THE ACTION OF RANEY NICKEL ON ORGANIC SULFUR COMPOUNDS

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(1) To the great regret of all who knew him, Prof. Dr. Heinrich Hauptmann died suddenly on July 21, 1960.

I. INTRODUCTION

Bougault, Cattelain and Chabrier (83, 84) observed in 1939 that in the presence of Raney nickel aliphatic organic sulfur compounds under very mild conditions loose their sulfur which is replaced by hydrogen. This is furnished, as was demonstrated later (72), by the Raney nickel which contains a considerable amount of it (76, 82, 179, 188, 245, 252, 305, 337, 407, 448, 484). The sulfur combines with the nickel to give nickel sulfide.

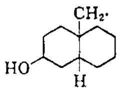
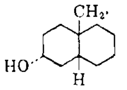
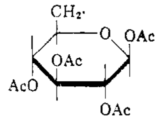
It is, however, largely due to the work of Mozingo, Wolf, Harris and Folkers (337), who in 1943 showed that the reaction could be applied to a greater variety of aliphatic and aromatic compounds containing divalent and oxidized sulfur, that hydrogenolytic desulfurization has had more and more applications and finally became an everyday procedure in research on organic sulfur derivatives. It has been used for the quantitative determination of sulfur (214, 444, 445), but has been employed mainly for the solution of organic structural and synthetical problems.

The Raney nickel used in the reactions reported below has been prepared by different ways. When the original procedure (369, 370, 371) or those of Mozingo and his group (336, 337) or of Ruggli and Preiswerk (389) was used or when no special mention of the method employed was made, the term "Raney nickel" will be used throughout this review. When, however, Raney nickel of special activity (W-1 to W-7) (4, 5, 59), deactivated (327, 328, 413) or degassed (248, 251, 252) Raney nickel was employed, this will be stated in the text.

It is the purpose of this review to report the results of the work done, mainly since 1953, on the action of the various types of Raney nickel on organic sulfur and the closely related selenium compounds. The authors do not claim that this review includes all the papers published where hydrogenolytic desulfurization has been used, but do hope that no important aspect of the problem has been overlooked.

TABLE 1

R—SH → R—H

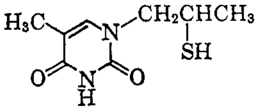
R	Yield, %	Reference
$CH_3\underset{\cdot}{C}HCHDCH_3$	77	254
$(CH_3)_3CCH_2CCH_3(OH)CH_2\cdot$	90	213
$C_6H_5CCH_3(OH)CH_2\cdot$	—	321
$(C_6H_5)_2\underset{\cdot}{C}COOH$	89	43
	85	274
	65–92	274
	70	418

II. THIOLS

A. SULFUR BOUND TO ALIPHATIC CARBON

During the past few years some aliphatic thiols have been submitted to hydrogenolytic desulfurization for synthetical or analytical purpose. The results are listed in Table 1.

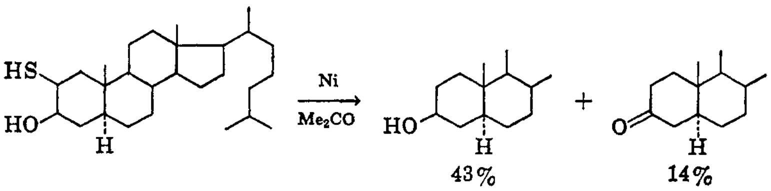
1,2′-Mercaptopropylthymine (I) was desulfurized with Raney nickel W_2 to 1-propylthymine in 23.5% yield. With Raney nickel W_7 only the corresponding disulfide was obtained (398).



I

Several substituted β-mercaptoethanols on desulfurization yielded the sulfur-free alcohols accompanied by the corresponding ketones and sometimes by the unsaturated or saturated hydrocarbons (149).

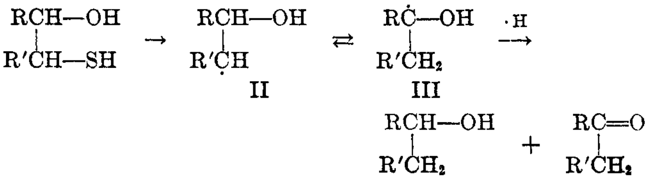
$$(C_6H_5)_2CHCH(OH)CH_2SH \xrightarrow[\text{MeCOEt}]{\text{Ni}} \underset{55\%}{(C_6H_5)_2CHCH(OH)CH_3} + \underset{24\%}{(C_6H_5)_2CHCOCH_3}$$



$$C_6H_5CH(SH)CH(OH)C_6H_5 \xrightarrow[\text{Me}_2\text{CO}]{\text{Ni}} \underset{32\%}{C_6H_5CH_2CH(OH)C_6H_5} + \underset{22\%}{C_6H_5CH_2COC_6H_5} + \underset{17\%}{C_6H_5CH_2CH_2C_6H_5}$$

$$C_6H_5CH(SH)CH(OH)C_6H_5 \xrightarrow[\text{C}_6\text{H}_6]{\text{Ni}} \underset{36\%}{C_6H_5CH_2CH(OH)C_6H_5} + \underset{16\%}{C_6H_5CH_2COC_6H_5} + \underset{15\%}{C_6H_5CH{:}CHC_6H_5}$$

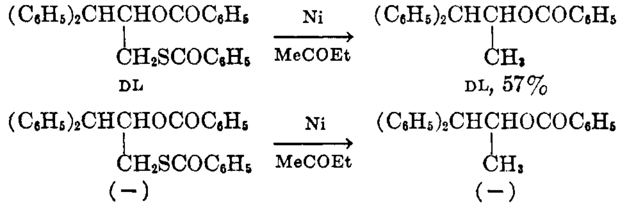
The mechanism shown was proposed for the reactions and it was suggested that "benzyl activation" was responsible for the formation of diphenylethane:



$$\begin{array}{c}\text{RCH—OH}\\ |\\ \text{R'CH—SH}\end{array} \rightarrow \underset{\text{II}}{\begin{array}{c}\text{RCH—OH}\\ |\\ \text{R'}\dot{\text{C}}\text{H}\end{array}} \rightleftarrows \underset{\text{III}}{\begin{array}{c}\text{R}\dot{\text{C}}\text{—OH}\\ |\\ \text{R'CH}_2\end{array}} \xrightarrow{\cdot\text{H}} \begin{array}{c}\text{RCH—OH}\\ |\\ \text{R'CH}_2\end{array} + \begin{array}{c}\text{RC=O}\\ |\\ \text{R'CH}_2\end{array}$$

In order to find out whether the alcohol was formed through radical II or radical III the optically active 1,1-diphenyl-3-mercapto-2-propanol and its dibenzoate were desulfurized (151), the results showing clearly that the configuration about carbon atom 2 is maintained:

$$\underset{(+)}{(C_6H_5)_2CHCH(OH)CH_2SH} \xrightarrow[\text{MeCOEt}]{\text{Ni}} \underset{(+),\ 49\%}{(C_6H_5)_2CHCH(OH)CH_3} + \underset{22\%}{(C_6H_5)_2CHCOCH_3}$$



$$\underset{\text{DL}}{\begin{array}{l}(C_6H_5)_2CHCHOCOC_6H_5\\ \qquad\quad |\\ \qquad\quad CH_2SCOC_6H_5\end{array}} \xrightarrow[\text{MeCOEt}]{\text{Ni}} \underset{\text{DL},\ 57\%}{\begin{array}{l}(C_6H_5)_2CHCHOCOC_6H_5\\ \qquad\quad |\\ \qquad\quad CH_3\end{array}}$$

$$\underset{(-)}{\begin{array}{l}(C_6H_5)_2CHCHOCOC_6H_5\\ \qquad\quad |\\ \qquad\quad CH_2SCOC_6H_5\end{array}} \xrightarrow[\text{MeCOEt}]{\text{Ni}} \underset{(-)}{\begin{array}{l}(C_6H_5)_2CHCHOCOC_6H_5\\ \qquad\quad |\\ \qquad\quad CH_3\end{array}}$$

Since only the alcohol formed through radical II should be optically active, intermediate formation of radical III can be excluded, it thus being shown that desulfurization of β-mercaptoethanols to the corresponding alcohols does not involve the α-carbon atom.

2-Anthraquinonylmethyl mercaptan (IV), when treated with Raney nickel alloy in alkali, gave these products (368, 453):

$$\underset{\text{IV}}{R—CH_2SH} \rightarrow R—CH_3 + R—CH_2OH + R—COOH \quad (R = \text{2-anthraquinonyl})$$

B. SULFUR BOUND TO AROMATIC CARBON

Thiophenol was desulfurized with Raney nickel to benzene (274).

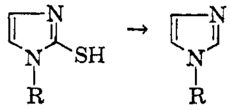
A thiol of unknown structure with an ultraviolet-spectrum similar to that of ethylthiophenol resulted from calcium hexammine reduction of dibenzothiophene. It yielded cyclohexylbenzene by desulfurization, its structure thus being classified as that of an *o*-cyclohexyl- or *o*-cyclohexenylthiophenol (395).

In another instance, a tetrachlorobenzenedithiol which was desulfurized (364) to 1,2,3,4-tetrachlorobenzene was thus shown to be a 1,2-dithiol.

C. SULFUR BOUND TO HETEROCYCLES

Various 2-mercaptoimidazoles have been desulfurized with Raney nickel, as shown in Table 2.

TABLE 2

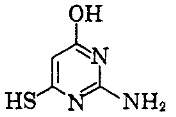


R	Yield, %	Reference
$(CH_3)_2CHCH_2CH_2\cdot$	70	101
$CH_3(CH_2)_6CH_2\cdot$	35	101
$CH_3CH_2CH(CH_3)CH_2\underset{\cdot}{C}HCH_3$	65	101
$C_6H_5(CH_2)_2CH_2\cdot$	68	101
$C_6H_5CH_2\underset{\cdot}{C}HCH_3$	66	101
$2\text{-}ClC_6H_4CH_2CH_2\cdot$	59	101
$4\text{-}ClC_6H_4CH_2CH_2\cdot$	74	101
$2,4\text{-}Cl_2C_6H_3CH_2CH_2\cdot$	63	101
$3,4\text{-}Cl_2C_6H_3CH_2CH_2\cdot$	70	101
$4\text{-}CH_3OC_6H_4CH_2CH_2\cdot$	55	101
$3,4\text{-}(CH_3O)_2C_6H_3CH_2CH_2\cdot$	60	101
$2\text{-}C_2H_5OCOC_6H_4\cdot$	14[a]	401

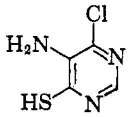
[a] Isolated as the hydrazide.

After Roblin, Lampen, English, Cole and Vaughan (384) first prepared pyrimidines by Raney nickel desulfurization of the corresponding mercapto compounds, the reaction has been widely used for this purpose (Table 3).

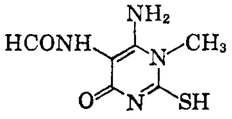
The pyrimidine derivatives V (277), VI (276) and VII (159) also were desulfurized (yields are given in parentheses), but no sulfur-free product could be isolated from the attempted desulfurization of VIII (330).



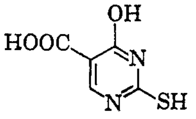
V (80%)



VI (25%)

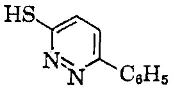


VII

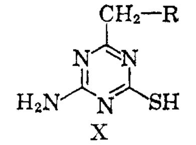


VIII

The 3-mercaptopyridazine IX (156), the 6-mercaptotriazines X (390), the 2-mercaptoquinazolones XI (354) and the 2-mercaptodihydroquinazolone XII (355) gave the expected sulfur-free products on desulfurization; the yields are given in parentheses.

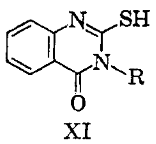


IX (49%)



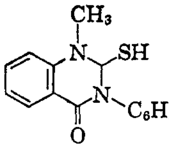
X

a, R = C_6H_5
b, R = $4\text{-}ClC_6H_4$ (32%)



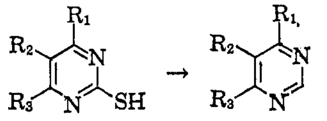
XI

a, R = H (92%)
b, R = C_6H_5 (80%).
c, R = $CH_2C_6H_5$ (57%)



XII (46%)

TABLE 3

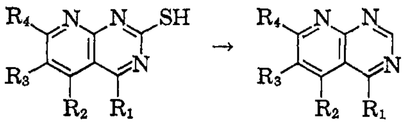


R_1	R_2	R_3	Yield, %	Reference
H	H	H	—[a]	71
CH_3	H	H	20	270
CH_3	H	CH_3	45–60[b]	71, 270
H	H	$NHCH_3$	54	87
H	H	$N(CH_3)_2$	50	87
OH	$COOC_2H_5$	H	14[c]	330
NH_2	H	OH	95	334
OH	H	$CH(OC_2H_5)_2$	89	91
OH	$OCH_2C_6H_5$	H	83	113
OH	$OCH_2C_6H_5$	OH	86	114
NH_2	NH_2	OH	96	160
NH_2	$CH_2CH(OH)CH_2OH$	OH	65	141
NH_2	$CH_2CH(OH)CH_2OH$	NH_2	63	141
NH_2	$CH_2CH(OC_2H_5)_2$	OH	75	141
NH_2	$CH_2CH(OC_2H_5)_2$	NH_2	70	141
NH_2	$CH_2C(OCH_2CH_2O)CH_3$	OH	86	141
NH_2	$CH_2C(OCH_2CH_2O)CH_3$	NH_2	51	141
OH	1-Piperidylmethyl	CH_3	83	408
OH	Diethoxyethyl	NH_2	76	466
OH	$N_2C_6H_5$	CF_3	50	55, 189
OH	H	CF_3	88	189
NH_2	H	CF_3	36	189

[a] Isolated as the $HgCl_2$-complex. [b] Desulfurization in neutral methanol was unsuccessful, either alkaline or acid solution had to be used. [c] Isolated as the free acid.

A great number of 2-mercaptopyrido[2,3-d]pyrimidines have been desulfurized with Raney nickel in the presence of ammonia for preparative purposes; the results are summarized in Table 4.

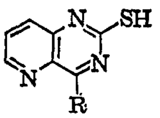
TABLE 4



R_1	R_2	R_3	R_4	Yield, %	Reference
NH_2	H	H	H	45	381
OH	H	H	H	30[a]	342
OH	CH_3	H	CH_3	83	383
OH	H	C_6H_5	$CH_2C_6H_5$	68	383
OH	H	CH_3	C_2H_5	80	383
OH	H	CH_3	CH_3	69	383
OH	H	C_2H_5	n-C_3H_7	80	383
OH	H	CH_3	n-C_4H_9	76	383
OH	H	H	4-ClC_6H_4	64	383
OH	H	H	iso-C_4H_9	66	383
OH	H	CH_3	C_6H_5	84	383
OH	H	H	C_6H_5	44	383
OH	H	H	4-ClC_6H_4	74	383
OH	H	C_2H_5	C_6H_5	58	383

[a] In presence of sodium hydroxide instead of ammonia.

4-Amino-2-mercaptopyrido[3,2-d]pyrimidine (XIII, R = NH_2) was desulfurized independently by two groups of workers (342, 382).



XIII

Since the yields and the reaction conditions differ widely, comparison of both is made in Table 5. It thus becomes evident that yields in desulfurization experiments mean very little and are not comparable, except when obtained under rigorously the same conditions.

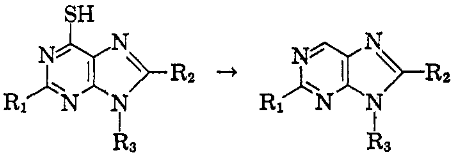
TABLE 5

Reference	382	342	
Weight of compound, g.	5	0.65	(ratio = 7.7:1)
Weight of Raney nickel, g.	15	3	(ratio = 5:1)
Volume of ethanol, l.	1.8	0.2	(ratio = 9:1)
Volume of ammonia, ml.	200	40	(ratio = 5:1)
Time, hr.	30	3	(ratio = 10:1)
Yield, %	29	94	

2,4-Dimercaptopyrido[3,2-d]pyrimidine (XIII, R = SH) on Raney nickel desulfurization gave pyrido-[3,2-d]pyrimidine, isolated as the picrate (342).

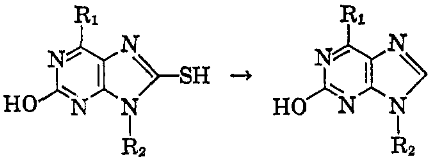
Raney nickel desulfurization has also been employed in the purine series; especially 6- and 8-mercaptopurines have been used, as may be seen from Tables 6 and 7, respectively.

TABLE 6



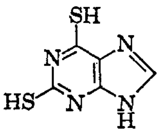
R_1	R_2	R_3	Yield, %	Reference
H	H	H	41–48	49
H	CH_3	H	79	307
CH_3	H	H	49	366
H	H	β-D-Ribofuranosyl	58	176
NH_2	H	β-D-Ribofuranosyl	69	176

TABLE 7 (306)

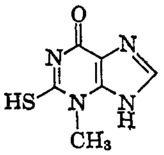


R_1	R_2	Yield, %
OH	CH_3	57
OH	iso-C_4H_9	58
OH	C_6H_5	46
OH	4-ClC_6H_4	36
NH_2	CH_3	64
NH_2	C_2H_5	58
NH_2	iso-C_4H_9	49

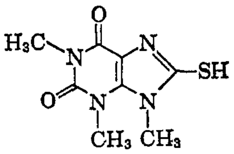
2,6 - Dimercaptopurine (XIV) was desulfurized to purine (49), 2-mercapto-3-methylhypoxanthine (XV) (159) and 1,3,9-trimethyl-8-mercaptoisoxanthine (XVI)



XIV (35%)



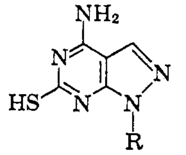
XV



XVI (53%)

(66) to the expected sulfur-free compounds. Yields are given in parentheses.

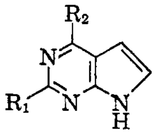
Some compounds with structure similar to purine, as the pyrazolo[3,4-d]pyrimidine derivatives XVIIa (168, 465) and XVIIb (116) yielded the expected sulfur-free substances when treated with Raney nickel:



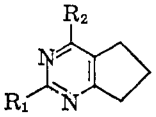
XVII

a, R = H (34%)
b, R = CH₃ (50%)

The pyrrolo[2,3-d]pyrimidine (XVIII) and trimethylenepyrimidine (XIX) (387) derivatives noted also were desulfurized with good results.



XVIII

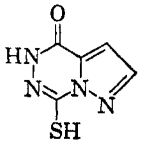


XIX

a, R_1 = H, R_2 = SH (67–69%) (141, 466).
b, R_1 = SH, R_2 = OH (52%) (466).

