-diphenyl-4-mercapto-2-butanol (VI). The earlier reported[6] synthesis of substituted β-mercaptoethanols by lithium aluminum hydride reduction of α-ketoxanthates did not appear feasible for the higher homolog and consequently the readily available[9] 1,1-diphenylbut-3-en-2-one (III) was treated with benzyl mercaptan in the presence of piperidine to afford 1,1-diphenyl-4-benzylthiobutan-2-one (IVa). It was intended to subject this substance to debenzylation[10] with sodium in liquid ammonia but irrespective of whether the ketone IVa, the alcohol IVb or the benzoate IVc was employed, none of the desired mercaptan VI was encountered.

An alternate and successful method involved the addition[11] of thiolacetic acid to the unsaturated ketone III followed by lithium aluminum hydride reduction of the thiolacetate V which yielded directly the required γ-mercaptopropanol VI. The latter was condensed with cholestan-3-one (VII) whereupon two of the four possible diastereoisomers of the hemithioketal VIII could be isolated and these served as important substrates for the desulfurization experiments described in the sequel.

Since free radicals may play an important role[12] in Raney nickel desulfurizations, it also was desirable to have available some hemithioketals in which a relatively stable benzyl free radical might be formed. For this purpose, acetophenone was condensed with 1,1-diphenyl-4-mercapto-2-butanol (VI) as well as with 1,1-diphenyl-3-mercapto-2-propanol[6] to yield 2-methyl-2-phenyl-6-benzhydryl-1,3-oxathiane (IX) and its 5-membered analog 2-methyl-2-phenyl-5-benzhydryl-1,3-oxathiolane (X). Then substituting *p*-methoxyacetophenone for acetophenone, 2-methyl-2-(*p*-methoxyphenyl)-5-benzhydryl-1,3-oxathiolane (XI) also was synthesized in order to be able to examine in at least one instance the effect of a *p*-methoxy substituent upon the course of the desulfurization.



(7) C. Djerassi and M. Gorman, THIS JOURNAL, **76**, 3704 (1953).
(8) M. Gorman, Ph.D. Thesis, Wayne State University, 1955, p. 138.
(9) W. Wilson and Z. Y. Kyi, *J. Chem. Soc.*, 1321 (1952).
(10) R. H. Sifferd and V. du Vigneaud, *J. Biol. Chem.*, **108**, 753 (1935).
(11) R. Brown, W. E. Jones and A. R. Pinder, *J. Chem. Soc.*, 2123 (1951), and references cited therein.
(12) For leading references see G. M. Badger and W. H. F. Sasse, *ibid.*, 3862 (1957).

TABLE I

DESULFURIZATION OF SPIRO-(5-BENZHYDRYL-1,3-OXATHIOLANE-2,3'-CHOLESTANE) (XII)

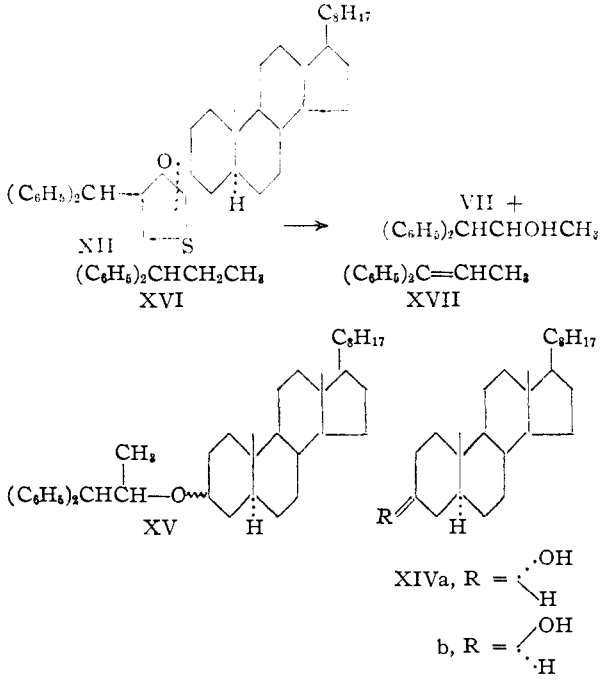
Expt.	Age of W-2 Raney nickel catalyst, days	Solvent	Reflux time, hr.	Yield, %, of desulfurization products: Cholestan-3-one (VII)	$(C_6H_5)_2CHCHOHCH_3$ (XIII)	$(C_6H_5)_2C{=}CHCH_3$ (XVII)	$(C_6H_5)_2CHCH_2CH_3$ (XVI)
1[e,f]	2	$C_2H_5COCH_3$[c]	19.5	85	89	..	..
2[a]	2	$C_2H_5COCH_3$	24.0	90[h]	64	..	..
3[b]	30	$C_2H_5COCH_3$[d]	24.0	55[i]	78	..	..
4[a,f]	30	C_6H_6–$C_2H_5COCH_3$ (3.1)	7.0	86	..	10	80
5[b,f]	12	C_6H_6	15.0	53[g]	..	20	78
6[b]	16	C_6H_6; N_2	8.0	56[g]	..	..	98
7[b,f]	17	C_6H_6; N_2	9.5	53[g]	..	..	81
8[a]	42	C_6H_6[e]; N_2	12.0	98	..	9	69
9[b]	55	C_6H_6[e]; N_2	12.0	93	..	84	..
10[a,f]	7	C_6H_6–BuOH (1.10)	14.0	42[g]	56–75	..	..

[a] Using isomer A (ref. 5). [b] Using mixture of isomers A, B and C (ref. 5). [c] Catalyst and substrate first azeotroped with benzene and the latter then displaced with freshly dried ethyl methyl ketone. [d] *p*H 6; adjusted by addition of acetic acid. [e] Some material may have been lost during the chromatographic purification. [f] This experiment was performed by Dr. John A. Zderic. [g] Catalyst first deactivated by boiling with acetone for 45 minutes. [h] In addition 7% of cholestan-3β-ol (XIVb) was isolated. [i] In addition, there was encountered 11% of cholestan-3α-ol (XIVa), 16% of cholestan-3β-ol (XIVb) and 9% of the ether XV.

Desulfurization of 1,3-Oxathiolanes.—The occurrence of "oxygen introduction" in the Raney nickel desulfurization (acetone or ethyl methyl ketone solution) of 1,3-oxathiolanes was demonstrated[5] with a variety of substituted 1,3-oxathiolanes (D) (among them spiro-(5-benzhydryl-1,3-oxathiolane-2, 3-cholestane) (XII)) and it was shown that the principal products were cholestanone (VII) and 1,1-diphenylpropan-2-ol (XIII). Proof[1,5] for the complete retention of optical activity (and most probably also of configuration) in the alcohol XIII suggested that the dotted bond in XII had undergone scission during the desulfurization step, but not further information could be provided about the mechanism of this reaction. Since the hemithioketal XII lends itself readily to identification of all desulfurization fragments, it was subjected to additional desulfurization experiments, the results of which are summarized in Table I.

Experiments 1, 2, 3 and 10 in Table I show that irrespective of the age of the catalyst (2–30 days) in the *p*H range 6–9 using ethyl methyl ketone or *t*-butyl alcohol as solvents the principal products are cholestan-3-one (VII) (up to 90%) and 1,1-diphenylpropan-2-ol (XIII) (up to 89%), thus demonstrating clearly that oxygen had to be introduced from an outside source. Small amounts of cholestan-3α-ol (XIVa) and cholestan-3β-ol (XIVb) as well as of the ether XV (see run 3 in Table I) were also encountered.

On the other hand, when the reaction was conducted in benzene solution (experiments 4–9 in Table I)—irrespective of whether the catalyst was initially deactivated with acetone or an atmosphere of nitrogen employed—the chief products were cholestan-3-one (VII) (up to 98%) and a mixture of 1,1-diphenylpropane (XVI) and 1,1-diphenylprop-1-ene (XVII).[13] The proportion of saturated and unsaturated hydrocarbon varied, depending on the age of the catalyst (older catalyst apparently being unable to effect further reduction of the olefin XVII) and possibly also on the rate of passage of nitrogen gas which may have removed some hydrogen from the site of reaction. In any event, the outcome of this series of desulfurizations can be summarized by stating that in an inert solvent such as benzene the principal products are the ketone and a hydrocarbon, the latter corresponding to the other structural fragment of the hemithioketal. Mechanistically, the most attractive interpretation for this second type of desulfurization is a 1,4-diradical intermediate (A'),[13] although the situation may well be more complicated as indicated below with certain 1,3-oxathianes.



That a further refinement in the product composition in the desulfurization of 1,3-oxathiolanes is possible could be demonstrated by the introduction of a structural alteration in the ketone moiety of the hemithioketal. As shown in Table III, de-

(13) The olefin expected from a 1,4-diradical mechanism such as A, would be 1,1-diphenylprop-2-ene, but it is conceivable that the double bond undergoes migration on the catalyst surface into conjugation with the aromatic nuclei.

TABLE II

DESULFURIZATION OF SPIRO-(6-BENZHYDRYL-1,3-OXATHIANE-2,3′-CHOLESTANE) (VIII)

Expt.	Age of W-2 Raney nickel catalyst, days	Solvent	Reflux time, hr.	Cholestan-3-one (VII)	Yield, %, of desulfurization products $(C_6H_5)_2CHCHOHC_2H_5$ (XXVII)	$(C_6H_5)_2CHCH_2CH_2CH_3$[c] (XXVIII)	$(C_6H_5)_2CHCH(C_2H_5)$-O-cholestanyl (XXVI)
1[a]	6	$C_2H_5COCH_3$	24	72[e]	67	..	..
2[b]	8	C_6H_6; N_2[d]	18	45	29	30	36
3[a]	40	C_6H_6; N_2[d]	9	56	17	21	24

[a] Using isomer B of VIII. [b] Using isomer A of VIII. [c] The ultraviolet absorption spectrum was identical with that of synthetic 1,1-diphenylbutane and ozonization precluded the presence of appreciable amounts of non-conjugation olefin. [d] Catalyst first deactivated by boiling with acetone for 45 minutes. [e] 13% of cholestan-3α-ol (XIVa) and 11% of cholestan-3β-ol (XIVb) were also isolated.

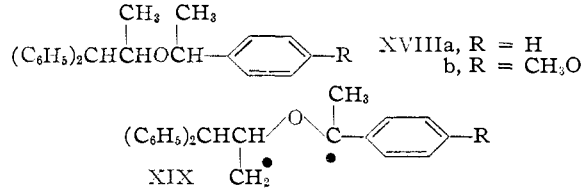
TABLE III

DESULFURIZATION OF 2-METHYL-2-PHENYL-5-BENZHYDRYL-1,3-OXATHIOLANE (X)

Expt.	Age of W-2 Raney nickel catalyst, days	Solvent	Reflux time, hr.	$C_6H_5COCH_3$[c]	Yield, %, of desulfurization products $(C_6H_5)_2CH$-$CHOHCH_3$ (XIII)	$(C_6H_5)_2CHCH(CH_3)$-$OCH(CH_3)C_6H_5$ (XVIIIa)	$(C_6H_5)_2C{=}CHCH_3$ (XVII)	$(C_6H_5)_2CHCH_2CH_3$ (XVI)
1	12	$C_2H_5COCH_3$	12	71	62	..	4	32
2	38[a]	CH_3COCH_3	12	64	37	27	..	30
3	62[a]	CH_3COCH_3	16	47	44	32	..	19
4	12	C_6H_6[b]; N_2	16	67	2	..	96	..
5	32	C_6H_6[b]; N_2	16	86	5	..	90	..

[a] For unknown reasons in a run with 48 day old nickel catalyst (different batch from experiments 2 and 3) in acetone solution, 16% of acetophenone, 16% of 1,1-diphenyl-2-propanol and 80% of ether (XVIIIa) was encountered. [b] Catalyst first deactivated by boiling with acetone for 45 minutes. [c] Identified by infrared spectrum and preparation of 2,4-dinitrophenylhydrazone.

sulfurization of 2-methyl-2-phenyl-5-benzhydryl-1,3-oxathiolane (X) in methyl ethyl ketone (expt. 1) or acetone (expt. 2–3) solution still results in predominant formation of the ketone (acetophenone) and alcohol (1,1-diphenylpropan-2-ol (XIII)), but in addition quite appreciable amounts (19–36%) of hydrocarbon (XVI and XVII) as well as of ether (XVIIIa)[14] also were produced. While the "oxygen introduction" path probably involves nucleophilic attack on carbon (see below), the free radical XIX derived[12] from the hemithioketal X, is more stable (tertiary benzyl free radical) than one derived from a hemithioketal such as XII and probably also more easily formed. Once formed, it can undergo either collapse—yielding acetophenone and hydrocarbon XVI and XVII—or capture hydrogen atoms thus accounting for increased ether (XVIIIa) production. In the benzene runs (4 and 5 in Table III), acetophenone and the hydrocarbon mixture (XVI, XVII) are observed almost exclusively and the absence of ether XVIIIa may be due to the fact that more active catalyst was employed in runs 4 and 5 as compared to 2 and 3.



The introduction of a *p*-methoxy substituent (XI) did not affect greatly the product composition of desulfurizations conducted either in benzene (72% *p*-methoxyacetophenone and 81% 1,1-diphenylpropane) or acetone (36% *p*-methoxyacetophenone, 27% 1,1-diphenylpropan-2-ol and 42% ether (XVIIIb)) solution and the quantitative differences between these results and the ones recorded in Table III may not be significant since different batches of Raney nickel catalyst were employed.[15]

Further work bearing on the possible mechanism of the "oxygen introduction" step was conducted with the (4,5)-unsubstituted hemithioketal XX derived[4] from β-mercaptoethanol and cholestan-3-one (VII). Desulfurization in acetone solution (run 1, Table V) yielded as the principal product the expected[4] cholestan-3-one (VII) accompanied by some cholestan-3α- and 3β-ol (XIVa, b), which are probably produced by further reduction of cholestan-3-one (VII).[16] Of interest is the observation that a small amount (*ca.* 3%) of the corresponding ethyl ether was isolated and this could be identified as cholestan-3α-ol ethyl ether (XXIa) by comparison with synthetic specimens of the 3α- (XXIa) and 3β- (XXIb) ethers prepared by Williamson syntheses from the corresponding alcohols (XIVa, b). The fact that none of the crystalline 3β-ether XXIb was isolated in any of the desulfurizations (see runs 1–4, 6, 7 in Table V) would appear to have a bearing on the stereochemistry of the hemithioketal XX and its mode of formation. The simplest explanation is that the hemithioketal has the stereochemistry implicit in structure XX and while initial attack by β-mercaptoethanol on C-3 of cholestan-3-one (VII) surely involves entrance of sulfur from the unhindered α-side to yield the intermediate XXII, subsequent ring closure to XX proceeds *via* an intermediate (2–3 double bond or C-3 carbonium ion) which

(14) The structure of the ether follows from the analytical and spectroscopic data as well as from analogy to the *p*-methoxy analog XVIIIb, whose constitution was established by synthesis.