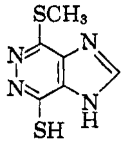
a, R_1 = H, R_2 = SH (58%)
b, R_1 = NH_2, R_2 = SH (55%)
c, R_1 = SH, R_2 = OH (70%)

7-Mercaptopyrazolo[1,5-d]*as*-triazin-4(5H)-one (XX) gave the expected product on desulfurization

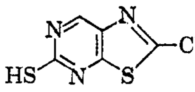


XX

(7), whereas from compound XXI only the mercapto group was removed, 4-methylmercaptoimidazo[4,5-d]-pyridazine being isolated in 41% yield (108):



XXI



XXII

2-Methyl-5-mercaptothiazolo[5,4-d]pyrimidine (XXII) too was only partially desulfurized with Raney nickel in aqueous ammonia solution (275), the thiazole ring remaining intact.

III. SULFIDES AND DISULFIDES

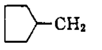
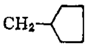
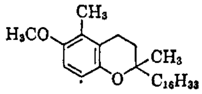
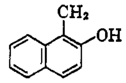
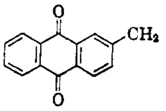
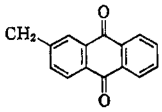
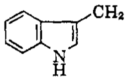
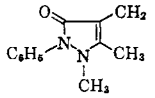
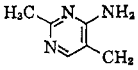
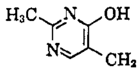
A. SULFIDES

1. *Alkyl and Alkyl-aryl Sulfides.*

Alkyl and alkyl-aryl sulfides substituted or not in the aliphatic chain, some of them occurring in nature, have been desulfurized with Raney nickel in order to determine their structures. The reactions are summarized in Table 8.

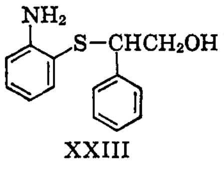
TABLE 8

$$R—S—R' \rightarrow R—H + R'—H$$

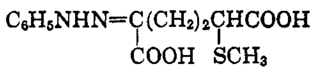
R	R'	Yield, % R–H	Yield, % R'–H	Reference
		—	—	60
C_6H_5	$CH{=}CHCH_3$	42	96[a]	289, 290
2-$CH_3C_6H_4$	$CH{=}CHCH_3$	78	—	289, 290
4-$CH_3C_6H_4$	$CH{=}CHCH_3$	44	81[a]	289, 290
C_6H_5	$CH_2CH{=}CHC_6H_5$	59	60[b]	283
$CH_3C(C_6H_5)_2CH_2CH_2$	n-C_4H_9	100	—	461
$C_6H_5CH_2NHCONH(CH_2)_8CH_2$	CH_3	—	—	302
$HOCH_2CHC_6H_5$	2-$NH_2C_6H_4$	—	—	266
$HO(CH_2)_2C(CH_3)_2$	$CH_2CH(NH_2)COOH$	—	—	469
$H_2NCH_2CHCOOH$	$CH_2C_6H_5$	49	—	226
$HOOCCH{=}CHCH{=}CCOOH$	CH_3	88[c]	—	229
$C_6H_5CH_2NHCH_2CHCOOH$	$CH_2C_6H_5$	18[d]	—	226
$H_3CCONHCH_2CHOCOCH_3$	C_2H_5	42	—	265
$C_6H_5N(COCH_3)CHC_6H_5$	4-$CH_3C_6H_4$	90	59	414
	CH_2CH_2OH	2[e]	—	326
	C_2H_5	75	—	365
		—[f]	—[f]	368, 453
	n-C_4H_9	62	—	365
	C_2H_5	56	—	365
	CH_2COOH	65	—	81
	CH_2COOH	55	—	81

[a] R'–H isolated as propane. [b] R'–H isolated as n-propylbenzene. [c] R–H isolated as adipic acid. [d] A small quantity of β-alanine, $H_2N(CH_2)_2COOH$, also was formed. [e] After demethylation R–H was isolated as 5-methyltocol. [f] Traces of anthraflavone were also formed.

2-Aminophenyl-2-hydroxy-1-phenylethyl sulfide (XXIII) was desulfurized to 2-phenylethanol with Raney nickel in ethanol, and with Raney nickel W-6 to a mixture of toluene and ethylbenzene (294; *cf.* Table 8, ref. 266), the products which result from treatment of 2-phenylethanol with Raney nickel W-6 (490). When desulfurized in sodium bicarbonate solution, the sulfide



XXIII



$$C_6H_5NHN{=}\underset{\displaystyle COOH}{C}(CH_2)_2\underset{\displaystyle SCH_3}{C}HCOOH$$

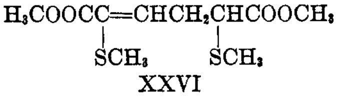
XXIV

XXIV gave 2-aminoadipic acid in 80% yield, together with some aniline (229).

The sodium salt of XXV was desulfurized in neutral solution giving an 85% yield of sodium propionate (228), XXVI gave dimethyl adipate in 74% yield (229), and from the tris-sulfide XXVII resulted 51% of trimethylamine and an unstated yield of di-isopropyl ketone (17).

$H_3CSCH{=}C(COOH)SCH_3$

XXV



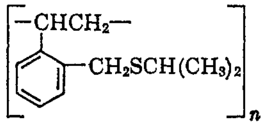
$$H_3COOC\underset{\displaystyle SCH_3}{\underset{|}{C}}{=}CHCH_2\underset{\displaystyle SCH_3}{\underset{|}{C}}HCOOCH_3$$

XXVI

$[(CH_3)_2CHCOC(CH_3)_2SCH_2]_3N$

XXVII

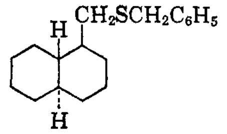
Poly-*o*-vinylbenzyl-D-*sec*-butyl sulfide (XXVIII) and a copolymer of *o*-vinylbenzyl-D-*sec*-butyl sulfide and methyl methacrylate, when treated with Raney nickel, yielded sulfur-free products (349).



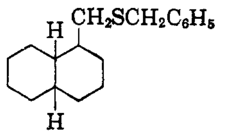
XXVIII

2. *Alkyl-Cycloalkyl Sulfides.*

Some sulfides containing cycloalkyl ring systems were also desulfurized with Raney nickel. From XXIX and XXX with deuteriated Raney nickel the deuteriated 1-methyl-decalins with the same configuration as the parent sulfides were obtained in 53 and 59% yield, respectively (272).



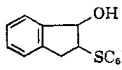
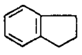
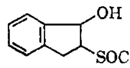
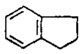
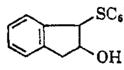
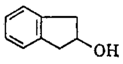
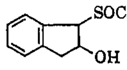
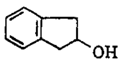
XXIX



XXX

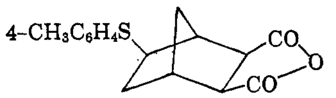
When the hydroxyindane derivatives shown in Table 9 were desulfurized with Raney nickel, the hydroxy groups located in the 2-position were stable, whereas those located in the 1-position were eliminated (174).

TABLE 9

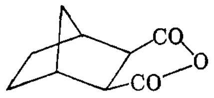
Sulfide	Product	Yield, %
		—
		—
		50
		20

This is another example for the ready dehydroxylation of derivatives of benzyl alcohols in the presence of Raney nickel (75, 77).

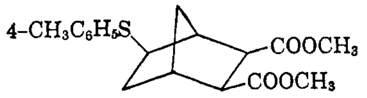
By desulfurization of 4-(4-tolylthio)-*exo-cis*-3,6-*endo*-methylene hexahydrophthalic anhydride (XXXI) the *exo*-anhydride XXXII was obtained in 38% yield. When XXXII was treated with fresh Raney nickel it could be recovered to about 40% only, so that some decomposition on the nickel surface must have occurred (56).



XXXI

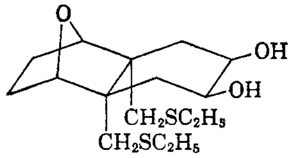


XXXII



XXXIII

On the other hand, desulfurization of the sulfide XXXIII containing two ester groups gave the normal product in 79% yield (56), and no difficulties were found in desulfurizing the bis-sulfide XXXIV, the yield being 75% (422).

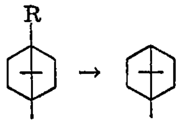


XXXIV

The first information about the stereochemistry of the hydrogenolytic desulfurization was forwarded by Bonner (73, 74) who showed that optically active 2-phenyl-2-phenylthio-propionamide and its sulfoxide were racemized when treated with Raney nickel in accordance with the radical mechanism previously proposed (111, 248, 249, 293). For desulfurization of the corresponding optically active sulfone which led to inversion, a different path of reaction was suggested.

Desulfurization of *cis*- and *trans*-3-methyl-3-benzylthiocyclohexyl 2-naphthoate and of its sulfone was accompanied by racemization (Table 10). Thus the sulfides behaved in the same manner in both cases, the sulfones, however, in a different one, no stereospecificity being observed in the latter case (434).

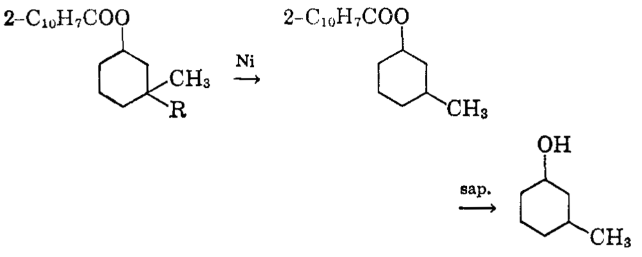
This could be further demonstrated by desulfurization of phenyl-4-camphyl-sulfone (434) which, by its endocyclic ring system, is not capable of inversion (yields are given in parentheses)



R = SC_6H_5 (53%)
R = $SO_2C_6H_5$ (61%)

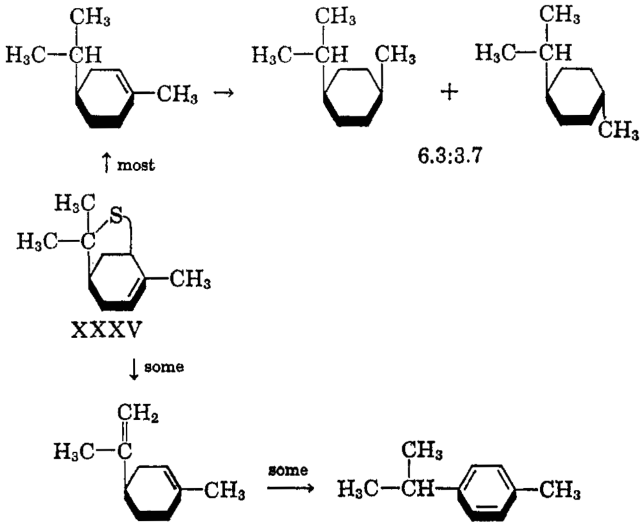
The authors remark that in these last reactions the least probable sulfur-free intermediate would be a carbonium ion and, although a S_Ni mechanism cannot be excluded, the results are not incompatible with a radical mechanism.

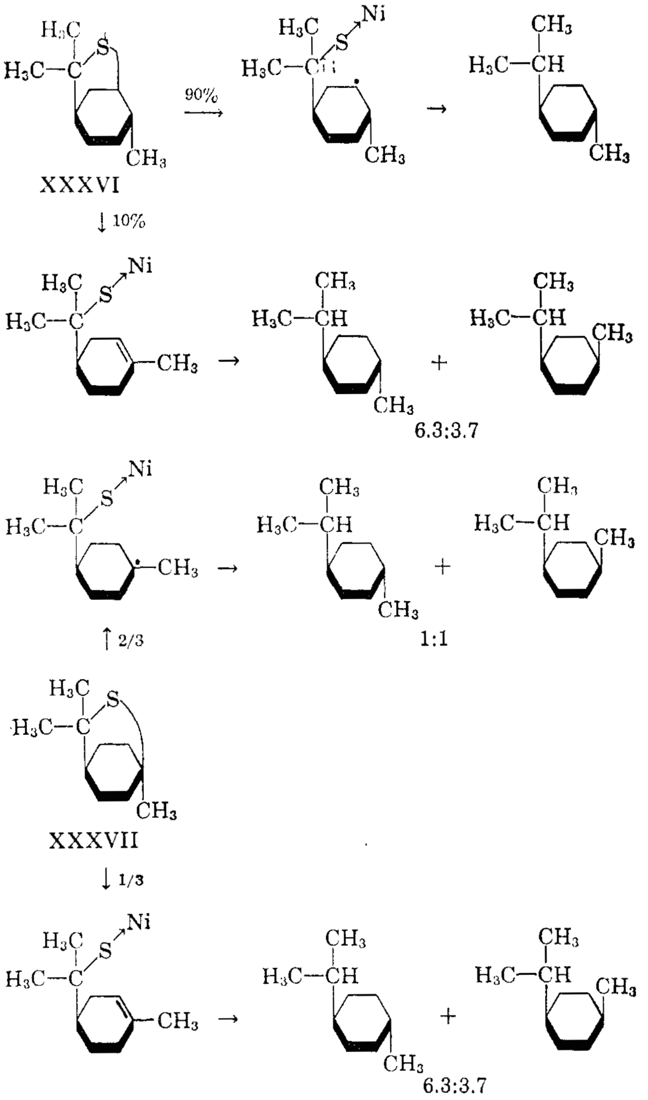
TABLE 10



R	Configuration of O and S	Yield, %, of 3-methylcyclohexyl 2-naphthoate	Total yield, %, 3-methylcyclohexanol	Yield, %, of *cis*-3-methylcyclohexanol
$C_6H_5CH_2S$	*cis*	88	87	56
$C_6H_5CH_2S$	*trans*	89	72	37
$C_6H_5CH_2SO_2$	*cis*	77	73	46
$C_6H_5CH_2SO_2$	*trans*	68	65	43

Desulfurization of *p*-menthenylene- and *p*-menthylenesulfides XXXV, XXXVI, and XXXVII in boiling methanol during 40 min. with great excess of Raney nickel yielded *cis*- and *trans*-*p*-menthane. When less Raney nickel was employed significant quantities of *1*-*p*-menthene and limonene were obtained. Racemization occurred when either the sulfur was connected to the asymmetric carbon atom or when this atom was in β-position to the sulfur and bore a double bond (463, 464). These schemes were given for the different sulfides:



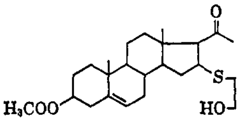
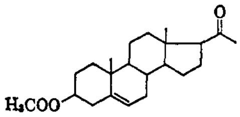
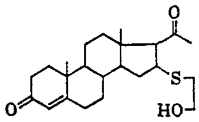
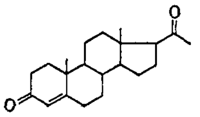
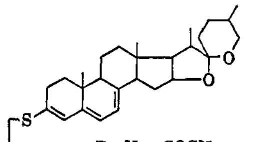
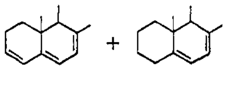
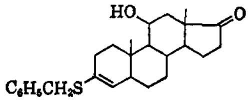
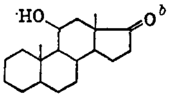
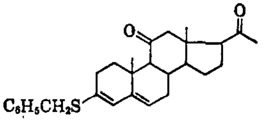
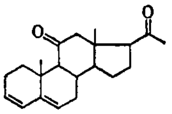


From these results the author concludes that desulfurization of the sulfides occurs *via* a radical mechanism, and in part through an unsaturated intermediate.

In this connection it should be considered that radicals disproportionate yielding olefins and paraffins. That this disproportionation occurs also when sulfur compounds, *e.g.*, cyclohexyl disulfide, are treated with Raney nickel (degassed at 200°), has been found recently (242). The amount to which the olefin appears as an intermediate would then be a question of the rate of hydrogenation and disproportionation of radicals which would explain the higher yield of 1-*p*-menthene with less Raney nickel (464) when hydrogen becomes scarce and hydrogenation is thus slow.

The corresponding sulfones, more resistant to hydrogenation, had to be refluxed with Raney nickel in 1-propanol for 20 hours. The more easily desulfurized 1,8-*p*-menthylene sulfone (XXXVIII) reacted in accordance with Bonner's findings (73) with complete inversion, which the author explains by assuming a

TABLE 11

Starting compound	Type of Ni used	Product	Yield, %	Reference
	W-2 in acetone		52	385
	W-2 in acetone		60	385
 R = H or $COCH_3$	Deactivated[a] W-2		—	148
	Not specified		—	23
	Deactivated[a] W-4		—	21, 22, 23

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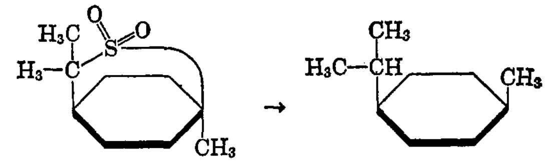
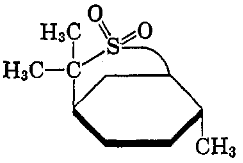
[a] By boiling previously in acetone for 1 hour. [b] Obtained after hydrogenation of the reaction product.

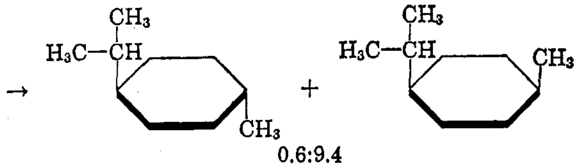
not specified S_N2 mechanism. The inversion observed with the 2,8-*p*-menthylene sulfone (XXXIX) cannot be explained by means of a simple displacement.



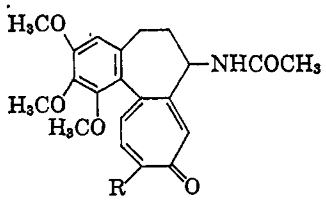
XXXVIII



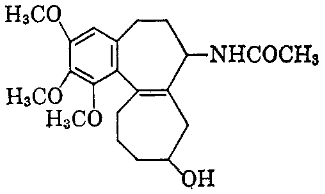
XXXIX



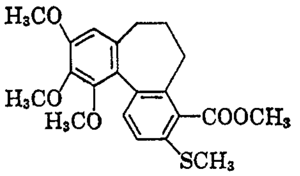
Raney nickel desulfurization was also used in work on the chemistry of colchicine. Demethoxycolchicine (XLa) was obtained in 61% yield from thiocolchicine (XLb) by treatment with Raney nickel deactivated by boiling acetone (373), whereas hexahydrodemethoxycolchicine (XLI) was obtained in yields up to 40% when active nickel was used (373, 452). The compound XLII was also desulfurized without hydrogenation of the aromatic ring (451).