(15) Although the catalyst used through this work was always prepared by the same procedure (R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., p. 181), the activity of different batches varied and in work extending over a period of two years, it is obviously impossible to eliminate this factor.

(16) The ease and steric course of reduction of 3-keto steroids is greatly dependent upon the age of catalyst and the solvent (see C. Djerassi, A. J. Manson and M. Gorman, THIS JOURNAL, **77**, 4925 (1955)), but in this instance fresh catalyst was employed.

TABLE IV

DESULFURIZATION OF 2-METHYL-2-PHENYL-6-BENZHYDRYL-1,3-OXATHIANE (IX)

Expt.	Age of W-2 Raney nickel catalyst, days	Solvent	Reflux time, hr.	Yield, %, of desulfurization products $C_6H_5COCH_3$	$(C_6H_5)_2CHCHOHC_2H_5$ (XXVII)	$(C_6H_5)_2CHCH(C_6H_5)$-$OCH(CH_3)C_6H_5$[a] (XXX)	$(C_6H_5)_2CHCH_2CH_2CH_3$[b] (XXVIII)
1	8	$C_2H_5COCH_3$	12	81	56	20	..
2	39	CH_3COCH_3	16	72	59	13	..
3	56	CH_3COCH_3	16	75	57	15	..
4	19	C_6H_6[c]; N_2	16	45	23	27	19
5	53	C_6H_6[c]; N_2	16	57	4	36	57

[a] Eluted in the chromatogram with hexane immediately after 1,1-diphenylbutane (XXVIII). The viscous oil exhibited no infrared hydroxyl or carbonyl absorption. *Anal.* Calcd. for $C_{24}H_{26}O$: C, 87.23; H, 7.93; O, 4.84. Found: C, 87.26; H, 7.38; O, 5.20. [b] The ultraviolet absorption spectrum was identical with that of synthetic 1,1-diphenylbutane and ozonization precluded the presence of appreciable amounts of non-conjugated olefin. [c] Catalyst first deactivated by boiling with acetone for 45 minutes.

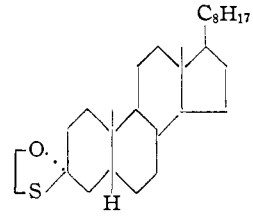
TABLE V

DESULFURIZATION OF SPIRO-(1,3-OXATHIOLANE-2,3′-CHOLESTANE) (XX)

Expt.	Age of W-2 Raney nickel catalyst, days	*p*H	Solvent	Reflux time, hr.	Yield, %, of desulfurization products Cholestan-3-one (VII)	Cholestanol 3α-(XIVa)	Cholestanol 3β-(XIVb)	3α-Ethoxycholestane (XXIa)
1	5	*Ca.* 8.5	CH_3COCH_3	4	64	12	19	3
2	8	6.75[a]	CH_3COCH_3	4	70	6	8	13
3	20	6.0[a]	CH_3COCH_3	4	67	6	8	12
4	67	4.2[a]–5.7[b]	CH_3COCH_3	5	87	2	6	5
5[c]	70, H_2-free		CH_3COCH_3	12	..	..	..	..
6	2	*Ca.* 8.5	C_6H_6	4	34[d]	..	..	31
7	13	*Ca.* 8.5	C_6H_6[e]; N_2	12	58	18	14	10

[a] *p*H adjusted by addition of acetic acid. [b] *p*H at end of reaction. [c] The unchanged hemithioketal was recovered. [d] Some material may have been lost during the chromatographic separation. [e] Catalyst first deactivated by boiling with acetone for 45 minutes.

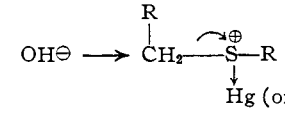
destroys the stereochemistry of XXII and permits again attack—this time by oxygen—from the unhindered α-side to furnish XX. If the latter postulate were not true, either a mixture of hemithioketals or the isomer with a C–S (α) and C–O (β) bond should be produced.



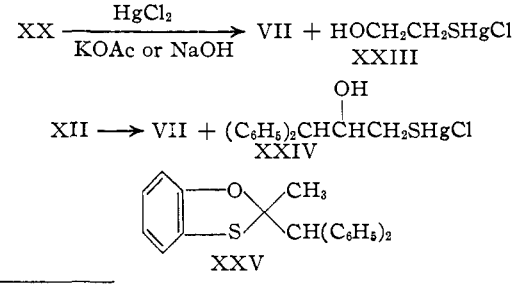
XX

XXIa, R = C_2H_5O; R_1 = H
b, R = H; R_1 = C_2H_5O
XXII, R = $HOCH_2CH_2S$–; R_1 = OH

Perhaps the most obvious factor responsible for "oxygen introduction" might be hydroxide ion, since Raney nickel catalyst is prepared by treatment of nickel–aluminum alloy with sodium hydroxide. Conventionally washed Raney nickel catalyst exhibits a *p*H of approximately 8–9 when suspended in water and several experiments were conducted (see runs 2, 3, 4, in Table V) in which it was attempted to eliminate this possibility by conducting the desulfurization on the acid side. The composition of the desulfurization products was substantially the same and it is probable that these experiments are of very little significance since it is virtually impossible to remove all base without affecting the composition of the catalyst. The *p*H adjustments indicated in Table V were carried out by addition of acetic acid and it was noted in blank experiments that the initial acidic *p*H slowly rose to neutrality or above, when stirring with water or solvent was carried out for several hours. Even in the most significant experiment (run 4, Table V) where the initial *p*H was 4.2 and had changed only to 5.7 at the end of the desulfurization, it is not certain whether all base had been removed. The important potential role of hydroxide ions is demonstrated by the work of Grob,[17] who has shown that certain substituted tetrahydrothiophenes readily undergo ring opening when treated with base in the presence of mercury or silver salts, probably by the mechanism



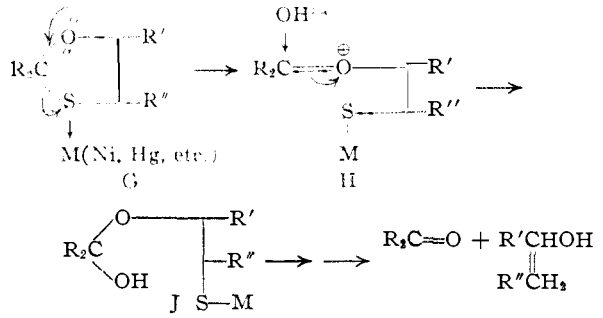
In point of fact when the hemithioketal XX was heated with acetic acid containing potassium acetate, no reaction occurred, but when mercuric chloride was added 80% of cholestanone (VII) and 77% of the mercuric chloride salt XXIII could be isolated. The reaction also could be conducted in ethanol solution with mercuric chloride and one equivalent of sodium hydroxide yielding 91% of



(17) C. A. Grob, unpublished observation. We are greatly indebted to Prof. Grob (University of Basel) for a stimulating discussion and for his courtesy in supplying us with experimental details of his unpublished experiments.

cholestan-3-one (VII) and 52%[18] of the salt XXIII. Similarly, the substituted hemithioketal XII gave cholestan-3-one (VII) and the mercuric chloride salt XXIV when treated in acetic acid solution with mercuric chloride and potassium acetate. The structures of the salts XXIII and XXIV were proved in each case by independent synthesis from the appropriate β-mercaptoethanol and mercuric chloride.