XLa, R = H
b, R = SCH_3



XLI

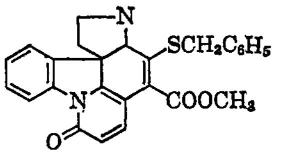


XLII

a, R = H.
b, R = SCH_3.

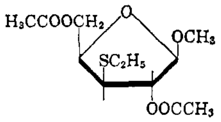
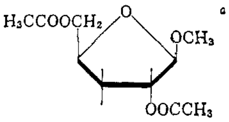
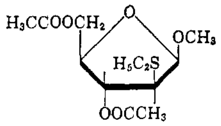
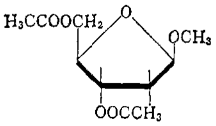
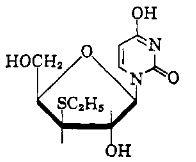
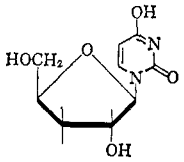
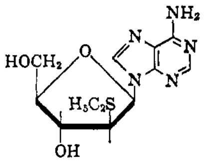
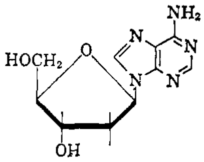
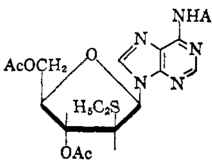
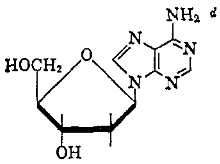
In the steroid series several thioethers and enolthioethers have been transformed into the sulfur-free products; the double bond of the thioenol ether remained unaltered when deactivated Raney nickel was used. The results are summarized in Table 11.

Compound XLIII, an intermediate in the strychnine synthesis, was desulfurized with Raney nickel and gave the expected sulfur-free product (477).



XLIII

TABLE 12

Starting compound	Type of Ni used	Product	Yield, %	Reference
	Not specified	 [a]	54	12
	Ni "C"[b]	 [a]	48	12
 [c]	Not specified, in presence of NH_4OH	 [d]	3[e]	88
	Ni "C"[b, f] in presence of NaOH		7[e, g]	13
	Ni "C"[b] in presence of NaOH	 [d]	13[e]	11, 13

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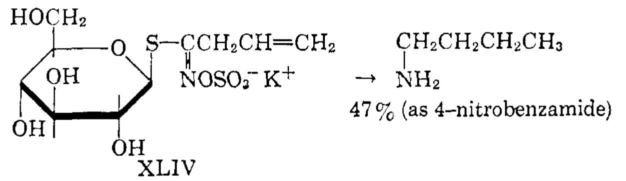
[a] Product reacetylated after desulfurization. [b] Ref. 271. [c] Compound acetylated prior to desulfurization. [d] Product deacetylated after desulfurization. [e] Part of the starting compound was recovered. [f] Urushibara nickel (341) gave similar results. [g] The yield of product was increased to 13% when sodium acetate was added to the reaction mixture.

3. *Sulfur Bound to Heterocycles*

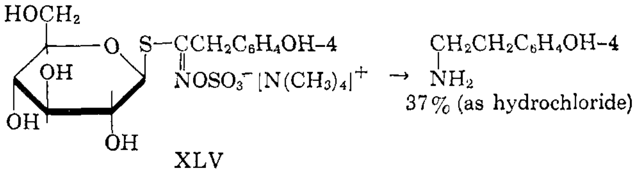
Deoxy-sugars and some of their pyrimidine- or purineglycosides which are important in cancer research have been prepared by Raney nickel desulfurization of the corresponding ethylthio derivatives. The results are tabulated in Table 12.

The structures of two mustard-oil glycosides, sinigrin (XLIV) and sinalbin (as tetramethylammonium sinalbate, XLV), were determined with the aid of Raney nickel desulfurization (165), which demonstrated that sulfur, nitrogen, and the allyl group were linked at the same carbon atom in the manner shown:



47% (as 4-nitrobenzamide)

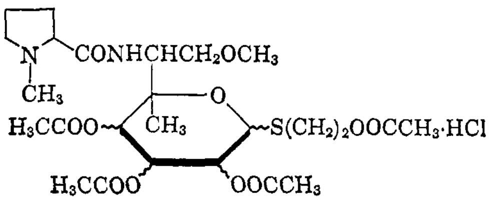
XLIV



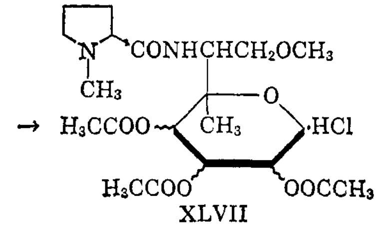
37% (as hydrochloride)

XLV

Tetraacetyl-desalicetin hydrochloride (XLVI) derived from a metabolism product of *Streptomyces celestis* NRLL 2418, was desulfurized with Raney nickel, yielding the hydrochloride of N-hygroylcelestitol triacetate (XLVII) (260).



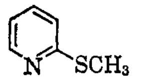
XLVI

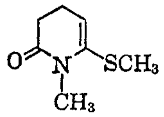


XLVII

Considering now sulfides with sulfur bound to nitrogen heterocycles, it may first be mentioned that 2-methylthiopyridine (XLVIII), when shaken with Raney nickel gave pyridine, whereas compound XLIX, which does not possess an aromatic system, gave N-methyl-2-piperidone, the ethylenic double bond being hydrogenated in this case (375).

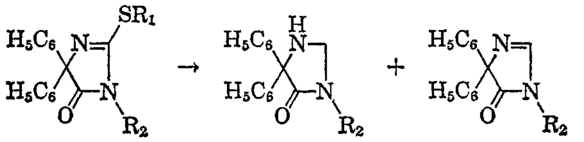
Some derivatives of 5,5-diphenyl-2-thiohydantoin


XLVIII


XLIX

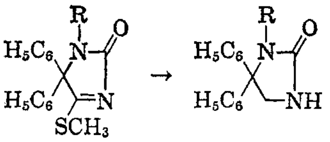
(L) have been desulfurized with Raney nickel in ethanol, as can be seen from Table 13. On the amount of Raney nickel present and on the alkalinity of the solution depends the ratio of saturated to unsaturated products: LII ($R_2 = CH_3$) could be hydrogenated with Raney nickel under desulfurization conditions to the saturated compound LI ($R_2 = CH_3$) in 75% yield (456), compounds L ($R_1 = CH_3$ or $CH_2\text{-}C_6H_5$, R_2 = H) gave the corresponding unsaturated LII in 84 and 85% yields, respectively, when sodium ethoxide was present (456).

TABLE 13

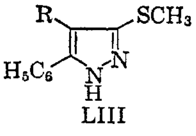

L LI LII

R_1	R_2	Yield of L, %	Yield of LI, %	Reference
CH_3	H	Main product	9	456
$CH_2C_6H_5$	H	Main product	25	456
CH_3	CH_3	24	75	456
CH_3	CH_3	—	66	102

5,5-Diphenyl-4-thiohydantoin derivatives also have been desulfurized (102), giving the normal, saturated products (yields are given in parentheses):

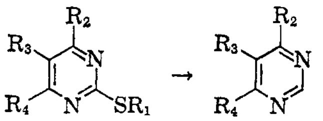

R = H (45%)
R = CH_3 (55%)

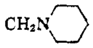
The pyrazole derivatives LIII (R = C_6H_5 or SH), when refluxed with Raney nickel in ethanol, gave the corresponding sulfur-free products; 3,4(4,5)-diphenylpyrazole was obtained in 55% yield (58).


LIII

Several 2-alkylthiopyrimidine derivatives have been desulfurized; the results are shown in Table 14.

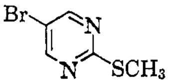
TABLE 14

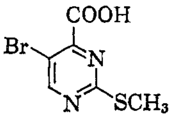


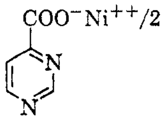
R_1	R_2	R_3	R_4	Yield, %	Reference
CH_2COOH	H	H	H	14	270
CH_3	CH_3	H	H	—	449
CH_3	CH_3	H	CH_3	77	270
CH_3	OH	H	CH_3	21	408, 415
CH_3	OH	 CH_2N	CH_3	10, 61[a]	408
C_2H_5	OH	NH_2	H	62	70
CH_3	OH	$NHCOC_6H_5$	H	57	70
CH_3	NH_2	H	OCH_3	50	363
CH_3	$NHCOCH_3$	H	OCH_3	35	363
CH_3	$N(CH_3)_2$	NHCOH	NH_2	69	9, 10
CH_3	$N(C_2H_5)_2$	NHCOH	NH_2	86	9, 10, 40
CH_3	$N(CH_3)C_6H_5$	NHCOH	NH_2	68	9, 40

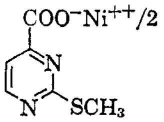
[a] Yields obtained under different reaction conditions: in the first run nickel prepared according to Brown (86) was used in a weight-ratio of 1 (compound):3(Ni); in the second, Hurd and Rudner's type "C" Raney nickel (271) in a ratio 1:5 was used.

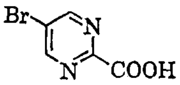
2-Methylthio-5-bromopyrimidine (LIV) gave 38% of pyrimidine (as $HgCl_2$ complex) on treatment with Raney nickel in ammonia-containing ethanol (329). Simultaneous splitting of the carbon–sulfur and the carbon–bromine bonds occurred also when 2-methylthio-5-bromo-4-pyrimidinecarboxylic acid (LV) was refluxed with five times its weight of Raney nickel, 4-pyrimidine carboxylate (LVI) being isolated in 48% yield. With three times its weight of Raney nickel 2-methylthio-4-pyrimidinecarboxylate (LVII) was the only reaction product (yield 39%); 5-bromo-2-pyrimidinecarboxylic acid (LVIII) under the same conditions was either recovered or completely degraded (329).


LIV

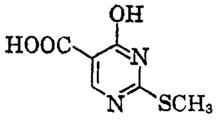

LV


LVI

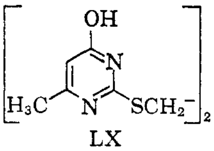

LVII

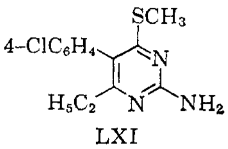

LVIII

On the other hand, no sulfur-free products could be isolated when the acid LIX or its methyl ester was treated with Raney nickel (330).


LIX

The bis-sulfide LX on treatment with Raney nickel in ethanol gave the expected 4-hydroxy-6-methylpyrimidine (415), and the derivative LXI of 4-methylthio-

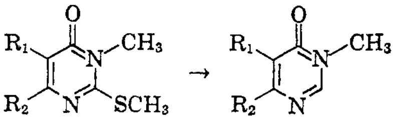

LX


LXI

pyrimidine gave the corresponding 2-amino-3-ethyl-4-(4-chlorophenyl)-pyrimidine (261).

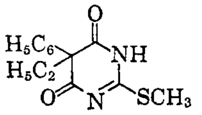
Some derivatives of 2-methylthio-3-methyl-4-oxo-dihydropyrimidine have been desulfurized with Raney nickel (see Table 15) without hydrogenation of the ring.

TABLE 15

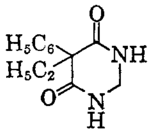


R_1	R_2	Yield, %	Reference
H	NH_2	52	363
H	$NHCOCH_3$	81	363
CH_3	NH_2	29	363
CH_3	NH_2	49	363
NH_2	NH_2	46	362
NHCOH	NH_2	—	159

Desulfurization with Raney nickel in ethanol of the tetrahydropyrimidine derivative LXII gave 5-ethyl-5-phenyl-4,6-dioxohexahydropyrimidine (LXIII), the ring double bond being hydrogenated during desulfurization (78).



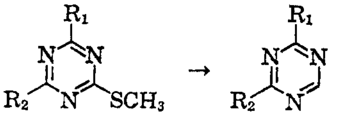
LXII



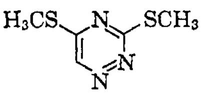
LXIII

1,3,5-Triazine and its derivatives can be prepared from the corresponding methylthiotriazine derivatives by Raney nickel desulfurization, as can be seen from Table 16. The nickel must be free from alkali in order to obtain maximum yields. 3,5-Bis-(methylthio)-1,2,4-triazine (LXIV) has been treated with Raney nickel in petroleum ether (224), but in this case extensive fargoing hydrogenolysis with formation of an unidentified amine $C_5H_{13}N$ took place.

TABLE 16



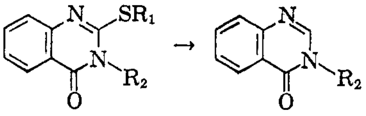
Starting compound		Product		Yield,	Refer-
R_1	R_2	R_1	R_2	%	ence
SCH_3	SCH_3	H	H	10	222
SCH_3	CH_3	H	CH_3	32	222
SCH_3	C_6H_5	H	C_6H_5	32	225
C_6H_5	C_6H_5	C_6H_5	C_6H_5	81	225
NHC_6H_5	NHC_6H_5	NHC_6H_5	NHC_6H_5	38	223



LXIV

Desulfurization of 2-alkylthio-4-quinazolones with Raney nickel gives the corresponding sulfur-free products; the reactions are summarized in Table 17.

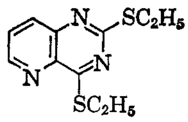
TABLE 17



R_1	R_2	Yield, %	Reference
CH_3	H	29	354
CH_3	C_6H_5	51	354
$CH_2C_6H_5$	C_6H_5	59	354
$CH_2CH(CH_3)N(CH_3)_2$	C_6H_5	46[a]	324

[a] Yield based on reacted starting compound; some of the latter was recovered, together with dimethyl-iso-propylamine.

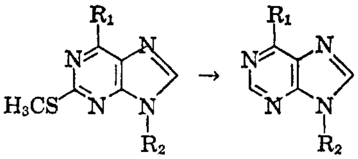
2,4-Diethylthiopyrido[3,2-d]pyrimidine (LXV), when treated with Raney nickel in aqueous ethanol, gave the expected pyrido[3,2-d]pyrimidine (342):

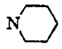


LXV

Many 2-methylthiopurine derivatives have been desulfurized in the course of the preparation of biologically interesting substances; the results are shown in Table 18.

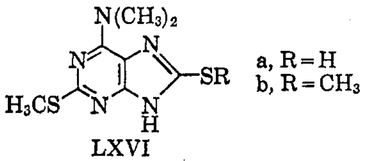
TABLE 18



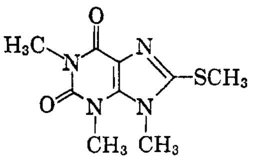
R_1	R_2	Yield, %	Reference
NH_2	H	51	439
$N(CH_3)_2$	H	—	9
$N(C_2H_5)_2$	H	32	9, 40
	H	28[a]	9, 40
$N(CH_3)C_6H_5$	H	23	9, 40
$N(C_4H_9)C_6H_5$	H	14	9, 40
NH_2	Tri-O-acetyl-β-D-ribofuranosyl	64	400
$N(CH_3)_2$	β-D-Ribofuranosyl	55	300
$N(CH_3)_2$	Tri-O-acetyl-β-D-ribofuranosyl	—	300
$N(CH_3)_2$	Tri-O-acetyl-β-D-ribofuranosyl	57[b]	14
$N(CH_3)_2$	Tri-O-benzoyl-β-D-ribofuranosyl	39[c]	300
$N(CH_3)_2$	2,5-Di-O-acetyl-3-acetamido-3-deoxy-β-D-ribofuranosyl	24	41
$N(CH_3)_2$	2,5-Di-O-benzoyl-3-acetamido-3-deoxy-β-D-ribofuranosyl	54	42
$N(CH_3)_2$	2,5-Di-O-benzoyl-3-acetamido-3-deoxy-β-D-ribofuranosyl	60	38
$N(CH_3)_2$	3,4,6-Tri-O-acetyl-2-acetamido-2-deoxy-β-D-glucopyranosyl	81	39
$N(CH_3)_2$	3,4,6-tri-O-acetyl-2-acetamido-2-deoxy-β-D-allopyranosyl	85[d]	325

[a] Isolated as picrate. [b] Yield of deacetylated product. [c] Yield of debenzoylated product. [d] In the presence of Amberlite IRC-50 ion exchange resin (to reduce alkalinity) and with Raney nickel deactivated by boiling acetone.

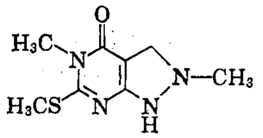
Compounds LXVIa and LXVIb also were desulfurized, yielding 6-dimethylaminopurine (9); 1,3,9-trimethyl-8-methylthio-isoxanthine (LXVII) gave 1,3,9-trimethylisoxanthine in 25% yield (66).

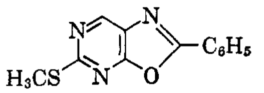

LXVI

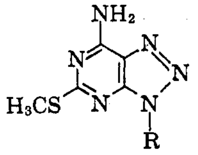
a, R=H
b, R=CH_3


LXVII

When heated with Raney nickel in ethanol, LXVIII yielded 61% of the corresponding pyrazolo[3,4-d]pyrimidine derivative (393), LXIX gave 2-phenyloxazolo[5,4-d]pyrimidine in 62% yield (70), and the

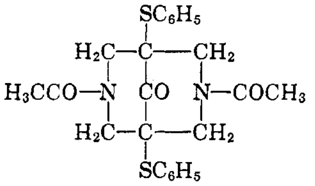

LXVIII

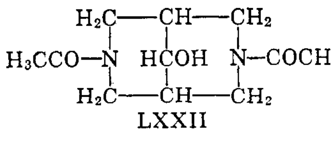

LXIX

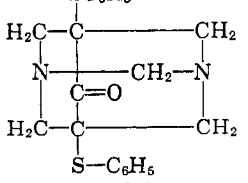

LXX

3H-*v*-triazolo[d]pyrimidine derivative LXX (R = tri-O-acetyl-β-D-ribofuranosyl) gave, after deacetylation, 21% of 3-(β-D-ribofuranosyl)-7-amino-3H-*v*-triazolo[d]pyrimidine (140).

Finally, the bispidone derivative LXXI after two treatments with Raney nickel in ethanol yielded 66% of the bispidinol derivative LXXII, whereas 5,7-bis(phenylthio)-1,3-diazaadamantan-6-one (LXXIII),


LXXI

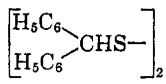

LXXII

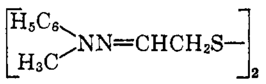

LXXIII

when refluxed with Raney nickel in dioxane, gave only 8% of 5,7-bis(phenylthio)-1,3-diazaadamantan-6-ol (420).

B. DISULFIDES

Relatively few disulfides have been subjected to hydrogenolytic desulfurization. Diphenyl disulfide, when treated with Raney nickel, gave benzene (278), the product of complete hydrogenolysis of the C-S bonds. On the other hand, bis(diphenylmethyl)disulfide (LXXIV), when refluxed with Raney nickel (ratio 1 : 15)

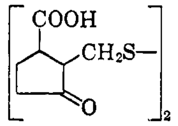

LXXIV


LXXV

in 70% ethanol, gave 1,1,2,2-tetraphenylethane in 56% yield (133), the "Wurtz like reaction" (337) between the two benzhydryl radicals probably being favored by resonance stabilization. Disulfide LXXV, when treated with Raney nickel, gave 15% of the corresponding monosulfide together with 59% of N-methylaniline (267), which was also obtained from acetaldehyde methylphenylhydrazone by identical treatment.

Disulfides LXXVI (100) and LXXVII (438) gave the normal products of hydrogenolytic desulfurization, but a mixture of products was obtained by treatment of

$[(CH_3)_2NC(CH_3)_2CH_2S-]_2$
LXXVI


LXXVII

bis(2-anthraquinonylmethyl) disulfide with Raney nickel alloy in sodium hydroxide (368, 453):

$$(R-CH_2S-)_2 \rightarrow R-CH_3 + R-CH_2OH + R-COOH$$
$$(R = \text{2-anthraquinonyl})$$

IV. THIOKETALS

Ever since Wolfrom and Karabinos (474) first desulfurized dithioketals of aliphatic and aromatic aldehydes and ketones with Raney nickel, this method has been used successfully to reduce the carbonyl to the methylene group, and has in many cases proved to be superior to the more drastic reduction methods by not affecting sensitive groups present in the molecule.

A. DITHIOKETALS DERIVED FROM ALDEHYDES OR ACYCLIC KETONES

The reactions of some ethylenedithioketals with Raney nickel are summarized in Table 19.

The diethyldithioketal derived from 2-(3′-oxobutyl)-6-hydroxy-3(2H)-pyridazinone (LXXVIII) on Raney nickel desulfurization gave N-butylsuccinamide (LXXIX) in 94% yield, but none of the expected pyridazinone derivative (170).

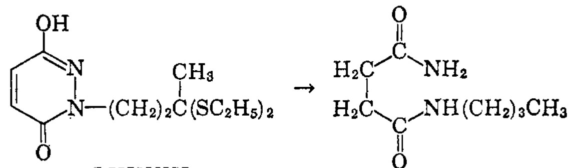
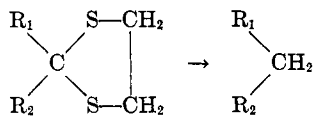
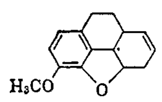
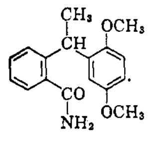
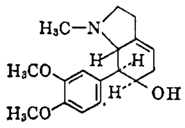

LXXVIII LXXIX

TABLE 19



R₁	R₂	Yield, %	Reference
H_3COCH_2	H	45	304
$H_2C(OH)CH(OH)CH(OH)CH_2$	H	—	135
$H_3C(CH_2)_{14}CH_2$	$CH_2CH(CH_3)CH_2CH(CH_3)CH_2COOCH_3$	—	6
	H	—	372
	CH_2CH_2COOH	89	184
	H	17[a]	301

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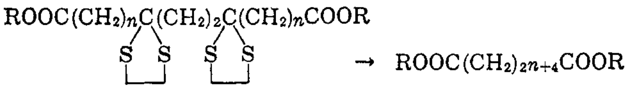
[a] The corresponding dihydro derivative was also formed.

Desulfurization by refluxing with Raney nickel in benzene–methanol of bis-ethylenedithioketals is the final step in the synthesis of the corresponding long chain dicarboxylic esters (see Table 20).

TABLE 20



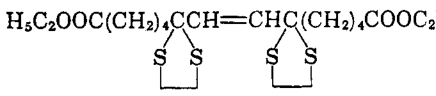
$$\mathrm{ROOC(CH_2)_nC(CH_2)_2C(CH_2)_nCOOR} \rightarrow \mathrm{ROOC(CH_2)_{2n+4}COOR}$$

R	n	Yield, %	Reference
C_2H_5	4	84	162
C_2H_5	5	54	162
C_2H_5	8	87	162, 262
CH_3	20	52[a]	262

---

[a] Based on diketo dioate.

Treatment of the unsaturated dithioketal LXXX with Raney nickel W-4 in boiling alcohol yielded diethyl tetradecanedioate. With deactivated Raney nickel unseparable mixtures were obtained which contained

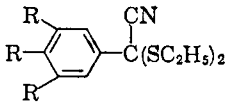


$$\mathrm{H_5C_2OOC(CH_2)_4CCH{=}CHC(CH_2)_4COOC_2H_5}$$

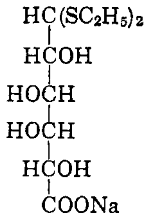
LXXX

the saturated and the unsaturated ester in different proportions depending on the time the nickel was refluxed in acetone. When this deactivation was extended to 12 hours, a small amount of dodec-6-ene-1,12-dicarboxylic acid could be isolated after saponification of the desulfurization product (163).

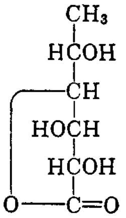
Desulfurization of LXXXIa and -b gave the normal products without hydrogenation of the cyano group (391), and the galacturonate dithioketal LXXXII yielded 48% of L-fuconic acid 1,4-lactone (LXXXIII) (459).



LXXXI
a, R = H (40%)
b, R = OCH_3 (55%)



LXXXII

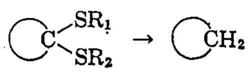


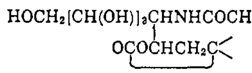
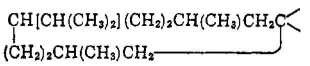
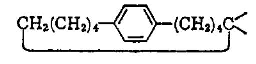
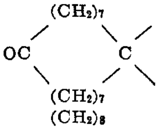
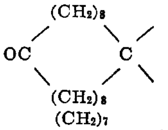
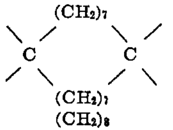
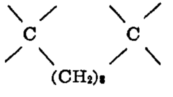
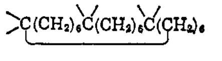
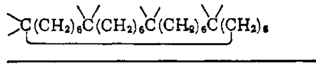
LXXXIII

B. DITHIOKETALS DERIVED FROM MONOCYCLIC KETONES

The Raney nickel desulfurizations of some dithioketals derived from monocyclic ketones are summarized in Table 21.

TABLE 21

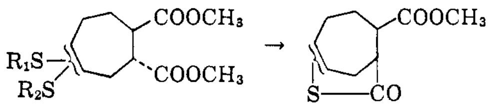


Ring	R₁	R₂	Yield, %	Reference
	C_2H_5	C_2H_5	70	310
	$\cdot CH_2CH_2\cdot$		—	423
	$\cdot CH_2CH_2CH_2\cdot$		69	125
	$\cdot CH_2CH_2\cdot$		90[a]	69
	$\cdot CH_2CH_2\cdot$		80[a]	69
	$\cdot CH_2CH_2\cdot$		42[a]	69
	$\cdot CH_2CH_2\cdot$		67[a]	69
	$\cdot CH_2CH_2\cdot$		90[b]	409
	$\cdot CH_2CH_2\cdot$		70[b]	409

---

[a] Nickel deactivated by refluxing in acetone. [b] Yields based on the corresponding ketones.

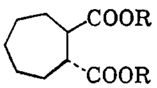
When the diethyldithioketal LXXXIV was treated with Raney nickel, ring closure to the thiolactone LXXXV was observed instead of formation of the expected diester LXXXVIa, which however was obtained in small yield (18%) from the ethylenedithioketal,



LXXXIV LXXXV

$R_1 = R_2 = C_2H_5$ (35%) $R_1, R_2 = CH_2CH_2$ (45%)

besides LXXXV (20).



LXXXVI

a, $R = CH_3$
b, $R = H$

LXXXV after mild alkaline hydrolysis could be desulfurized to LXXXVIb, wherefrom its structure was deduced (20).

C. DITHIOKETALS DERIVED FROM POLYCYCLIC KETONES

1. Terpene Derivatives

Several dithioketals of terpene ketones have been desulfurized to the corresponding methylene compounds (name of reaction product, yield and reference are given below each formula):

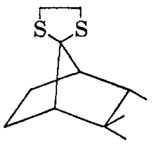
2. Steroid Derivatives

Desulfurization of dithioketals of steroid ketones, first used for the transformation of 4-cholesten-3-one into 4-cholestene by Hauptmann (237), has been applied widely in this field. In addition to the advantages already mentioned (p. 354, it permits the selective reduction of certain keto groups which form dithioketals more easily, as was demonstrated with derivatives of dehydrocholic acid (238, 240).

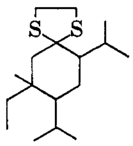
Some of the dithioketals which have been desulfurized to yield the corresponding methylene compounds are tabulated (yields of reaction products and references are given below each formula) (see pages 361 and 362).

Hydrogenolysis of C–O bonds in addition to C–S bonds occurred in some instances, only hydroxy or acetoxy groups neighboring the sulfur-bearing carbon atom being split off, as may be seen from Table 22. Neighboring carbonyl groups are unaffected (see foregoing list of dithioketals).

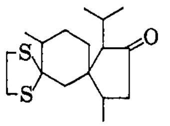
That desulfurization is a fast reaction becomes evident from the experiments (15) summarized in Table 23.



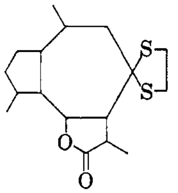
Isocamphane, 24% (435)



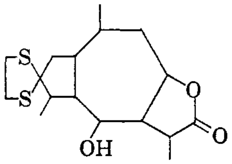
Elemane, 82% (from the ketone) (343)



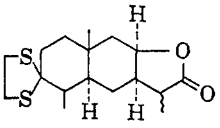
Acoranone, —(431)



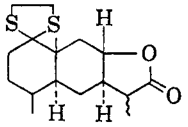
8,12-Guaianolide, —(109)



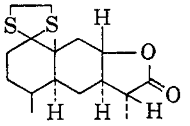
Desoxytetrahydrohelenaline, quantitative (257)



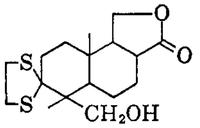
Tetrahydroalantolactone, —(437)



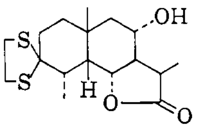
$C_{(8)}$-Epimer of tetrahydroalantolactone, —(120)



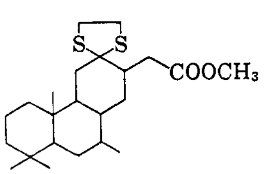
8α-Hydroxy-4,5,11α-(H)-eudesman-13-oic acid (after hydrolysis of primary product),—(121)



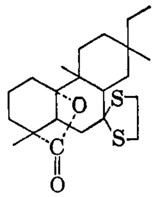
3-Deoxydihydroiresin, 56% (147)



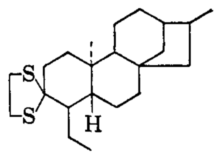
"γ"-Desoxytetrahydroartemisin, 72% (425)



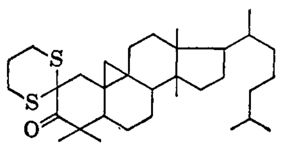
—(298)



12-Hydroxy-iso(?)rosan-16-oic acid lactone, 58% (233)

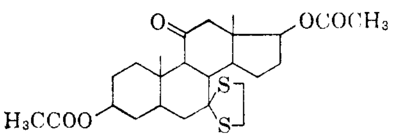


33% (146)

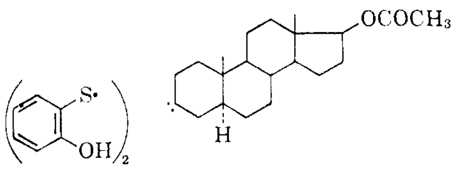


Cycloartanone, 70% (124)

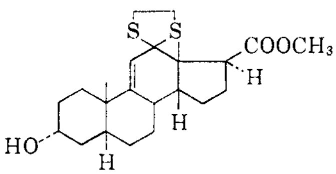
The nature of the reaction products often depends on the activity of the Raney nickel. Thus, the dithioketal LXXXVII, when refluxed with Raney nickel alloy in dioxane, gives the saturated product LXXXVIII, whereas with less active nickel (type not specified) the double bond at C(22) remains intact after desul-



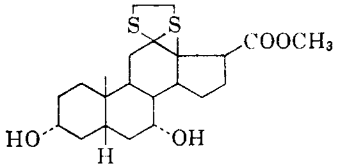
– (117)



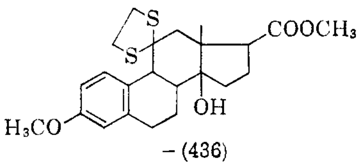
67% (150) (together with phenol)



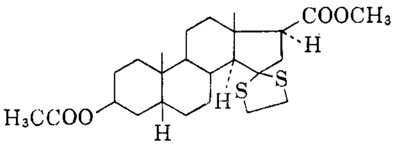
94% (107)



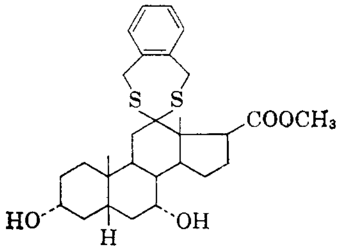
49% (404)



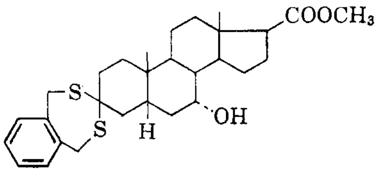
– (436)



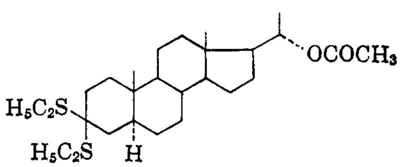
75% (311)



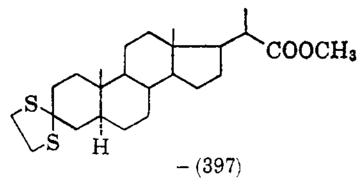
53% (282)



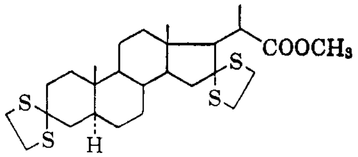
85% (282)



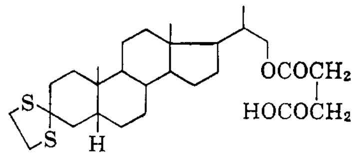
– (as 20-hydroxy deriv.) (344)



– (397)



36% (397)



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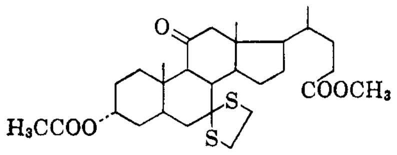
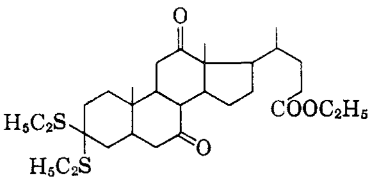
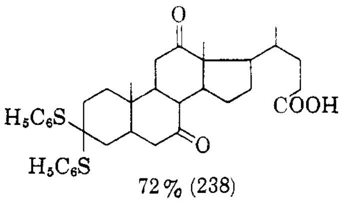


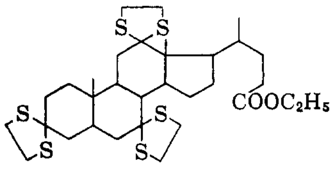
– (117)



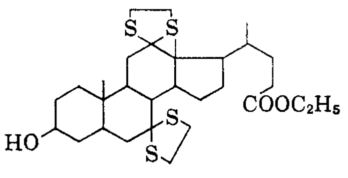
91% (238)



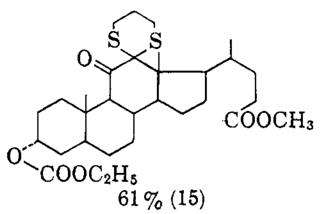
72% (238)



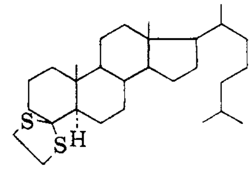
86% (238)



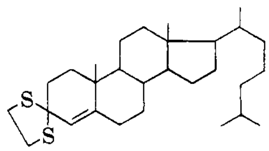
60% (as methyl ester) (238)



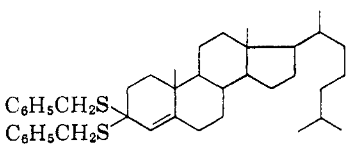
61% (15)



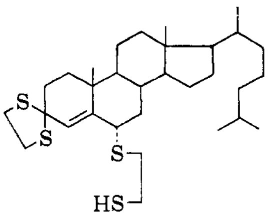
63% (421)



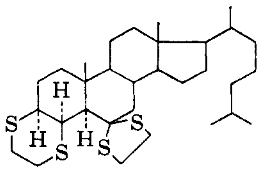
69% (238) 91% (421)



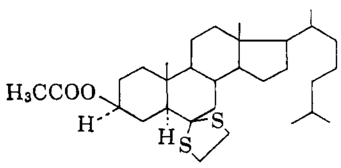
92% (238)



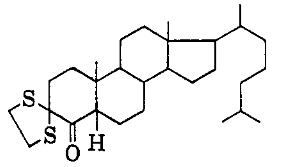
74% (as cholestane) (171)



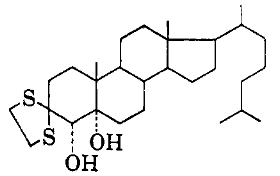
74% (as cholestane) (171)



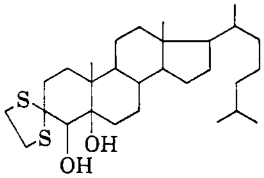
68% (171)



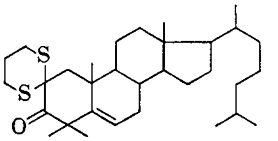
44% (421)



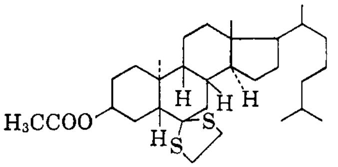
74% (157)



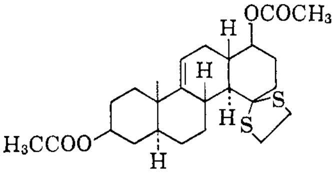
55% (157)



75% (478)



72% (from the ketone) (323)



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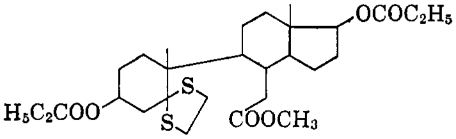
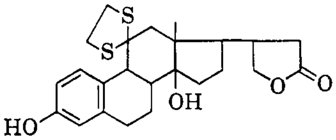