The above experiments not only demonstrate further the utility of the hemithioketal moiety as a protecting group for carbonyl derivatives—removable by Raney nickel treatment as well as by Grob's method[17]—but also suggest a possible mechanism for the "oxygen introduction" step in the desulfurization of cyclic hemithioketals. Coördination of the electron-deficient metal with sulfur yields a species (G), which—aided by the electron pair on oxygen—opens to H. The latter can now suffer attack by hydroxide ion present in the reaction medium (or chemically combined with the catalyst) leading to the hemiketal (J) which is cleaved in the subsequent work-up. The sulfur is lost by the usual[12] free-radical desulfurization mechanism—either at the hemiketal stage or after decomposition (into ketone and β-mercaptoethanol)—depending upon the composition of the solution.



In order to demonstrate that Raney nickel can fulfill the role of the metal (see G), thus strengthening the above proposed mechanism, a sample of old W-2 Raney nickel catalyst was rendered hydrogen-free[19] by heating at 200° *in vacuo*. The resulting catalyst in acetone solution did not affect the hemithioketal XX (see experiment 5 in Table V), but when the same sample was suspended in acetic acid solution containing some potassium acetate, 67% of cholestan-3-one (VII) was isolated in addition to 28% of unreacted hemithioketal (XX).

In order to rationalize the absence of "oxygen introduction" when the desulfurization is conducted in benzene rather than acetone or methyl ethyl ketone solution,[20] it probably can be assumed that in benzene no ionic intermediates are involved and the reaction proceeds chiefly by a free radical pathway.

(18) The actual yield of this salt is certainly appreciably higher, but in that particular medium difficulties are encountered in isolating all of it.

(19) H. Hauptmann, B. Wladislaw, L. L. Nazario and W. F. Walter, *Ann.*, **576**, 45 (1952).

(20) It should be appreciated that such solutions contain large amounts of isopropyl alcohol or 2-butanol—formed by Raney nickel catalyzed reduction of the ketones—in which a high concentration of hydroxide ion can be expected.

Incidental to the above studies there was also examined the behavior of a 1,3-oxathiolane derived from *o*-mercaptophenol and for that purpose the readily available[6] 2-benzhydryl-2-methyl-1,3-benzoxathiole (XXV) was selected. In this case irrespective of the reaction conditions (fresh catalyst in acetone solution or old catalyst in benzene) only phenol and hydrocarbon (XVI or XVII) were produced.

The results obtained in the desulfurization of cyclic 5-membered hemithioketals (1,3-oxathiolanes) can now be summarized as follows: (a) Desulfurization in hydroxylic solvents (alcohols or ketones[20]) yields chiefly *two* oxygenated fragments—the parent ketone and the alcohol corresponding to the original β-mercaptoethanol. The reaction presumably involves nucleophilic attack by hydroxide ion on C-2 of the 1,3-oxathiolane (G → H → J) followed by decomposition of the resulting hemiketal. Some change in the composition of the reaction products is possible by structural alterations of the hemithioketal and is ascribed to increased stability and ease of formation of intermediate free radicals.

(b) In a non-polar solvent, the main products are the ketone and the hydrocarbon (saturated or unsaturated depending upon activity of catalyst), the latter corresponding to the original β-mercaptoethanol. A certain amount of ethyl ether—resulting from simple desulfurization—is also encountered and the formation of all these products is rationalized *via* a free radical intermediate (*e. g.*, A′).

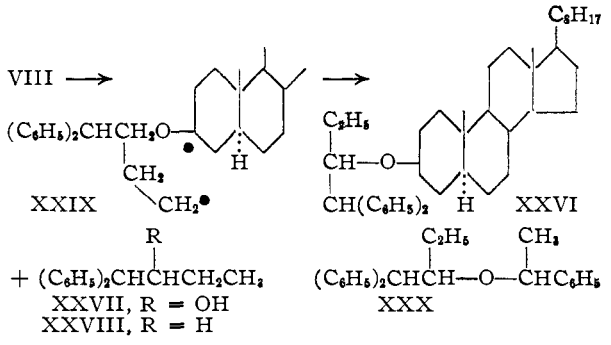
Substitution of a 6-membered hemithioketal (1,3-oxathiane) would, therefore, not be expected to affect postulate (a), but might well give different results in so far as (b) is concerned.

Desulfurization of 1,3-Oxathianes.—Comparative studies were carried out with the 1,3-oxathianes (VIII, IX) derived from cholestan-3-one (VII) and acetophenone and the relevant data are collected in Tables II and IV. As far as the experiments in acetone or ethyl methyl ketone are concerned (run 1, Table II, and runs 1–3, Table IV) the results are substantially the same as those encountered with the corresponding 5-membered analogs (Tables I and III) since in each case "oxygen introduction" was observed to occur as the principal course of the reaction. As indicated above, this is in accord with the suggested mechanism which should not be affected by the size of the heterocyclic ring.

Rather interesting differences were noted when the desulfurization was run in benzene solution. Turning first to spiro-(6-benzhydryl-1,3-oxathiane-2,3′-cholestane) (VIII), run 3 of Table II can be compared with the results of the 5-membered analog (XII) in experiment 8 (Table I) which were performed under substantially the same conditions. Since a 1,4-diradical mechanism (A′) is impossible in the 1,3-oxathiane series and assuming that a cyclopropane intermediate (F) is not involved, one would expect as the major product the ether XXVI. Indeed 24% (36% in run 2 of Table II) of the ether XXVI was isolated in contrast to the complete absence of such ether production in

the 5-membered case. However, the major product (56%) was represented by cholestan-3-one (VII) and in addition there was isolated 17% of 1,1-diphenylbutan-2-ol (XXVII) (the corresponding alcohol XIII was not formed in the 5-membered analog) and 21% of 1,1-diphenylbutane (XXVIII) (compared to 78% of hydrocarbon in the 5-membered analog).

These results, which differ greatly from those encountered with the 5-membered hemithioketal, certainly do not disprove the existence of the 1,4-diradical collapse mechanism (A') for the latter, but they do indicate that the reaction can proceed by several paths. Considerable additional work with differently substituted[21] 1,3-oxathianes would be required to clarify this point, but one possible mechanism—hydrogenolysis[22] of the intermediate ether (*e. g.*, XXVI)—has been excluded by the experimental observation that the substance is recovered in quantitative yield when treated with Raney nickel in benzene solution.



An examination of the benzene desulfurizations (experiments 4 and 5, Table IV) of 2-methyl-2-phenyl-6-benzhydryl-1,3-oxathiane (IX) show, just as with VIII, that the major difference between the 6-membered (IX) and 5-membered (X) hemithioketals lies in the formation (by the former) of appreciable quantities of ether XXX and reduced amounts of hydrocarbon XXVIII. The same explanation offered above in the case of VIII should also apply here.

Experimental[23]

General Procedure Desulfurizations.—The W-2 Raney nickel catalyst was prepared according to Mozingo[15] and ten times the weight of hemithioketal was employed. All reactions were carried out in three-necked flasks with vigorous agitation. The *p*H of catalyst batches was measured with a Beckman *p*H meter and ordinarily washed[15] Raney nickel catalyst exhibited *p*H 8–9. The amount of solvent ranged between 100–200 cc./g. of hemithioketal in different experiments. When acetone or ethyl methyl ketone was employed, the catalyst was first heated under reflux for 30 min. before adding the hemithioketal. In the benzene runs, the catalyst was washed with benzene and then co-distilled with fresh portions of benzene. The hemithioketal was subjected to similar treatment before both solutions were mixed and nitrogen was passed through the reaction mixture continuously unless not indicated in the tables.