81% (284)



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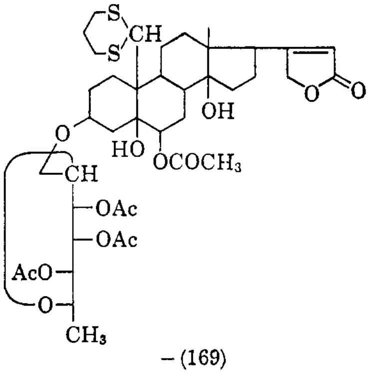

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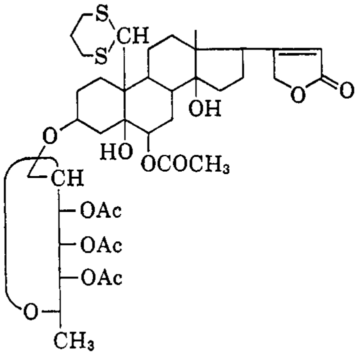

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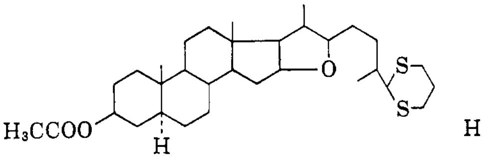
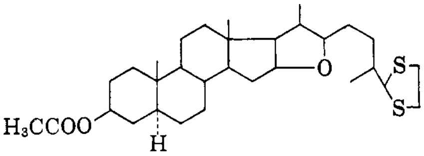
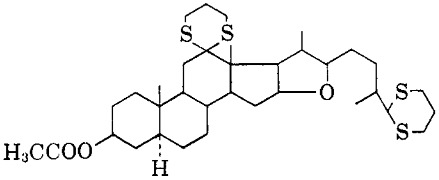


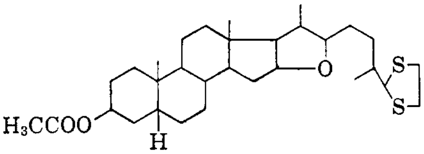
67% (152)



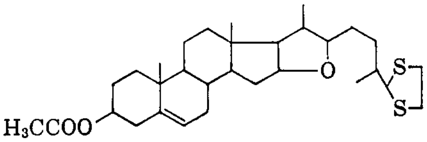
75% (152)



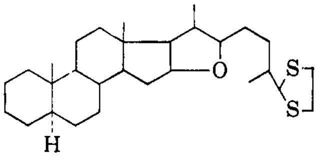
67% (152)



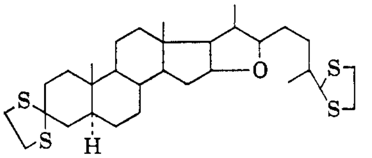
75% (152)



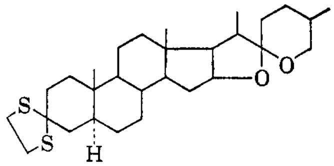
60% (152)



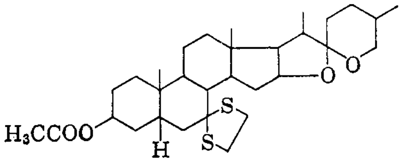
87% (152)



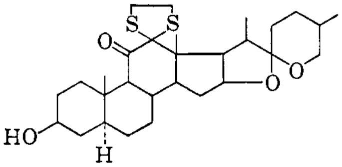
69 76% (152)



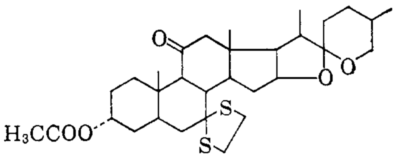
50% (361)



65% (386)



61% (153)



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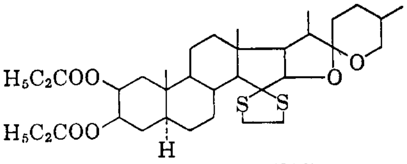
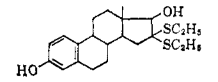
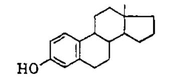
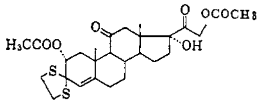
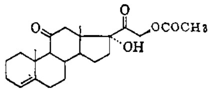
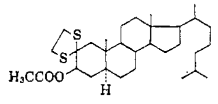
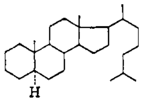
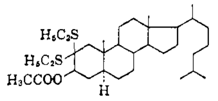
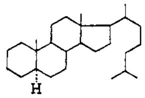
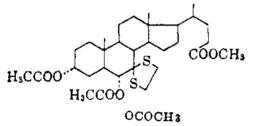
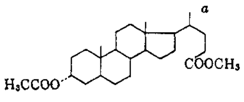
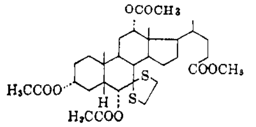
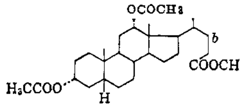
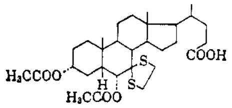
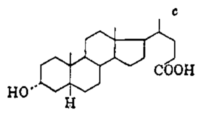


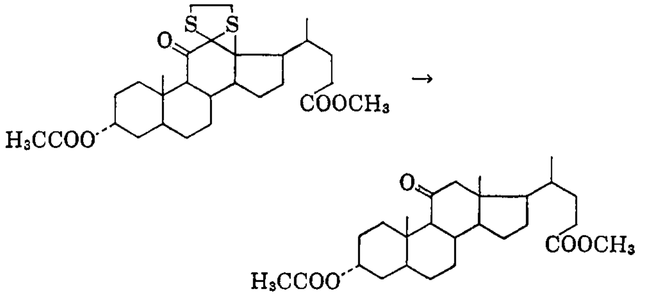
69% (as diacetate) (303)

TABLE 22

Starting compound	Reaction product	Yield, %	Reference
		—	269
		10	232
		80	399
		70	399
	 [a]	78	273
	 [b]	—	236
	 [c]	38	268

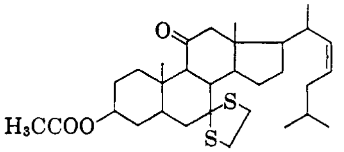
[a] Together with some 3,6-diacetoxy derivative. [b] Together with the 3,6,12-triacetoxy derivative. [c] After hydrolysis with KOH, together with 10% of the 3,6-dihydroxy derivative.

TABLE 23

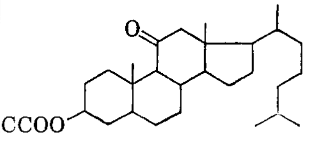


Reaction time	Temperature	Yield, %
6 hours	Room	95
1 hour	Reflux	90
15 minutes	Room	86

furization (117).

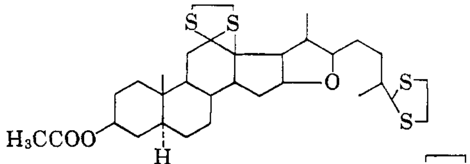


LXXXVII

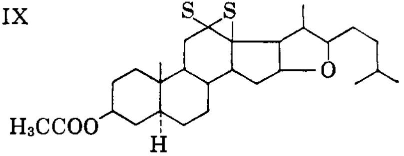


LXXXVIII

The bis-dithioketal LXXXIX was partially desulfurized in 60% yield to the 12-dithioketal XC, when it was refluxed with five times its weight of W-2 Raney nickel, it thus being demonstrated that desulfurization at the 12-position is slower than that at carbon 26. With W-4 Raney nickel in a 1:14 (weight ratio) the completely desulfurized substance XCI was obtained in 76% yield (152).

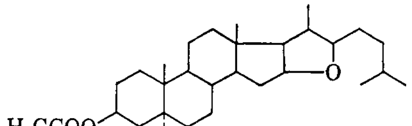


LXXXIX

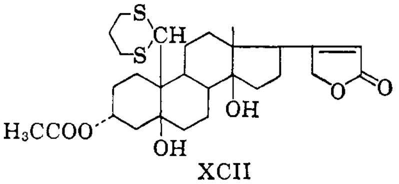


XC

This result may derive from different quantities of nickel used, since W-2 and W-4 Raney nickel do not differ too much in their activity.



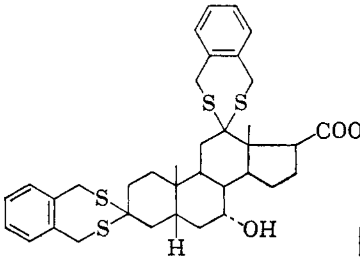
XCI



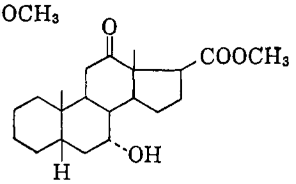
XCII

When heated with Raney nickel, previously deactivated by refluxing in acetone, dithioketal XCII yielded 17% of the expected reaction product (396). With active Raney nickel at room temperature, the yield of the sulfur-free product was 43%, 25% of unchanged starting compound being recovered (292).

Desulfurization of the bis-dithioketal XCIII in methanol gave 39% of the normal desulfurization product accompanied by a very small quantity of the ketone XCIV (282). This compound was certainly obtained from desulfurization of some 12-keto-7-hydroxy-3-xylylenedithioketal which was present in the amorphous bis-dithioketal XCIII (374).



XCIII

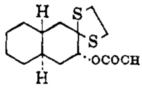
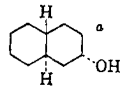
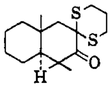
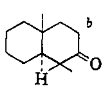
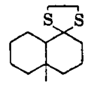
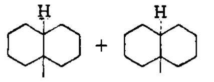
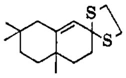
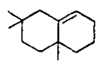
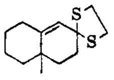
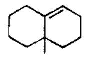
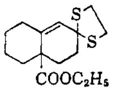
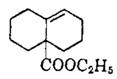
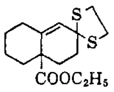
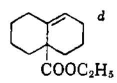


XCIV

3. Other Carbocyclic Derivatives

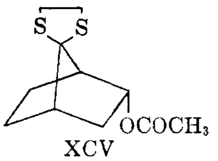
A series of dithioketals derived from deca- and octahydronaphthalene have been desulfurized with Raney nickel, yielding the expected products. The reactions are assembled in Table 24.

TABLE 24

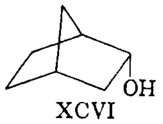
Starting compound	Reaction product	Yield, %	Reference
	 [a]	63	161
	 [b]	79	183
		89[c]	410
		81	411
		61	410
		56	388
	 [d]	—	134

[a] Product was deacetylated after desulfurization. [b] Deactivated Raney nickel (boiling in ethyl acetate and acetone) was used. [c] Over-all yield from the corresponding ketone. [d] Some unchanged starting material was recovered.

The bicyclic dithioketal XCV on Raney nickel desulfurization and hydrolysis with KOH gave *endo*-norborneol (XCVI) in an over-all yield of 68% from the parent ketone (142).

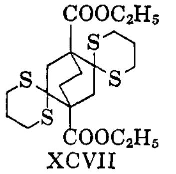


XCV

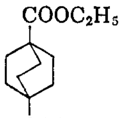


XCVI

The bis-dithioketal XCVII gave the corresponding methylene compound XCVIII in 70% yield (380) and 83% yield (316). Several attempts to reduce the parent 2,5-diketone by the Wolff–Kishner and Clemmensen methods gave less than 15% of diethyl bicyclo[2,2,2]-octane 1,4-dicarboxylate (XCVIII) (380).



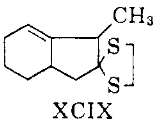
XCVII



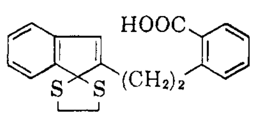
XCVIII

Desulfurization of dithioketals containing the dispiro[5,1,5,1]tetradecane skeleton and of others derived from polynuclear ketones with condensed rings has been accomplished successfully. The results are summarized in Table 25.

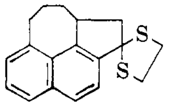
In some cases Raney nickel desulfurization failed to give the desired products. Dithioketal XCIX with W-2 Raney nickel gave a brown oil which decomposed on distillation; treatment with other types of Raney nickel gave either the unchanged starting material or resulted in complete decomposition (235).



XCIX



C

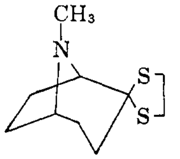


CI

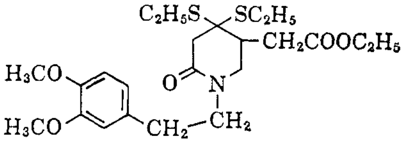
Dithioketal C on desulfurization gave "a vitreous, non-crystallizable material of acid character" (256) and CI "did not yield the hydrocarbon" (182).

4. Heterocyclic Derivatives

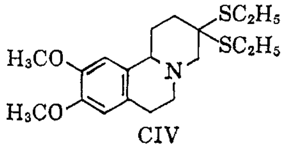
Some dithioketals of heterocyclic ketones also were desulfurized with Raney nickel. Thioketal CII gave the expected tropane (19), and CIII (426) and CIV (424) afforded the corresponding sulfur-free compounds in 93 and 37% yields, respectively.



CII

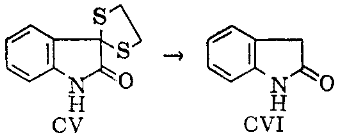


CIII



CIV

Isatin ethylenedithioketal CV, when refluxed for four hours in benzene or ethanol with Raney nickel (ratio 1 : 10), was transformed into oxindole (CVI) (467):

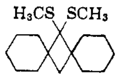
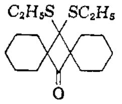
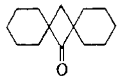
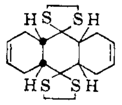
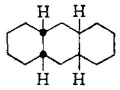
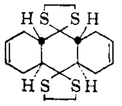
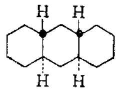
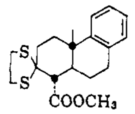
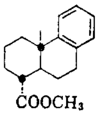
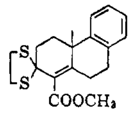
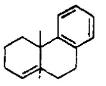
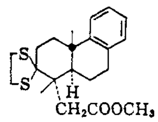
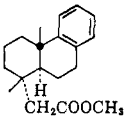
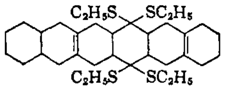
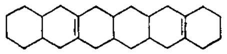
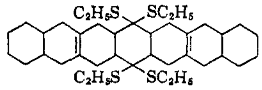
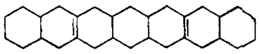


CV CVI

However, in methanol, ethanol, or 2-propanol with increased reaction time 3-alkyloxindoles resulted from the desulfurization. The results are shown in Table 26.

Oxindole itself gave 3-ethyloxindole in 90% yield when refluxed for 72 hours with Raney nickel in ethanol, and 10% when the reflux time was reduced to 24 hours. In the latter case addition of *p*-thiocresol or ethanedithiol raised the yields of 3-ethyloxindole to 20% and

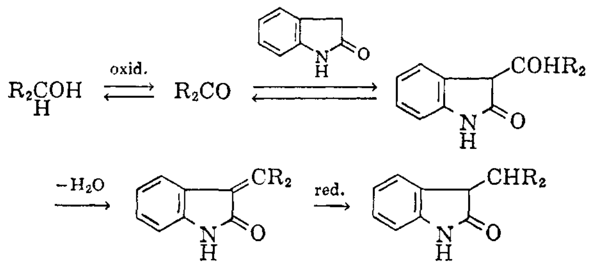
TABLE 25

Starting Compound	Reaction Product	Yield, %	Reference
		17	457
		73	457
		—	259
		—	259
		88	468
		68	468
		65	186
		42[a]	37
		35[a]	37

[a] Over-all yield from the corresponding diketone.

50%, respectively. Finally, oxindole, refluxed with Raney nickel in methanol for 70–84 hours gave 18% of polymeric 3-methyloxindole.

Based on these results the authors (467) propose a reaction scheme:

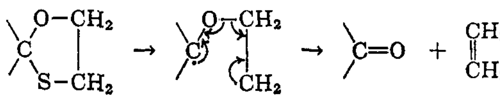


(R = H or alkyl)

D. MONOTHIOKETALS[2]

A new trend in hydrogenolytic desulfurization was opened when Romo, Rosenkranz and Djerassi (385) started studying the behavior of cyclic monothioketals and found that in this case the parent ketone is regenerated (see Table 27).

The following mechanism was suggested in order to explain the ketone formation, but the existence of other possibilities was admitted:

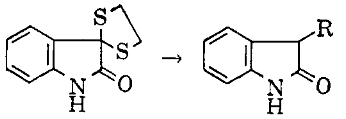


However, a surprising observation was made when compound CVII was treated with Raney nickel in acetone solution. No oxygen-free product could be isolated, the yields of the oxygenated products mounting to over 100%, so that oxygen must have been introduced from an outside source during the reaction. This observation was confirmed with other steroid monothioketals (149).

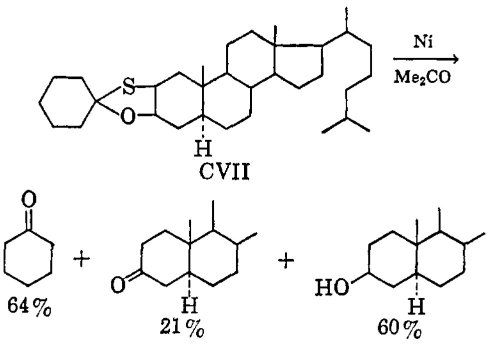
---

(2) These compounds are frequently called hemithioketals. This name, however, seems ambiguous since hemiketals have the formula $R_1R_2C(OH)OR$ and hemithioketals could therefore be compounds of the type $R_1R_2C(OH)SR$.

TABLE 26



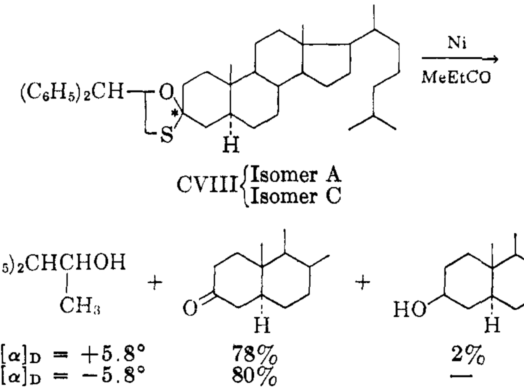
Solvent	Refluxing Time, hr.	R	Yield, %
C_2H_5OH	4	H	63
C_2H_5OH	8	C_2H_5	21
C_2H_5OH	24	C_2H_5	83
$(CH_3)_2CHOH$	84	$(CH_3)_2CH$	32
H_3COH	36	CH_3	16



CVII

64% 21% 60%

By employing monothioketals of optically active mercaptoalcohols it could be shown that the oxygen originally present in the monothioketal remains in the alcohol portion, since desulfurization of two of the three synthesized monothioketals CVIII yielded the two enantiomers of 1,1-diphenyl-2-propanol with the same absolute value of $[\alpha]_D$ (149):



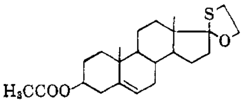
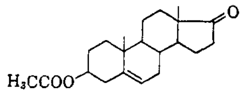
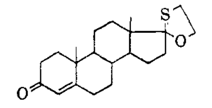
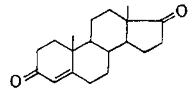
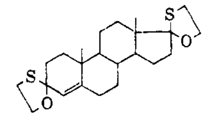
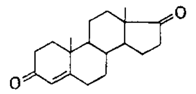
CVIII {Isomer A, Isomer C}

$(C_6H_5)_2CH\underset{\displaystyle CH_3}{C}HOH$

52%, $[\alpha]_D = +5.8°$ 78% 2%
57%, $[\alpha]_D = -5.8°$ 80% —

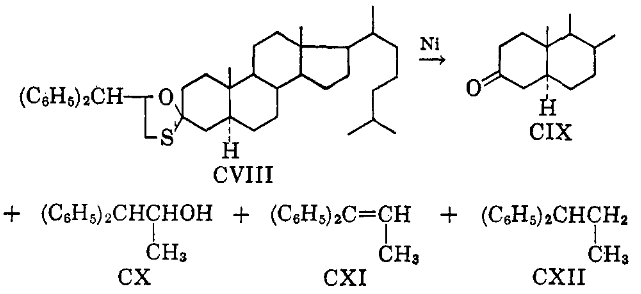
In spite of the specific rotation of pure 1,1-diphenyl-2-propanol not being known the authors conclude from the isolation of the two enantiomeric alcohols that the configuration about the carbon atom 2 of the 1,1-diphenyl-2-propanol has been retained during the desulfurization, since it is highly improbable that partial racemization should have occurred to exactly the same extent in both desulfurizations. Retention of configuration, however, indicates that the starred bond only had been broken and no radical $(C_6H_5)_2$-$CHCHCH_3$, which would racemize quickly, had been formed during the reaction (149).

TABLE 27

Starting compound	Reaction product	Yield, %
		80
		70
		22

The introduction of oxygen occurs only in polar solvents, as ketones or alcohols. When the reaction is performed in benzene, a different pattern is observed as is shown in Tables 28 and 29.

TABLE 28



CVIII CIX

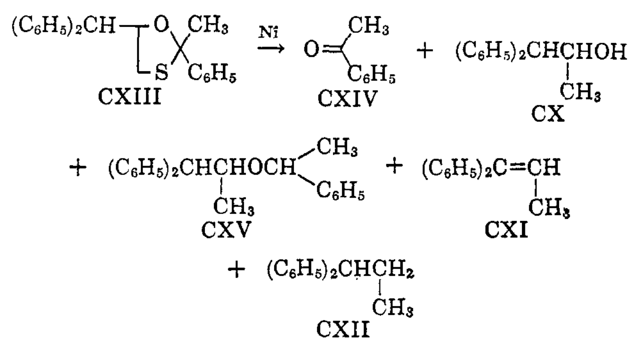
$+ (C_6H_5)_2CH\underset{\displaystyle CH_3}{C}HOH + (C_6H_5)_2C{=}\underset{\displaystyle CH_3}{C}H + (C_6H_5)_2CH\underset{\displaystyle CH_3}{C}H_2$

CX CXI CXII

No.	Solvent	CIX, %	CX, %	CXI, %	CXII, %
1	MeEtCO	85	89	0	0
2	C_6H_6, *t*-BuOH	42	56–75	0	0
3	C_6H_6	53	0	20	78
4	C_6H_6, N_2[a]	98	0	9	69
5	C_6H_6, N_2[b]	93	0	84	0

[a] 42 day old Raney nickel deactivated by boiling in acetone. [b] 55 day old Raney nickel similarly deactivated.

TABLE 29



CXIII CXIV

$+ (C_6H_5)_2CH\underset{\displaystyle CH_3}{C}HOH$ CX

$+ (C_6H_5)_2CH\underset{\displaystyle CH_3}{C}HOCH\begin{smallmatrix}CH_3\\C_6H_5\end{smallmatrix}$ CXV $+ (C_6H_5)_2C{=}\underset{\displaystyle CH_3}{C}H$ CXI

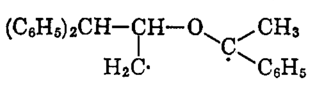
$+ (C_6H_5)_2CH\underset{\displaystyle CH_3}{C}H_2$ CXII

Solvent	CXIV, %	CX, %	CXV, %	CXI, %	CXII, %
MeEtCO	71	62	0	4	32
Me_2CO[a]	64	37	27	0	30
C_6H_6[b]	67	2	0	96	0

[a] 38 day old Raney nickel. [b] Raney nickel deactivated by refluxing in acetone.

In benzene little, if any, alcohol CX is formed from the β-mercapto-alcohol portion of the hemithioketal but a mixture of two hydrocarbons, a saturated (CXII) and an unsaturated (CXI) one, is isolated and in some cases an ether (CXV) which contains the ketone as well as the mercaptoethanol moiety of the hemithioketal (154).

The 1,4-diradical mechanism holds for this reaction too. The formation of ether CXV is explained by the fact that the diradical contains a benzyl radical which is more stable than the corresponding one from CVIII



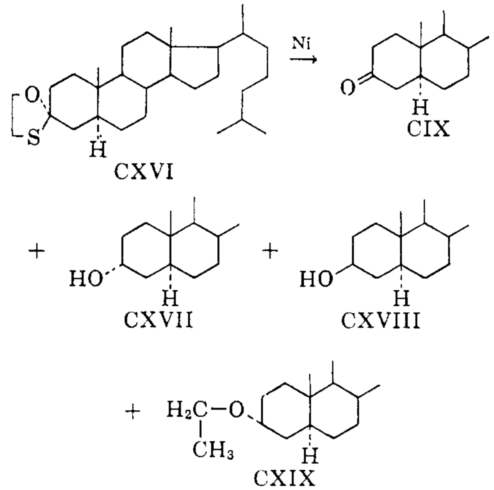
$$(C_6H_5)_2CH{-}\underset{H_2C\cdot}{CH}{-}O{-}\overset{\cdot}{C}(CH_3)(C_6H_5)$$

(p. 366) and may either collapse with formation of acetophenone and the hydrocarbons or react with hydrogen to give the ether (154).

It is to be noted that 1,1-diphenyl-1-propene (CXI) is obtained instead of the expected 1,1-diphenyl-2-propene, which should result from the 1,4-diradical postulated; this is explained by the assumption that isomerization by double bond migration may occur on the nickel surface (154).

The introduction of the extra oxygen is attributed to the action of hydroxyl ions adsorbed on the surface of the Raney nickel, where they could have remained from the preparation. The alkaline reaction of aqueous Raney nickel suspension is well established since it was shown that it had a pH of 8–9 (154); later work (253) confirmed this finding. Experiments were performed (154) at different pH in order to eliminate the effect of hydroxyl ions. As can be seen from Table 30 there are significant differences in the results obtained at different pH. It is indeed dubious whether acidification of the solution even to pH 4.2 is sufficient for removing all or at least most of the hydroxyl ions from the nickel surface or whether this can be done at all without affecting the structure of the Raney nickel composition.

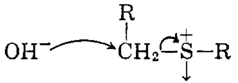
TABLE 30



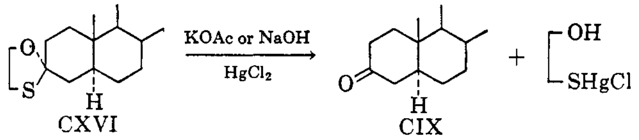
Solvent	pH	CIX, %	CXVII, %	CXVIII, %	CXIX, %
Me_2CO	~8.5	64	12	19	3
Me_2CO	6.75[a]	70	6	8	13
Me_2CO	4.2[a]–5.7[b]	87	2	6	5
C_6H_6	~8.5	34	0	0	31
C_6H_6, N_2[c]	~8.5	58	18	14	10

[a] pH adjusted by addition of acetic acid. [b] Final pH. [c] Raney nickel deactivated by refluxing in acetone.

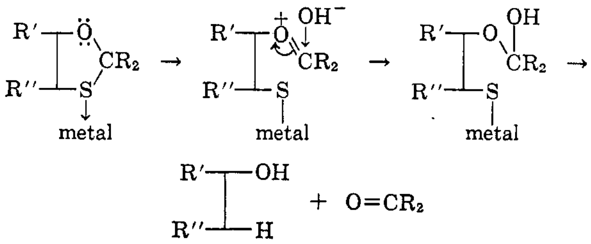
Therefore, another mechanism was proposed based on Grob's observation (218) that certain tetrahydrothiophenes easily undergo ring opening when treated with base in the presence of silver or mercury salts, probably through a reaction such as



Mercuric chloride had the same effect on the hydrolysis of monothioketals CXVI and CVIII, which did not react with acetic acid and potassium acetate but were split easily by either potassium acetate or sodium hydroxide when mercuric chloride was present (154):



In order to demonstrate that Raney nickel may act in the same manner as mercuric chloride, a sample of the metal, degassed at 200° *in vacuo*, which did not react with hemithioketal CXVI in acetone, was shown to produce 67% of cholestanone (CIX) when acetic acid and potassium acetate were added. This mechanism is suggested (154) for the reaction:

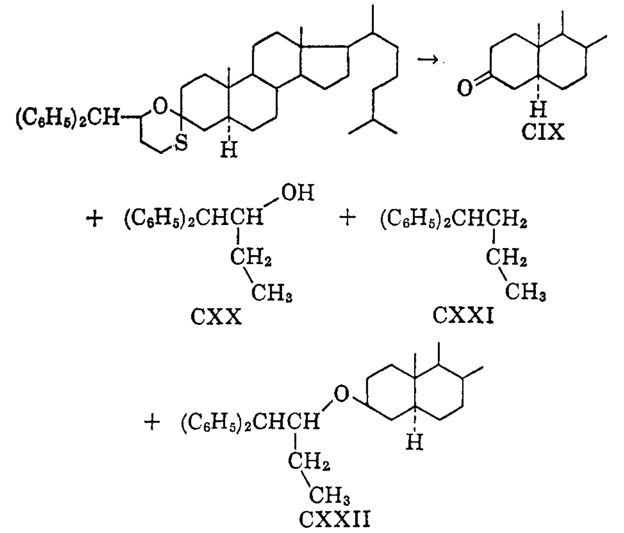


The fact that no extra oxygen is introduced in benzene solution is explained by the assumption that in this solvent the reaction proceeds mainly through radicals since no ionic intermediates can be formed.

Oxathianes (six-membered cyclic hemithioketals of γ-mercaptoalcohols) behaved essentially in the same way as oxathiolanes (154) as can be seen from Tables 31 and 32.

In benzene, however, formation of the ether was enhanced, being observed also with cholestane derivatives (Table 31, No. 2), in contrast to the corresponding oxathiolanes (p. 366, Table 28, No. 4). If a 1,4-diradical were an intermediate, as assumed for the oxathiolanes,

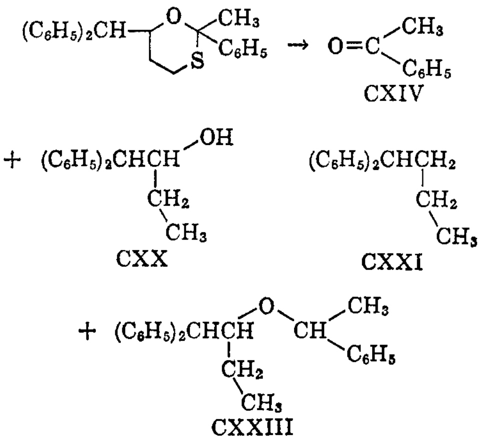
TABLE 31



No.	Solvent	CIX, %	CXX, %	CXXI, %	CXXII, %
1	MeEtCO	72[b]	67	0	0
2	C_6H_6, N_2[a]	56	17	21	24

[a] 13% of 3α-cholestanol and 11% of 3β-cholestanol also were isolated.
[b] Raney nickel deactivated by refluxing in acetone.

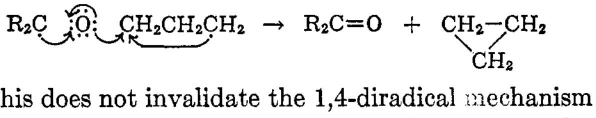
TABLE 32



Solvent	CXIV, %	CXX, %	CXXI, %	CXXIII, %
MeEtCO	81	56	0	20
Me_2CO	72	59	0	13
C_6H_6, N_2[a]	45	23	19	27

[a] Raney nickel deactivated by refluxing in acetone.

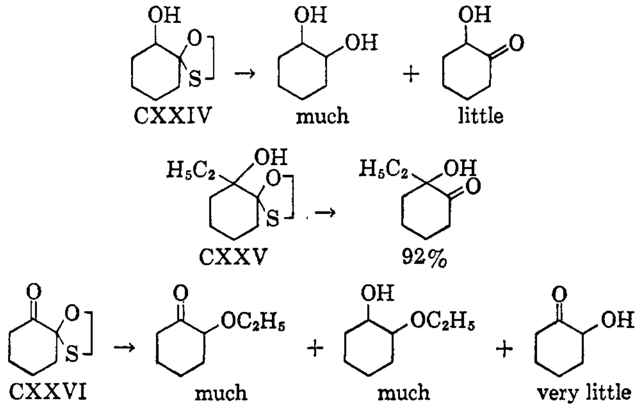
a cyclopropane derivative should be formed in the case of the oxathianes, which has never been observed:



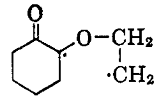
$$R_2C\,\dot{O}\,\dot{C}H_2CH_2\dot{C}H_2 \rightarrow R_2C{=}O + \underset{CH_2}{CH_2{-}CH_2}$$

This does not invalidate the 1,4-diradical mechanism since it has been shown in the meantime that cyclopropane derivatives are transformed into propane derivatives under desulfurization conditions (34). If no 1,4-diradical mechanism is operative one should expect the ether to be the principal desulfurization product. Indeed ethers CXXII and CXXIII were isolated but the main reaction products continued being the ketones CIX and CXIV together with alcohol CXX and hydrocarbon CXXI. These did not originate from hydrogenolysis of an ether like CXXII, which was shown to be stable in the presence of Raney nickel under the usual desulfurization conditions. Therefore it was suggested (154) that the reaction may perhaps proceed through several pathways.

While the work on steroid monothioketals was in progress the behavior of some oxathiolanes derived from cyclohexane-1,2-dione and its derivatives during desulfurization was studied (279). When they were refluxed with Raney nickel the following results were obtained:



Desulfurization of the oxathiolanes CXXIV and CXXV proceeds essentially by the already proposed "normal" mechanism (149) accompanied by some reduction of the keto group. The desulfurization of CXXVI apparently was anomalous, ether formation being possibly favored by the influence of the electron-attracting carbonyl group which stabilizes the adjacent unpaired electron, so that addition of hydrogen to the diradical



becomes the faster reaction.

The results obtained by desulfurization of the compounds shown in Table 33, which have a carbonyl group in the oxathiolane ring, can be explained by assuming intermediate formation of the 1,4-diradical CXXVII, which rearranges to the original carbonyl compound CXXVIII and 1,2-diradical CXXIX, which

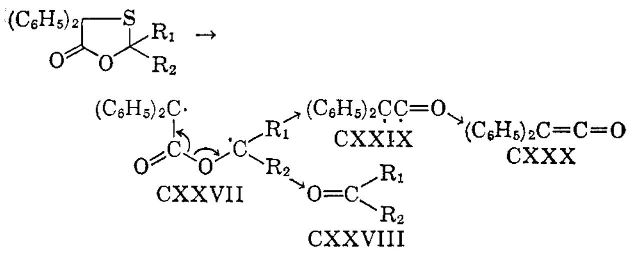
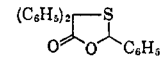
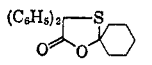
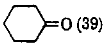
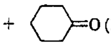
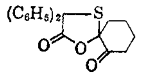
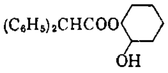
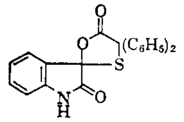
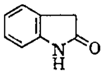
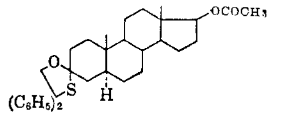
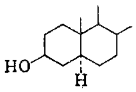
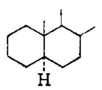
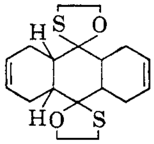


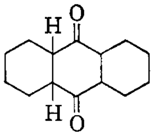
TABLE 33

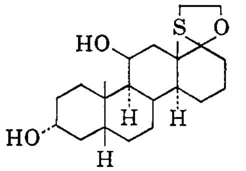
Oxathiolanone	Solvent	Reaction products and yields, %
	Ethanol Acetone Benzene	$(C_6H_5)_2CHCOOH(2) + (C_6H_5)_2CHCOOC_2H_5(12)$ $(C_6H_5)_2CHCOOH(18) + C_6H_5CHO(5)$ $(C_6H_5)_2CHCOOH(4) + C_6H_5CHO(38)$
	Ethanol	$(C_6H_5)_2CHCOOH(3) + (C_6H_5)_2CHCOOC_2H_5(35) + (C_6H_5)_2CHCH_2OH(4)$
	Acetone	$(C_6H_5)_2CHCOOH$ (14) +  (39)
	Benzene	$(C_6H_5)_2CHCOOH$ (0.2) + $(C_6H_5)_2CHCH_2OH$ (12) +  (17)
	Benzene + Aniline	$(C_6H_5)_2CHCONHC_6H_5$ (43) +  (8)
	Ethanol	 (37)
	Ethanol	$(C_6H_5)_2CHCOOH$ (28) +  (9)
	Ethanol	$(C_6H_5)_2CHCOOC_2H_5$ (6) +  (48) +  (6)

may further rearrange to diphenylketene CXXX. Either CXXIX or CXXX may react with the solvent, with water or with hydrogen present in the Raney nickel to give the isolated reaction products (455).

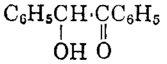
The regeneration of ketones by Raney nickel desulfurization of cyclic hemithioketals has been further confirmed by some recent investigations. Thus, the bismonothioketal CXXXI on treatment with Raney nickel in ethanol, gave the saturated diketone CXXXII (259) and the D-homosteroid monothioketal CXXXIII in acetone gave the corresponding ketone (119).