After filtering the catalyst, it was extracted with chloroform to remove adhering products and the chloroform extracts were added to the filtrate before processing. In some cases (*e.g.*, desulfurization of XI described below), the ketonic product was separated by Girard fractionation, but in most cases separation was accomplished by careful chromatography. As a concrete example, a **desulfurization of spiro-(6-benzhydryl-1,3-oxathiane-2,3'-cholestane)** (VIII) is described.

The crude product (950 mg.) from the desulfurization of 1.0 g. of hemithioketal VIII (experiment 2 in Table II) in hexane solution was adsorbed on 50 g. of Merck acid-washed alumina. Elution with hexane provided 540 mg. of oil (see below) while further development with hexane–benzene (8:2) led to 305 mg. of cholestan-3-one (VII) identified by mixture melting point determination and infrared comparison. Washing of the column with benzene afforded 105 mg. of (−)-1,1-diphenyl-2-butanol (XXVII),[24] which was distilled at a bath temperature of 140° and 0.03 mm. whereupon it crystallized, m.p. 42–44°, $[\alpha]_D$ −3.7° (*c* 1.2).

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02; O, 7.07. Found: C, 84.43; H, 8.02; O, 7.58.

The 3,5-dinitrobenzoate was prepared in pyridine solution and recrystallized from dilute methanol, m.p. 109–111°, $[\alpha]_D$ +47.9° (*c* 1.1).

Anal. Calcd. for $C_{23}H_{20}N_2O_6$: C, 65.70; H, 4.80; N, 6.66; O, 22.83. Found: C, 65.67; H, 4.75; N, 6.75; O, 22.60.

Thd 540-mg. sample of oil, eluted originally, was rechromatographed on 20 g. of Woelm alumina (activity I). The first hexane eluates yielded 212 mg. of 1,1-**diphenylbutane (XXVIII)**, whose infrared and ultraviolet absorption spectrum[25] was identical with that of a synthetic specimen described below. No appreciable amounts of unconjugated olefin were present as shown by the absence of volatile material (passed into 2,4-dinitrophenylhydrazine solution) produced during ozonolysis of an aliquot.

Anal. Calcd. for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.24; H, 8.87.

Further elution with hexane gave 350 mg. of a thick, pale yellow oil which could not be crystallized but whose analysis indicated that it was the **ether XXVI**, $[\alpha]_D$ +9° (*c* 0.82).

Anal. Calcd. for $C_{42}H_{64}O$: C, 86.51; H, 10.81; O, 2.68. Found: C, 86.40; H, 10.59; O, 2.50.

In all other desulfurizations listed in Tables I–V, the products were identified in each case by infrared comparison and where applicable also by mixture melting point determinations with authentic samples. The only exceptions were **α-phenyl-α'-benzhydryl diethyl ether (XVIIIa)** isolated in experiments 2 and 3 (Table III) as a non-crystallizable oil ($n^{22.5}D$ 1.5692) whose structure followed from its analysis (*Anal.* Calcd. for $C_{23}H_{24}O$: C, 87.30; H, 7.65. Found: C, 86.85; H, 7.74.) and from analogy to the *p*-methoxy derivative (see below), and **α-(benzhydryl)-ethyl cholestanyl ether (XV)**, thick, uncrystallizable oil, $[\alpha]_D$ ±0°.

Anal. Calcd. for $C_{42}H_{62}O$: C, 86.53; H, 10.72. Found: C, 86.16; H, 10.37.

Desulfurization of 2-Methyl-2-(*p*-methoxyphenyl)-5-benzhydryl-1,3-oxathiolane (XI).—A mixture of 0.7 g. of the hemithioketal XI, 7 g. of 6 day old Raney nickel catalyst and 100 cc. of acetone was heated with stirring under reflux for 24 hr. Filtration of the catalyst, evaporation of the filtrate to dryness and boiling of the residue (580 mg.) in 40

(21) In order to exclude the possibility that some of the results are due to participation of the benzhydryl substituent.

(22) J. A. Zderic, W. A. Bonner and T. W. Greenlee (THIS JOURNAL, **79**, 1696 (1957)) have shown that 1,1-diphenyl-2-ethanol undergoes ready hydrogenolysis with Raney nickel catalyst in ethanol solution. The only ether described by them, 1-methoxy-2-phenylpropane, did not react under their conditions but it might have been conceivable that cleavage could occur with other ethers, notably benzyl ethers (as would be derived from IX).

(23) Melting points were determined on the Kofler block and boiling points are uncorrected. Unless noted otherwise, rotations were obtained in chloroform solution. We are indebted to Mrs. Dolores Phillips for the infrared and ultraviolet spectral measurements and to Dr. A. Bernhardt (Mülheim, Germany) for the microanalyses.

(24) Both isomers A and B of the hemithioketal VIII led to the (−)-alcohol XXVII.

(25) In other runs with 1,3-oxathiolanes (Tables I and III) where the hydrocarbon fraction consisted of a mixture of saturated (XVI) and unsaturated (XVII) hydrocarbon, the composition of the mixture always was determined by ultraviolet spectral determination since 1,1-diphenyl-1-propene (XVII) exhibited a maximum at 248 mμ (log ε 3.94), while 1,1-diphenylpropane (XVI) showed considerable amount of fine structure between 240–270 mμ with log ε 2.65–2.83. Furthermore, several samples were subjected to ozonolysis and benzophenone isolated as the 2,4-dinitrophenylhydrazone.

cc. of ethanol and 2 cc. of glacial acetic acid with 2.0 g. of Girard reagent T yielded 400 mg. of non-ketonic and 100 mg. of ketonic material. The latter crystallized on standing and was identified as *p*-methoxyacetophenone by infrared comparison and conversion to the 2,4-dinitrophenylhydrazone, m.p. and mixture m.p. 220–221°. Chromatography of the non-ketonic fraction on 15 g. of Merck acid-washed alumina yielded two products. The first, eluted with hexane, constituted the oily **α-(*p*-methoxyphenyl)-α'-benzhydryl diethyl ether (XVIIIb)**, $n^{24}D$ 1.5708, whose infrared spectrum was identical with that of a synthetic sample described below.

Anal. Calcd. for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56. Found: C, 83.25; H, 7.63.

Further elution with benzene provided 106 mg. of **1,1-diphenyl-2-propanol (XIII)**, m.p. 61–63°, undepressed upon admixture with an authentic sample.[5]

When the desulfurization was performed in dry benzene solution with 16 day old Raney nickel for 8 hr. in a current of nitrogen and the product subjected to Girard separation, there was isolated 72% of *p*-methoxyacetophenone and 81% of 1,1-diphenylpropane (XVI).

α-(*p*-Methoxyphenyl)-α'-benzhydryl Diethyl Ether (XVIIIb).—A 3.0-g. sample of α-(*p*-methoxyphenyl)-ethanol,[26] prepared by lithium aluminum hydride reduction of *p*-methoxyacetophenone, was cooled to −9° and hydrogen bromide gas was passed through for 15 min. The crude α-(*p*-methoxyphenyl)-ethyl bromide crystallized and was drained from adhering liquid by pressing between sheets of filter paper. The substance (3.2 g.) fumed on exposure to air and due to its instability was not submitted for analysis. It could, however, be preserved in an evacuated desiccator in a refrigerator for several weeks. A solution of 1.25 g. of the bromide in 25 cc. of toluene was added dropwise over a period of 20 min. with stirring to a refluxing solution of 0.15 g. of sodium in 1.8 g. of 1,1-diphenyl-2-propanol and 50 cc. of toluene and heating was continued for an additional hour. The cooled toluene reaction mixture was washed with water, dried, evaporated and the residue was chromatographed on 90 g. of basic alumina (activity I). Elution with hexane furnished 0.406 g. of oil, whose infrared spectrum was identical in every respect with the ether isolated in the desulfurization of the hemithioketal XI.