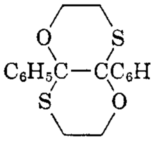

CXXXI

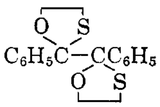

CXXXII


CXXXIII

Two isomers of benzil bis-(ethylenemonothioketal) were reported, which both gave benzoin (CXXXIV) on treatment with Raney nickel in acetone (320); CXXXV and CXXXVI were, therefore, suggested as possible formulas of the isomers.


$$C_6H_5\underset{OH}{CH}\cdot\underset{\overset{\|}{O}}{C}C_6H_5$$
CXXXIV

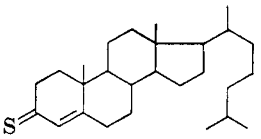

CXXXV

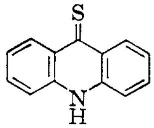

CXXXVI

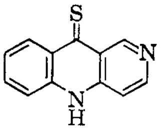
V. Thiones and Related Compounds

A. THIONES

To our knowledge, during the last few years very few thiones have been desulfurized; 3-thiono-4-cholestene (CXXXVII), when refluxed in dioxane with Raney nickel, gave 4-cholestene in unstated yield (85). Thioacridone (CXXXVIII) yielded a maximum of 25% of acridine, and desulfurization of pyrido[4,3-b]quinolin-10(5H)-thione (CXXXIX) was accompanied by extensive reduction of the ring system (123).

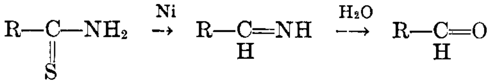

CXXXVII


CXXXVIII


CXXXIX

B. THIOAMIDES

Desulfurization with Raney nickel of simple or substituted thioamides, easily obtained from nitriles, has been used for the preparation of aldehydes, supposedly by a two-step reaction (129):


$$R—\underset{\underset{S}{\|}}{C}—NH_2 \xrightarrow{Ni} R—\underset{H}{C}{=}NH \xrightarrow{H_2O} R—\underset{H}{C}{=}O$$

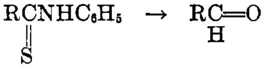
The highest yield of benzaldehyde obtained from thiobenzamide was 32% (nickel deactivated with acetone and ammonia at 25°, ratio thioamide : nickel = 1 : 41, reaction in ethanol at 25° during 15 minutes).

Thioanilides, which however are difficult to prepare, were also treated with Raney nickel, higher yields of aldehydes being obtained as expected, because of the greater stability of the intermediate anils (see Table 34).

The thioanilides were refluxed in acetone for 1 hour with Raney nickel (ratio 1 : 15) previously deactivated by heating in the same solvent (129).

No aldehyde could be obtained by Raney nickel

TABLE 34



$\mathrm{R\underset{\underset{S}{\|}}{C}NHC_6H_5 \rightarrow R\underset{H}{C}{=}O}$

R	Yield, %[a]
C_6H_5	84
$4\text{-}CH_3OC_6H_4$	96
$4\text{-}OHC_6H_4$	78
$CH_3CH_2CH_2$	32
$(CH_3)_2CHCH_2$	32

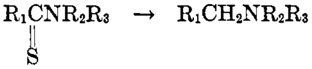
[a] As 2,4-dinitrophenylhydrazones.

treatment of the thioamide CXL; no details were given (8).

CXL

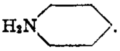
Various substituted thioamides have been desulfurized with Raney nickel to the corresponding substituted amines (Table 35).

TABLE 35



$\mathrm{R_1\underset{\underset{S}{\|}}{C}NR_2R_3 \rightarrow R_1CH_2NR_2R_3}$

R_1	R_2	R_3	Yield, %	Reference
Ferrocenyl-$CH_2\cdot$	CH_3	CH_3	—	348
$3,4\text{-}(CH_3)_2C_6H_3CH_2\cdot$[a]	$\cdot CH_2(CH_2)_3CH_2\cdot$		55	118
$4\text{-}ClC_6H_4$	$2\text{-}C_5H_4N$	$\cdot(CH_2)_2N(CH_3)_2$	70[b]	378
$4\text{-}ClC_6H_4$	$2\text{-}C_5H_4N$	$\cdot(CH_2)_2N(CH_3)_2$	60[b,c]	443
$4\text{-}CH_3OC_6H_4$	2-pyrimidyl	$\cdot(CH_2)_2N(CH_3)_2$	51	333

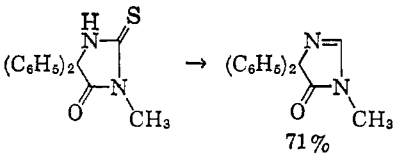
[a] Starting compound could also be $3,4\text{-}(CH_3)_2C_6H_3C(:S)CH_2N$.

[b] Raney nickel deactivated by refluxing in acetone. [c] With active nickel $2\text{-}C_5H_4NNH(CH_2)_2N(CH_3)_2$ was obtained.

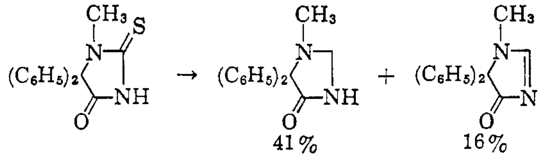
C. THIOHYDANTOINS, THIOBARBITURIC ACIDS, AND RELATED COMPOUNDS

A great number of 2-thiohydantoins, which, being easy to prepare, are a convenient starting material for the preparation of imidazolidones, have been desulfurized with Raney nickel (Table 36).

Sometimes 2-thiohydantoins on Raney nickel desulfurization yield the corresponding imidazolinones either exclusively or together with the imidazolidones (102):



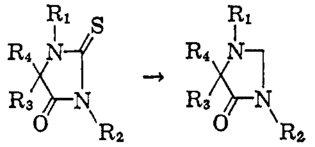
71%



41%

16%

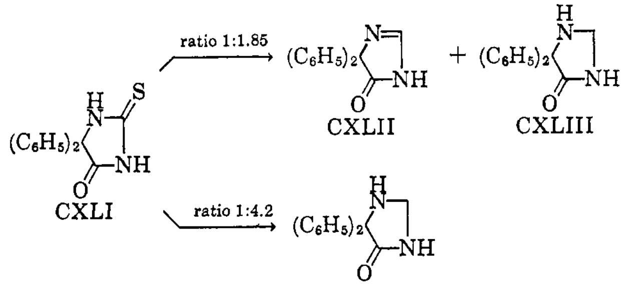
TABLE 36



R_1	R_2	R_3	R_4	Yield, %	Reference
$COCH_3$	H	H	H	—	158
$COCH_3$	H	H	H	—	158
H	$COOCH_2C_6H_5$	H	H	23–34[a]	180
H	H	CH_3	H	—[b]	470
H	H	C_6H_5	H	—[b]	470
$COCH_3$	H	CH_3	H	—	158
$COCH_3$	H	$CH_2C_6H_5$	H	—	158
H	H	C_6H_5	C_6H_5	64	102
H	H	$4\text{-}CH_3OC_6H_4$	$4\text{-}CH_3OC_6H_4$	22	102
H	H	C_6H_5	CH_3	21	102
H	H	C_6H_5	C_2H_5	46	102
CH_3	H	C_6H_5	CH_3	10	102
CH_3	CH_3	C_6H_5	C_6H_5	48[c]	102

[a] Raney nickel previously refluxed with absolute ethanol; the same result was obtained by heating the nickel *in vacuo* at 100° according to (248). [b] Viscous brown oils were obtained which could not be crystallized. [c] Only in methanol, propanol, or cyclohexane was the corresponding imidazolidone obtained; for the reaction product in ethanol see p. 371.

That the amount of Raney nickel influences the course of the reaction was shown (416, 417) when 5,5-diphenyl-2-thiohydantoin (CXLI), treated with Raney nickel in a weight-ratio of 1 : 1.85, gave mainly the unsaturated product (CXLII) along with a little of the corresponding imidazolidone (CXLIII), whereas the latter was obtained almost pure when a ratio of 1 : 4.2 was used.



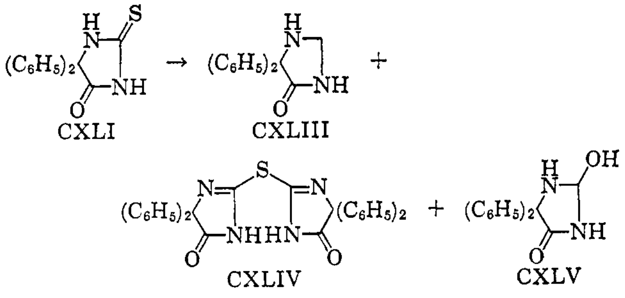
CXLI

CXLII

CXLIII

CXLIII

Compound CXLII, when treated with fresh Raney nickel, gave 45% of CXLIII (416, 417). When the same thiohydantoin CXLI was refluxed with three-week-old Raney nickel in a ratio of 1 : 5, these products were obtained (470):



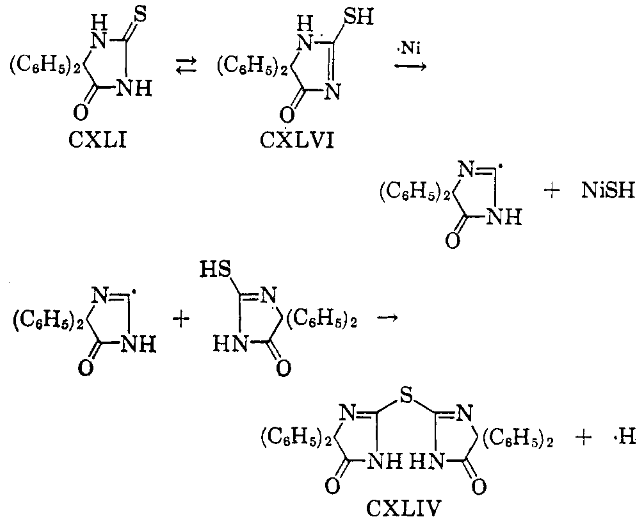
CXLI

CXLIII

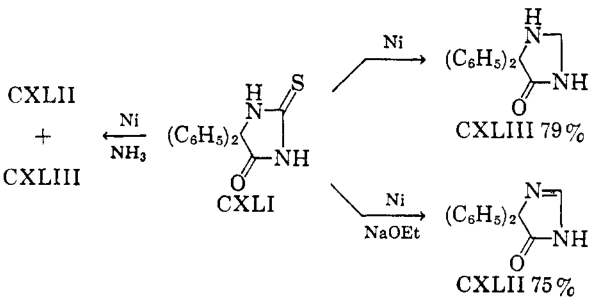
CXLIV

CXLV

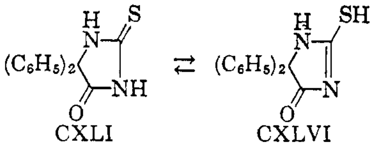
The sulfide CXLIV and the hydroxy compound CXLV could be transformed quantitatively into CXLIII by treatment with fresh Raney nickel. In the opinion of the authors (470), the formation of the sulfide indicates that the reduction proceeds by way of the mercapto form of the thiohydantoin, a radical mechanism being involved:



Another factor which strongly influences the course of the desulfurization of CXLI is the alkalinity of the reaction medium, as can be seen from the scheme below (456):



When CXLI is desulfurized in ethanol containing ammonia, increasing concentration of ammonia favors formation of CXLII at the expense of CXLIII (456) (see Table 37). The already mentioned equilibrium



which in alkaline medium would be shifted to the right side may be involved.

In this connection it should be remembered that desulfurization of 2-alkylthio-5,5-diphenyl-4-imidazolinones, which are derivatives of form CXLVI, gives also mixtures of saturated and unsaturated compounds (see p. 356, Table 13), the yields being comparable to those cited in Table 37. Therefore, it seems likely that desulfurization of 5,5-diphenyl-2-thiohydantoins occurs at least in part on the thiol form CXLVI, the double bond being but partially hydrogenated during this reaction, possibly due to deactivation of the nickel in the alkaline medium.

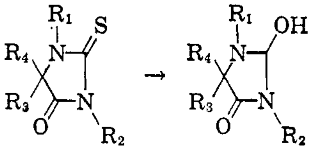
TABLE 37

CXLI → CXLII + CXLIII

NH_3 in ethanol, M	Yield of CXLII, %	Yield of CXLIII, %
0	0	75
0.05	4	72
0.5	8	63
5	11	57

Frequently, 2-hydroxyimidazolidones are formed during the desulfurization of 2-thiohydantoins, especially when position 5 is substituted by alkyl or alkylene groups (102). It may be recalled that substitution of oxygen for sulfur is easily performed in 2-thiohydantoins; from the reagents used, *e.g.*, chloroacetic or hydrochloric acids but also sodium hydroxide and ferrous sulfide, it seems very likely that this reaction has an ionic mechanism (460). The Raney nickel desulfurizations are tabulated in Table 38.

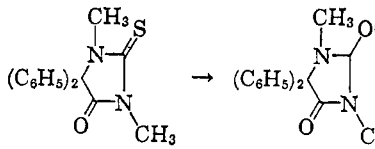
TABLE 38



R_1	R_2	R_3	R_4	Yield, %
H	H	CH_3	CH_3	39
H	H	$\cdot CH_2(CH_2)_3CH_2\cdot$		40[a]
H	H	$\cdot CH_2(CH_2)_2CH_2\cdot$		26
H	H	$\cdot CH_2CH_2CH(CH_3)CH_2CH_2\cdot$		43
H	CH_3	$\cdot CH_2(CH_2)_3CH_2\cdot$		17[b]
CH_3	H	$\cdot CH_2(CH_2)_3CH_2\cdot$		55
CH_3	CH_3	$\cdot CH_2(CH_2)_3CH_2\cdot$		7

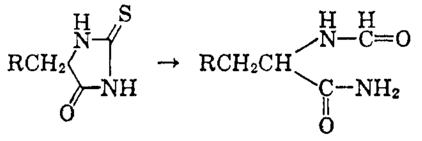
[a] Together with a small quantity of the hydroxyl-free product. [b] Together with 16% of the hydroxyl-free product.

When 1,3-dimethyl-5,5-diphenyl-2-thiohydantoin (CXLVII) was refluxed with Raney nickel in ethanol, the 2-ethoxy compound (CXLVIII) was obtained in 38% yield (102).



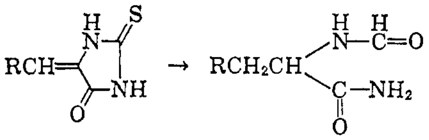
Sometimes desulfurization of thiohydantoins is accompanied by opening of the ring. Thus, 5-monosubstituted-2-thiohydantoins, when treated with Raney nickel in tetrahydrofuran or dioxane, both containing 10% of water, give the amides of the corresponding

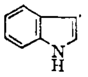
TABLE 39



R	Yield, %
H	34
$(CH_3)_2CHOCOCH_2$	43
C_6H_5	64
$4\text{-}OHC_6H_4$	61

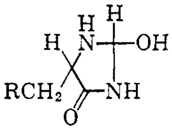
TABLE 40



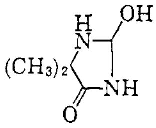
R	Yield, %
$(CH_3)_2CH$	44
$4\text{-}CH_3OC_6H_4$	67
$3,4\text{-}CH_2O_2C_6H_3$	56
$4\text{-}ClC_6H_4$	15
C_6H_5	60
	50

α-formylamino acids (53) (see Tables 39 and 40), which are easily hydrolyzed to α-amino acids.

However, the tautomer ring structure (CXLIX) which had already been proposed (102) (see Table 38) is also under consideration (53).

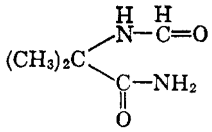


CXLIX

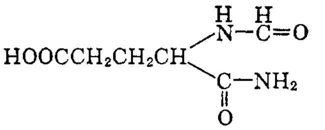


CL

5,5-Dimethyl-2-thiohydantoin on Raney nickel desulfurization gave 66–88% of a product which was formulated as either CL or CLI (470), the latter being in better accordance with the infrared spectrum (53).



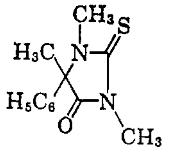
CLI



CLII

dl-4-Formamidoglutaramic acid (CLII) results from desulfurization of 2-thio-5-hydantoinpropionic acid (483).

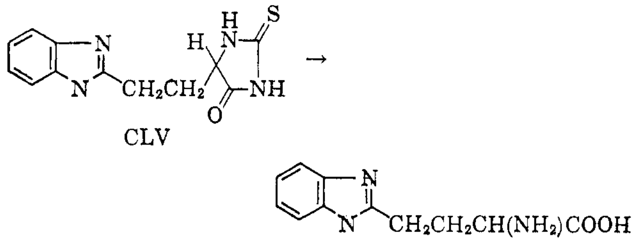
Sometimes more extensive degradation takes place when thiohydantoins are treated with Raney nickel. Thus, 1,3,5-trimethyl-5-phenyl-2-thiohydantoin (CLIII) gave N-methyl-α-phenylpropionamide (CLIV) (102), and 1-(2-benzimidazolyl)-2-(2-thio-5-hydantoinyl)ethane (CLV) in moist tetrahydrofuran gave α-amino-γ-(2-benzimidazolyl)butyric acid (CLVI) (51):



CLIII

→ $C_6H_5CH(CH_3)CONHCH_3$

CLIV

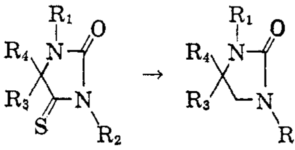


CLV

CLVI

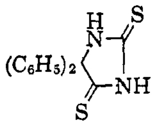
Some 4-thiohydantoins also have been desulfurized to the corresponding imidazolidones (102), as can be seen from Table 41.

TABLE 41



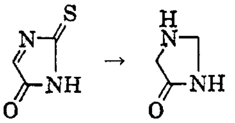
R_1	R_2	R_3	R_4	Yield, %
H	H	C_6H_5	CH_3	60
H	CH_3	C_6H_5	C_6H_5	56
H	CH_3	C_6H_5	CH_3	44
CH_3	CH_3	C_6H_5	C_6H_5	43
H	H	$\cdot CH_2(CH_2)_3CH_2\cdot$		61
H	CH_3	$\cdot CH_2(CH_2)_3CH_2\cdot$		46

On the other hand, attempts to desulfurize 5,5-diphenyl-2,4-dithiohydantoin (CLVII) were unsuccessful (416).



CLVII

That 3,4-dehydro-2-thiohydantoin (CLVIII), when treated with Raney nickel, gives the unstable 4(5)-imidazolidone (CLIX) was concluded from chromatographic evidence (R_f, color reactions) (180).