Desulfurization of 2-Benzhydryl-2-methyl-1,3-benzoxathiole (XXV).—A mixture of 0.7 g. of the hemithioketal XXV,[6] 7 g. of 1 day old Raney nickel catalyst and 100 cc. of acetone was stirred and heated under reflux for 24 hr. The crude product was separated into phenolic and neutral fractions and the latter (395 mg., 90%) identified as 1,1-diphenylpropane (XVI) by ultraviolet spectral determination and elementary analysis.

Anal. Calcd. for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.67; H, 8.27.

The alkali-soluble material (200 mg.) was identified as phenol by its infrared spectrum and 2,4,6-tribromo derivative, m.p. 93–95°. The reaction proceeded by substantially the same path when 40 days old Raney nickel catalyst in benzene solution was employed except that the ultraviolet absorption spectrum of the hydrocarbon fraction indicated the presence of *ca.* 10% of 1,1-diphenyl-1-propene (XVII).

1,1-Diphenyl-4-benzylthiobutan-2-one (IVa).—About 15 cc. of benzene was distilled from a mixture of 1.2 g. of 1,1-diphenylbut-3-en-2-one (III),[9] 2.0 g. of benzyl mercaptan, 0.3 g. of piperidine and 100 cc. of benzene, and after heating under reflux for 5 hr. the reaction mixture was left at room temperature overnight. The solution was washed successively with dilute sodium hydroxide, dilute hydrochloric acid, water, dried and evaporated. Crystallization from hexane afforded 1.4 g. of colorless crystals, m.p. 48–50°, raised to 54–55° upon further recrystallization from hexane–ether.

Anal. Calcd. for $C_{23}H_{22}OS$: C, 79.74; H, 6.40; O, 4.62; S, 9.24. Found: C, 80.04; H, 6.44; O, 4.78; S, 9.02.

Reduction of the ketone IVa with lithium aluminum hydride in ether solution proceeded in nearly quantitative yield and the alcohol IVb was obtained as a pale yellow oil, b.p. 200–205° at 0.003 mm.

Anal. Calcd. for $C_{23}H_{24}OS$: C, 79.28; H, 6.94. Found: C, 79.26; H, 6.92.

(26) A. Klages, *Ber.*, **36**, 3584 (1903).

For further characterization a sample of the alcohol IVb was benzoylated with benzoyl chloride in pyridine solution and the benzoate IVc was recrystallized from methanol, m.p. 99–101°.

Anal. Calcd. for $C_{30}H_{28}O_2S$: C, 79.62; H, 6.24; O, 7.07; S, 7.07. Found: C, 79.99; H, 6.27; O, 7.03; S, 7.08.

1,1-Diphenyl-4-mercapto-2-butanol (VI).—Thiolacetic acid (1.1 g.) was added dropwise with vigorous shaking to 1.55 g. of 1,1-diphenylbut-3-en-2-one (III)[9] containing 2 mg. of benzoyl peroxide. After standing overnight, ether was added and the solution was washed well with 5% sodium bicarbonate, water, dried and evaporated. Crystallization of the residue from hexane at −70° provided 1.4 g. of the thiolacetate V, m.p. 69–71°.

Anal. Calcd. for $C_{18}H_{18}O_2S$: C, 72.46; H, 6.08. Found: C, 72.39; H, 6.15.

A 1.2-g. sample of the thiolacetate V in ether solution was heated under reflux with 4 g. of lithium aluminum hydride for 14 hr. Decomposition with sulfuric acid, washing with water, drying and distillation afforded 1.0 g. of the desired mercaptan VI as an oil (b.p. 205–210° at 0.01 mm.) with a very disagreeable odor.

Anal. Calcd. for $C_{16}H_{18}OS$: C, 74.39; H, 7.02; O, 6.20; S, 12.40. Found: C, 73.80; H, 7.00; O, 6.73; S, 12.89.

Spiro-(6-benzhydryl-1,3-oxathiane-2,3'-cholestane) (VIII).—A mixture of 3.7 g. of 1,1-diphenyl-4-mercapto-2-butanol (VI), 3.5 g. of cholestan-3-one (VII), 4.0 g. of anhydrous sodium sulfate, 4.0 g. of freshly fused zinc chloride and 20 cc. of dioxane was stirred magnetically for 3 days at room temperature in a closed vessel. Ether was added and after washing with sodium bicarbonate solution, water, drying and evaporating, there was left a thick yellowish oil. Successive concentrations of an acetone solution and separate recrystallizations of the two main crops from methanol–chloroform yielded two isomers of the hemithioketal VIII: **isomer A**, m.p. 216–218°, $[\alpha]$ +98°. *Anal.* Calcd. for $C_{43}H_{62}OS$: C, 82.37; H, 9.97. Found: C, 81.90; H, 9.76. Isomer B: m.p. 184–185°, $[\alpha]D$ −41°. *Anal.* Found: C, 81.67; H, 10.00.

The remaining mother liquors crystallized (m.p. 114–121°) but no pure isomer could be separated even after chromatography.

2-Methyl-2-phenyl-6-benzhydryl-1,3-oxathiane (IX).—A solution of 1.8 g. of 1,1-diphenyl-4-mercapto-2-butanol (VI), 1.8 g. of acetophenone and 70 mg. of *p*-toluenesulfonic acid monohydrate was heated under reflux for 24 hr. under a water separator. The benzene solution was cooled, washed with dilute bicarbonate and water, dried and evaporated. Repeated crystallization from methanol–ether led to 2.0 g. of the hemithioketal, m.p. 116–118°, which showed no infrared hydroxyl or carbonyl absorption.

Anal. Calcd. for $C_{24}H_{24}OS$: C, 79.97; H, 6.71; O, 4.44; S, 8.88. Found: C, 79.35; H, 6.77; O, 4.88; S, 9.01.

2-Methyl-2-phenyl-5-benzhydryl-1,3-oxathiolane (X).—The hemithioketal X was prepared by the zinc chloride technique from 1.5 g. of acetophenone, 3.1 g. of 1,1-diphenyl-3-mercapto-2-propanol,[6] 4.0 g. of sodium sulfate, 5.0 g. of zinc chloride and 25 cc. of dioxane. After two days, the mixture was processed as described above and yielded 1.7 g. of colorless crystals with m.p. 130–134°. Further recrystallization from methanol–acetone furnished 1.32 g. of a pure isomer, m.p. 138–139°.

Anal. Calcd. for $C_{23}H_{22}OS$: C, 79.74; H, 6.40; S, 9.24. Found: C, 79.55; H, 6.64; S, 9.17.

2-Methyl-2-(*p*-methoxyphenyl)-5-benzhydryl-1,3-oxathiolane (XI).—The condensation of *p*-methoxyacetophenone with 1,1-diphenyl-3-mercapto-2-propanol was carried out exactly as described above and gave 88% of hemithioketal, m.p. 112–116°, which was used in the desulfurizations.

Anal. Calcd. for $C_{24}H_{24}O_2S$: C, 76.57; H, 6.43. Found: C, 76.87; H, 6.62.

Repeated recrystallization of this material from methanol yielded one pure isomer melting at 125–126°.

Anal. Found: C, 76.52; H, 6.45.

1,1-Diphenyl-3-butanol (XXVII).—This alcohol was required as an authentic specimen for the desulfurizations described in Tables II and IV and was obtained in 88% yield

by lithium aluminum hydride reduction of 1,1-diphenyl-2-butanone.[9] After chromatography on Merck acid-washed alumina and crystallization from hexane it melted at 44–46°.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02; O, 7.07. Found: C, 85.04; H, 7.92; O, 7.20.

The 3,5-dinitrobenzoate was recrystallized from hexane whereupon it exhibited m.p. 108–110°. Its infrared spectrum in solution was identical with that of the optically active form obtained in the desulfurizations reported in Table II.

Anal. Calcd. for $C_{23}H_{20}N_2O_6$: C, 65.70; H, 4.80; N, 6.66. Found: C, 66.34; H, 4.97; N, 6.55.

1,1-Diphenylbutane (XXVIII).—A synthetic sample of the hydrocarbon was needed as an infrared standard for the product identification of the desulfurizations reported in Tables II and IV. Consequently, 1,1-diphenyl-2-butanone[9] was reduced by the Huang-Minlon modification of the Wolff–Kishner reduction by heating under reflux for 1 hr. 1.0 g. of the ketone, 1 g. of potassium hydroxide, 7 cc. of 85% hydrazine hydrate and 100 cc. of diethylene glycol. The condenser was removed, the temperature was permitted to rise to 200–210° and heating under reflux was continued for 3 hr. After pouring into water, isolating with ether and chromatographing on 30 g. of Merck acid-washed alumina, hexane eluted 700 mg. of the hydrocarbon, b.p. 80–90° at 0.02 mm. The substance exhibited no infrared carbonyl absorption and its ultraviolet absorption spectrum indicated fine structure between 240–270 mμ, log ε 2.6–2.8.

Anal. Calcd. for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.38; H, 8.16.

1,1-Diphenylpropane (XVI) was prepared in an identical manner from 1,1-diphenylacetone[27] and its ultraviolet absorption spectrum (λ_{max}^{EtOH} 254, 260, 263 and 270 mμ, shoulders at 245, 250 and 265 mμ) was identical with that of the butane XXVIII. For analysis, a sample was distilled at a bath temperature of 130–140° and 15 mm.

Anal. Calcd. for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.56; H, 8.47.

1,1-Diphenylprop-1-ene (XVII)[28] was isolated in a desulfurization similar to run 9 in Table I and was purified by rechromatography and distillation at a bath temperature of 130–140° and 15 mm. The position of the double bond was confirmed by ozonolysis to benzophenone, and by its ultraviolet spectrum (λ_{max}^{EtOH} 248 mμ, log ε 3.94; λ_{max}^{EtOH} 235 mμ, log ε 3.87).

Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.27; H, 7.29.

3α-Ethoxycholestane (XXIa).—Cholestan-3α-ol (XIVa), prepared according to ref. 16, was ethylated with ethyl iodide and emulsified potassium in benzene solution exactly as described for the corresponding methyl ether.[29] Repeated chromatography and attempts at crystallization failed and the ether (42% yield) was distilled for analysis at a bath temperature of 185–195° and 0.01 mm., $[\alpha]_D$ +22.4°. The infrared spectrum (CS_2 solution) differed appreciably in the 8–12 μ region from the 3β-isomer XXIb but proved to be completely identical with the product of the desulfurization experiments (Table V).

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58; O, 3.84. Found: C, 83.76; H, 12.13; O, 4.00.

3β-Ethoxycholestane (XXIb) was prepared in an analogous fashion in 53% yield and crystallized from hexane, m.p. 77–79°, $[\alpha]_D$ +20.8°.

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58; O, 3.84. Found: C, 83.22; H, 12.22; O, 4.10.

Cleavage of Spiro-(1,3-oxathiolane-2,3′-cholestane) (XX). (a) In the Presence of Potassium Acetate and Mercuric Chloride.—To a solution of 0.5 g. of hemithioketal **XX** in 30 cc. of glacial acetic acid was added quickly a warm solution of 0.31 g. of mercuric chloride in 8 cc. of acetic acid followed by 0.30 g. of potassium acetate in 10 cc. of acetic acid. After heating on the steam-bath for 30–60 min., the hot solution was filtered and the precipitate of the mercuri-**chloride salt XXIII**[30] was washed with ether and then recrystallized from acetic acid–methanol to afford colorless crystals (270 mg.), m.p. 158–160°.

Anal. Calcd. for $C_2H_5ClHgOS$: C, 7.67; H, 1.56; Cl, 11.35; Hg, 63.89; O, 5.11; S, 10.22. Found: C, 8.03; H, 1.52; Cl, 10.96; Hg, 63.45; O, 5.24; S, 10.53.

The combined filtrate and ether washings were diluted with more ether, washed with dilute sodium carbonate solution, water, dried and evaporated. The residue was crystallized from methanol–ether yielding 360 mg. of cholestan-3-one (VII), m.p. 128–130°, which was identified further by its infrared spectrum.

The hemithioketal was recovered in quantitative yield when it was heated alone with acetic acid or with acetic acid and potassium acetate for 3 hr. in the absence of mercuric chloride.

(b) In the Presence of Sodium Hydroxide and Mercuric Chloride.—A solution of 200 mg. of the hemithioketal XX in 50 cc. of absolute ethanol was mixed with a solution of 125 mg. of mercuric chloride in 10 cc. of ethanol. While maintaining vigorous stirring at room temperature there was added dropwise over a period of 30 min. a solution of 20 mg. of sodium hydroxide in 5 cc. of water. A yellow precipitate of the oxide formed upon each addition of the alkaline solution but soon disappeared. At the end of the reaction, a small amount (30 mg.) of mercuric oxide was filtered and the filtrate was evaporated to dryness and stirred with ether. Filtration and recrystallization of the ether-insoluble material from acetic acid–methanol provided 75 mg. (52%) of the salt XXIII, m.p. and mixed m.p. 158–160°. The ether solution was evaporated and the residue recrystallized to furnish 158 mg. of cholestan-3-one (VII), m.p. 128–129°.

(c) In the Presence of Potassium Acetate and Hydrogen-free Raney Nickel.—Raney nickel (70 days old) was rendered hydrogen-free by the procedure of Hauptmann, *et al.*,[19] and when 5 g. of this catalyst was heated under reflux overnight with 0.5 g. of the hemithioketal XX in acetone solution, 94% of starting material was recovered.

On the other hand, when a suspension of 2.0 g. of the identical hydrogen-free Raney nickel in 160 cc. of glacial acetic acid containing 0.3 g. of potassium acetate and 0.5 g. of hemithioketal was heated on the steam-bath for 90 min., the nickel filtered and the solution worked up in the usual manner including chromatography on Merck acid-washed alumina, there was isolated 140 mg. of recovered hemithioketal XX, 290 mg. of cholestan-3-one (VII) and 20 mg. of cholestan-3β-ol (XIVb). Identification was confirmed in each case by mixture melting point and infrared examination.

Substitution of nickel hydroxide or nickel chloride for the hydrogen-free Raney nickel preparation led to quantitative recovery of the hemithioketal.

Cleavage of Spiro-(5-benzhydryl-1,3-oxathiolane-2,3′-cholestane) (XII).—A mixture of 0.5 g. of isomer A^5 of the hemithioketal XII, 0.22 g. of mercuric chloride, 0.4 g. of potassium acetate and 200 cc. of glacial acetic acid was heated for 2.5 hr. on the steam-bath. The clear solution was diluted with water, extracted with ether, dried and concentrated whereupon a white precipitate of the mercuri-chloride salt XXIV separated. After recrystallization from acetic acid–ethanol (180 mg.), it melted at 110–113°, $[\alpha]_D$ +33° dimethylformamide, and exhibited an infrared spectrum identical with that of an authentic sample of the racemic salt.[31]

Anal. Calcd. for $C_{15}H_{15}ClHgOS$: C, 37.58; H, 3.13;

(27) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 343.

(28) This substance was first encountered and characterized by Dr. J. A. Henry in this Laboratory (see last paragraph of discussion in ref. 5).

(29) J. R. Lewis and C. W. Shoppee, *J. Chem. Soc.*, 1375 (1955), have shown that these conditions do not cause inversion.

(30) This salt was obtained in 73% yield when a solution of 150 mg. of β-mercaptoethanol in 30 cc. of acetic acid was treated in rapid succession with 610 mg. of mercuric chloride in 20 cc. of acetic acid and then 600 mg. of potassium acetate in 20 cc. of the same solvent. After heating for 1 hr., the precipitate was filtered and recrystallized from acetic acid–methanol, m.p. 156–158°. Identity was established by mixture melting point determination and infrared spectral comparison (potassium bromide pellet).

(31) Prepared in 58% yield from 0.4 g. of 1,1-diphenyl-3-mercapto-2-propanol,[6] 0.44 g. of mercuric chloride and 0.6 g. of potassium acetate in 140 cc. of glacial acetic acid; m.p. 113–115°. *Anal.* Calcd. for $C_{15}H_{16}ClHgOS$: C, 37.58; H, 3.13; Hg, 41.88; O, 3.34; S, 6.68. Found: C, 37.30; H, 3.21; Hg, 41.95; O, 3.41; S, 6.24.

Cl, 7.41; Hg, 41.88; O, 3.34; S, 6.68. Found: C, 37.21; H, 3.27; Cl, 7.01; Hg, 41.50; O, 3.14; S, 6.32.

The residue from the ether solution was chromatographed on 20 g. of Merck acid-washed alumina and yielded 110 mg. of recovered hemithioketal XII and 235 mg. of cholestan-3-one, m.p. and mixture m.p. 128–129°.

DETROIT, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

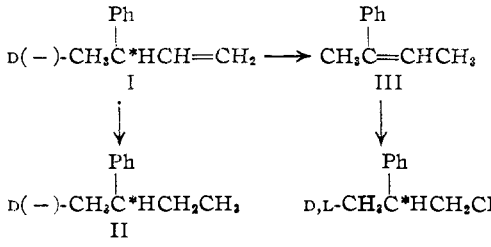
The Catalytic Hydrogenation of 3-Phenyl-1-butene-2-C^{14}

BY WILLIAM A. BONNER, CHARLES E. STEHR AND JEFFERSON R. DO AMARAL[1]

RECEIVED APRIL 9, 1958

D(−)-3-Phenyl-1-butene undergoes varying extents of racemization on catalytic hydrogenation to D(−)-2-phenylbutane.[2,3,4] A rationalization[2] of this fact, involving double bond migration to 2-phenyl-2-butene prior to reduction, appears[4] untenable. An alternative rationalization, involving partial hydrogenation to a 3-phenyl-2-butyl radical followed by non-stereospecific phenyl migration, has been tested by hydrogenation of uniquely labeled 3-phenyl-1-butene-2-C^{14} (IV) under a variety of conditions. The resulting labeled 2-phenylbutane samples have been oxidized to benzoic acid samples, radioactivity assays of which indicate the extents of net phenyl migration attending each catalytic hydrogenation. The net phenyl migrations observed were uniformly less than one per cent., eliminating both the above rationalization and a bridged radical intermediate as important mechanisms for racemization. An alternative mechanism involving hydrogen migration is suggested.

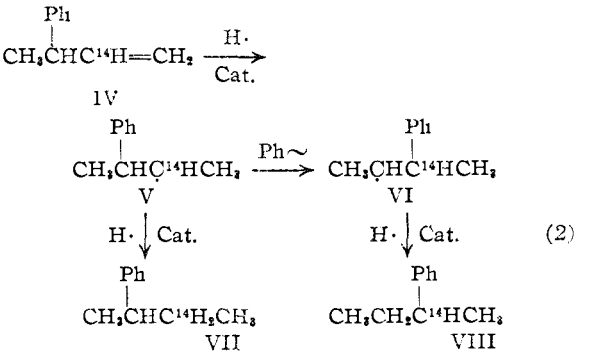
In 1952, Cram observed[2] that when D(−)-3-phenyl-1-butene (I) was catalytically hydrogenated under a variety of conditions the resulting D(−)-2-phenylbutane[3] (II) was racemized to the extent of 1 to 11%. Since D(−)-2-phenylbutane itself was optically stable under the experimental conditions of the catalytic hydrogenation, Cram concluded[2] that the racemization must have occurred prior to or during the hydrogenation process, and suggested that the olefin I might have rearranged partially into conjugated 2-phenyl-2-butene (III) prior to hydrogenation (equation 1), subsequent reduction



(1)

of III producing the racemic 2-phenylbutane. More recently Huntsman and Schlesinger, in a study of double bond migration and racemization during the hydrogenation of olefins, have similarly observed[4] extensive racemization (*ca.* 60%) during the hydrogenation of optically active 3-phenyl-1-butene in the presence of palladium–charcoal catalyst. They have reported further that double bond migration is much slower than hydrogenation in this case and that racemization failed to occur in the absence of hydrogen. They concluded, therefore, that racemization of optically active 3-phenyl-1-butene during hydrogenation must occur by some mechanism other than double bond migration to the asymmetric center.

An alternative mechanism to double bond migration which would account for the racemization of 3-phenyl-1-butene during hydrogenation occurred to us in 1954 and will now be described. If a portion of the starting olefin underwent *partial, stepwise* reduction, rather than instantaneous complete reduction by addition of hydrogen atom pairs,[5] an intermediate secondary free radical such



(2)

as V could result. If V were sufficiently long-lived, phenyl migration might occur yielding the equivalent rearranged radical VI, with its radical site at the previous asymmetric center. Lacking any marked stereospecificity in the phenyl migration step or in the subsequent further reduction of rearranged radical VI, the final 2-phenylbutane from such a process should be substantially racemic. Reduction of the unrearranged radical V would, of course, yield unracemized 2-phenylbutane. A racemization mechanism such as (2) is a reasonable one in view both of the demonstrated[6–11] tendencies of the phenyl group to undergo migration in reactions known to involve free radical intermediates and of the recent report[12] that rearrangement accompanies the palladium–charcoal catalyzed reduction of certain halogenated bicyclo[2,2,1]heptane compounds.

The intervention of a mechanism such as (2) to engender racemization during the hydrogenation

(1) We are indebted to the National Science Foundation for its support of a portion of this investigation.

(2) D. J. Cram, THIS JOURNAL, **74**, 5518 (1952).

(3) D. J. Cram, *ibid.*, **74**, 2150 (1952).

(4) W. D. Huntsman and S. I. Schlesinger, Abstract in "A Report on Research under Sponsorship of the Petroleum Research Fund Administered by the American Chemical Society," 1954–1956, p. 18.

(5) R. P. Linstead and co-workers, THIS JOURNAL, **64**, 1983 (1942).

(6) W. H. Urry and M. S. Kharasch, *ibid.*, **66**, 1438 (1944).

(7) S. Winstein and F. H. Seubold, *ibid.*, **69**, 2916 (1947).

(8) D. Y. Curtin and M. S. Hurwitz, *ibid.*, **74**, 5381 (1952).

(9) S. Winstein, *Experientia*, **12**, 138 (1956).

(10) D. F. DeTar and A. Hlynsky, THIS JOURNAL, **77**, 4411 (1955).

(11) E. Grovenstein, Jr., *ibid.*, **79**, 4985 (1957).

(12) H. Kwart and G. Null, *ibid.*, **80**, 248 (1958).