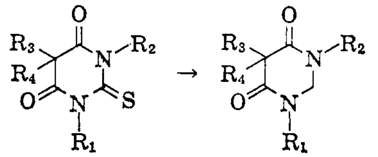


CLVIII CLIX

Considering now six-membered rings, it may be mentioned first that piperidine-2-thione when treated with Raney nickel in ethanol gave piperidine (416).

2-Thiobarbituric acid and many of its derivatives have been desulfurized with Raney nickel, as can be seen from Table 42.

TABLE 42

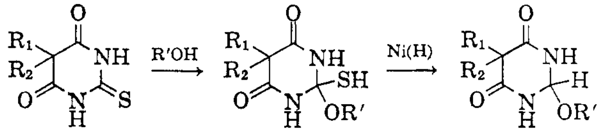


R_1	R_2	R_3	R_4	Yield, %	Reference
H	H	H	H	—	416
H	H	C_2H_5	C_2H_5	70	470
H	H	C_2H_5	iso-C_5H_{11}	71	470
H	H	C_2H_5	cyclo-C_6H_{11}	—[a], [b]	78
H	H	C_2H_5	C_6H_5	45[a], [c]	78
H	H	C_2H_5	C_6H_5	High	470
H	H	C_2H_5	2-ClC_6H_4	—[a], [d]	78
H	H	C_2H_5	3-ClC_6H_4	—[a]	78
H	H	C_2H_5	4-ClC_6H_4	—[a]	78
H	CH_3	C_2H_5	C_6H_5	—[a]	78
H	C_6H_5	C_2H_5	C_6H_5	—[a]	78
CH_3	CH_3	H	C_6H_5	—[a]	78
CH_3	CH_3	C_2H_5	C_6H_5	—[a]	78
C_6H_5	C_6H_5	H	H	—	416

[a] Refluxed in ethanol with W-5 Raney nickel. [b] Starting compound was 5-ethyl-5-cyclohexenyl-2-thiobarbituric acid. [c] Refluxed with W-1 Raney nickel or "W-5" Raney cobalt in 1- or 2-propanol. [d] Dehalogenation took place.

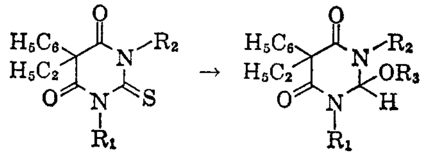
2-Alkoxyhexahydropyrimidine derivatives are obtained, sometimes besides the normal products, with W-1 Raney nickel (which very likely contains less hydrogen than the W-5 type) or with deactivated Raney nickel (see Table 43); the alkoxy derivatives, when treated with fresh Raney nickel, give 5-ethyl-5-phenylhexahydropyrimidine-4,6-dione in almost quantitative yields (470).

Introduction of hydroxy or alkoxy groups into the 2-position during desulfurization of 2-thiobarbituric acids or 2-thioimidazolones (p. 370) does not occur when highly active Raney nickel preparations are used. Formation of an intermediate CLX by addition of water or alcohol to the thiocarbonyl group followed by hydrogenolytic desulfurization was admitted as explanation in the barbituric acid series (470).



CLX

TABLE 43



R_1	R_2	R_3	Yield, %	Reference
H	H	CH_3	—[a]	78
H	H	CH_3	4[b]	470
H	H	C_2H_5	—[a]	78
H	H	C_2H_5	48[b]	470
H	H	C_3H_7	41[b]	470
H	H	C_4H_9	30[b]	470
H	CH_3	CH_3	—[a]	78
CH_3	CH_3	CH_3	—[a]	78

[a] Refluxed in methanol, resp. ethanol, with W-1 Raney nickel or "W-5" Raney cobalt. [b] Refluxed in the appropriate alcohol with Raney nickel deactivated by heating with another portion of the 2-thiobarbituric acid dissolved in the same alcohol.

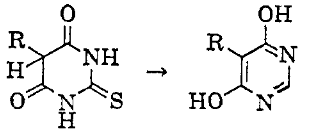
Another possibility would be the recently reported addition of water or alcohol to the double bond of an intermediate tetrahydropyrimidine-4,6-dione (79). However, introduction of hydroxy or alkoxy groups has never been observed during desulfurization of 2-alkylthio derivatives of 2-imidazolinones (Table 13, p. 356) or of partially hydrogenated pyrimidones (Table 15, p. 357; cpd. LXII, p. 357) where the unsaturated compound is likely to be an intermediate.

On the other hand, 2-hydroxy or alkoxy derivatives are obtained from 1,3-dialkyl-2-thiohydantoin derivatives (Table 38, p. 371; cpd. CXLVII, p. 371) and 2-thiobarbituric acid (Table 43, p. 373), where no intermediate with a double bond on carbon 2 can appear.

Therefore, formation of intermediates like CLX, possibly aided by polarization of the carbon–sulfur bond during adsorption on the nickel surface, seems to be a satisfactory pathway for the anomalous reactions.

Finally, 5-monosubstituted-2-thiobarbituric acids, reacting obviously in the tautomeric form containing the aromatic system, may give 4,6-dihydroxypyrimidine derivatives, as can be seen from Table 44.

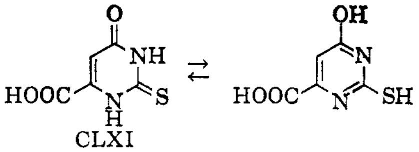
TABLE 44



R	Yield, %	Reference
C_2H_5	37	470
iso-C_5H_{11}	58	470
C_6H_5	—	78
$CH_2C_6H_5$	69	470

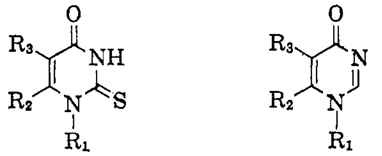
The results of desulfurization of 2-thiouracil derivatives are shown in Table 45.

Thioorotic acid (CLXI), tautomer of 2-mercapto-4-hydroxypyrimidine-6-carboxylic acid, on treatment



CLXI

TABLE 45



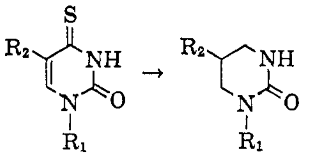
R_1	R_2	R_3	Yield, %	Reference
H	H	CH_3	91–93[a, b]	408
H	H	$CH(OC_2H_5)_2$	—[c]	450
H	H	NH_2	86[a]	363
H	CH_3	H	—	449
H	CH_3	NH_2	80	363
CH_3	H	NH_2	53	363
CH_3	CH_3	NH_2	65	363

[a] In the presence of ammonia. [b] Product formulated as 4-hydroxy-6-methylpyrimidine. [c] The diacetal of 4-formyl-6-pyrimidone was obtained.

with Raney nickel, is either recovered unchanged or totally decomposed (450).

Hexahydropyrimidine derivatives were obtained by treating 4-thiouracil derivatives with Raney nickel (175), as can be seen from Table 46.

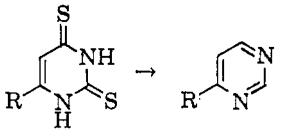
TABLE 46



R_1	R_2	Yield, %
H	H	60
CH_3	H	70
2,3,5-Tri-O-benzoyl-β-D-ribosyl	H	55
2-Deoxy-β-D-ribofuranosyl	CH_3	29
3,5-Di-O-benzoyl-2-deoxy-β-D-ribosyl	CH_3	64

2,4-Dithiouracils on Raney nickel desulfurization gave the corresponding pyrimidines (see Table 47):

TABLE 47



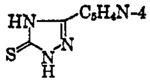
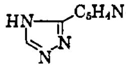
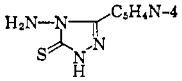
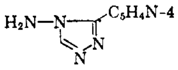
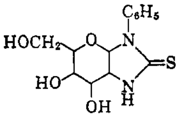
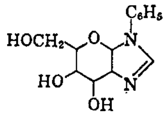
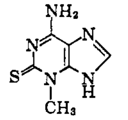
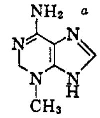
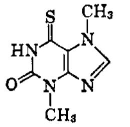
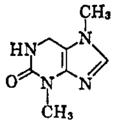
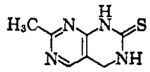
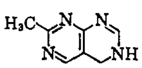
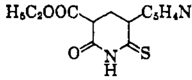
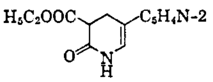
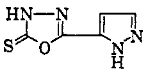
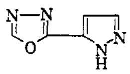
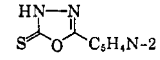
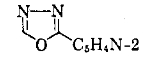
R	Yield, %	Reference
H	17[a]	71
CH_3	—	449

[a] Product isolated as $HgCl_2$-complex.

D. OTHER COMPOUNDS

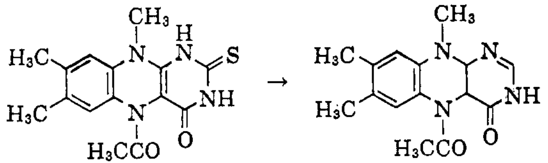
Many heterocyclic compounds of various classes containing the thione group have been desulfurized with Raney nickel, mostly in ethanol. The reactions are summarized in Table 48.

TABLE 48

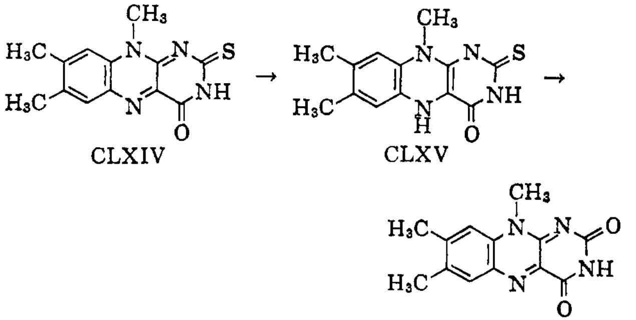
Starting compound	Reaction product	Yield, %	Reference
		73	487
		—	488
		—	181
	 [a]	—	159
		33	285
		—	115
		23	433
		12	7
		57	488

[a] Product named 3-methyladenine in *Chemical Abstracts*.

When 10-acetyl-1,10-dihydro-2-thiolumiflavine (CLXII) was heated with Raney nickel in the presence of ammonia, 2-deoxy-10-acetyl-1,10-dihydrolumiflavine (CLXIII) was obtained in 67% yield (255). 2-Thiolumiflavine (CLXIV) gave at room temperature 1,10-dihydro-2-thiolumiflavine (CLXV), which was desulfurized, giving on heating lumiflavine (CLXVI) formed by air oxidation of the expected 2-deoxylumiflavine.

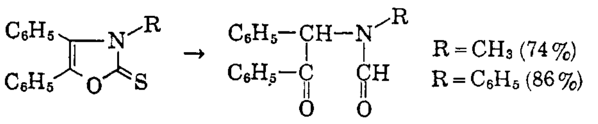


CLXII → CLXIII

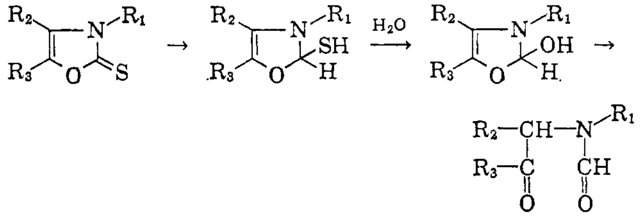


CLXIV CLXV CLXVI

Desulfurization of substituted Δ^4-oxazolines with Raney nickel in ethanol was accompanied by ring opening due to the action of water contained either in the ethanol or the Raney nickel (212):

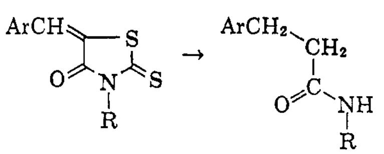


The reaction scheme shown is assumed, in analogy to the formation of hydroxycompounds from thiohydantoins (Table 38, p. 371) and of alkoxy compounds from thiobarbituric acids (Table 43, p. 372).



β-Arylpropionamides have been prepared by Raney nickel desulfurization of rhodanines (50). The results are shown in Table 49.

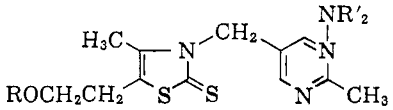
TABLE 49



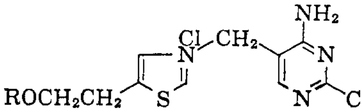
Ar	R	Yield, %
C_6H_5	H	70
4-ClC_6H_4	H	62
4-$CH_3OC_6H_4$	H	86
4-$(CH_3)_2NC_6H_4$	H	78
3,4-$CH_2O_2C_6H_3$	H	73
2-Tetrahydrofuryl[a]	H	85
4-$NH_2C_6H_4$[b]	H	60
4-$CH_3OC_6H_4$	C_2H_5	89
4-$(CH_3)_2NC_6H_4$	C_2H_5	77
2-Tetrahydrofuryl[a]	C_2H_5	54
4-$NH_2C_6H_4$[b]	C_2H_5	78

[a] Starting from furfurylidenerhodanine. [b] Starting from (4-nitrophenyl)-rhodanine.

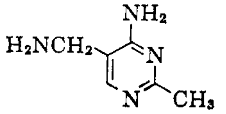
Vitamin B_1 or its acetyl derivative (CLXVIII) was obtained in good yields when 3-(2-methyl-4-amino-5-pyrimidylmethyl)-4-methyl-5-(2-hydroxyethyl)-4-thiazoline-2-thione (CLXVII) or its acetyl derivative was refluxed with Raney nickel in a 1 : 3 ratio in slightly acidic solution for 30 minutes. Longer reflux time, greater excess of Raney nickel and neutral alcoholic solution favor degradation of the thiazole ring with formation of 4-amino-5-(aminomethyl)-pyrimidine hydrochloride (CLXIX) (447). The results are summarized in Table 50.



CLXVII

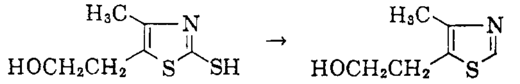


CLXVIII



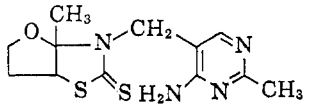
CLXIX

The simple thiazoline-2-thione analog, 2-mercapto-4-methyl-5-(2-hydroxyethyl)thiazole (CLXX), on heating with Raney nickel in water gave CLXXI, without fission of the thiazole ring (447):

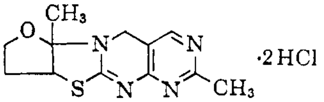


CLXX CLXXI

Finally, 3-(2-methyl-4-amino-5-pyrimidylmethyl)-3a-methyl-3a,5,6,6a-tetrahydrofuro[2,3-d]thiazoline-2-thione (CLXXII), on heating with Raney nickel in diluted HCl (pH 3–3.5), gave 14% of the hydrochloride of CLXIX and, with cyclization, 62% of 6a,8,9,9a-tetrahydro-2,6a-dimethyl-5-H-furo[2,3-h]thiachromine hydrochloride (CLXXIII) (489).



CLXXII



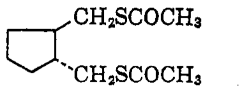
CLXXIII

VI. THIOL ESTERS

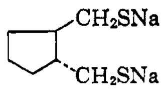
Preparation of aldehydes by hydrogenolytic desulfurization of thiol esters has first been described by Wolfrom and Karabinos (475, 476); however, Prelog, Jeger, Norymberski, and Szpilfogel (280, 367) obtained alcohols by the same reaction. Levin, McIntosh, Meinzer, Searcy, and Spero (115, 460, 475) used Raney nickel deactivated by refluxing with acetone or formaldehyde successfully to stop the reaction at the aldehyde stage, whereas with not pretreated Raney nickel alcohols were the reaction products.

Mono- and bis-thiolacetates have been desulfurized with Raney nickel to the corresponding sulfur-free products. The experiments are summarized in Table 51.

The bis-thiolacetate CLXXIV, after being transformed into the not isolated CLXXV by alkaline hydrolysis, was treated with Raney nickel in aqueous solution.



CLXXIV



CLXXV

Besides a small amount of *trans*-1,2-dimethylcyclopentane, the main reaction product was the cyclic sulfide CLXXVI, which is insoluble in water and therefore not further desulfurized. The diradical CLXXVII

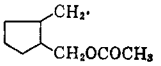
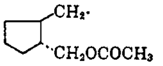
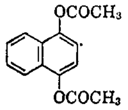
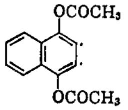
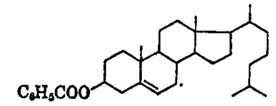
TABLE 50

CLXVII R	CLXVII R′	Cpd.:Ni (weight)	Solvent	pH	Reflux time, min.	Reaction product[a]	R	Yield, %
H	H	1:3	EtOH 50%	7.8	30	CLXVIII	H	18[b]
H	H[a]	1:3	HCl-H_2O	4.6	30	CLXVIII	H	74
CH_3CO	H	1:3	HCl-H_2O	4.4	—	CLXVIII	CH_3CO[c]	89
CH_3CO	CH_3CO	1:10	HCl-H_2O	4	—	CLXVIII	H	68
H	H	1:10	EtOH 96%	—	120	CLXIX		—

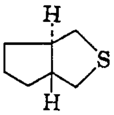
[a] As hydrochloride. [b] Besides 50% of starting material. [c] Besides unspecified amount of CLXVIII (R = H).

TABLE 51

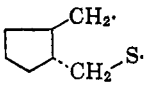
$RSCOCH_3 \rightarrow RH$

R	Yield, %	Reference
$CH_3C(C_6H_5)_2CH_2CH_2\cdot$	90	461
	—	351
	—	351
	—	331
	—	331
	77	239

is postulated as an intermediate (351). The ring closure



CLXXVI

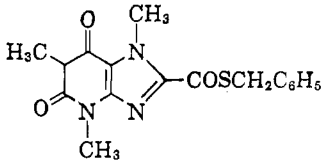


CLXXVII

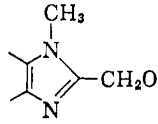
to CLXXVI is also strongly favored by steric factors.

Alcohols were obtained by Raney nickel desulfurization of thiol esters (Table 52).

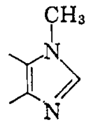
When the thiol ester CLXXVIII was treated with Raney nickel in dioxane at room temperature, a mixture of CLXXIX and CLXXX was obtained; the same procedure in 80% ethanol gave 89% of CLXXX (211).



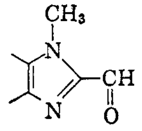
CLXXVIII



CLXXIX



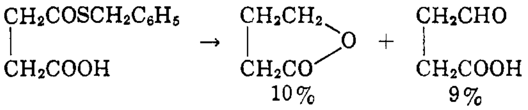
CLXXX

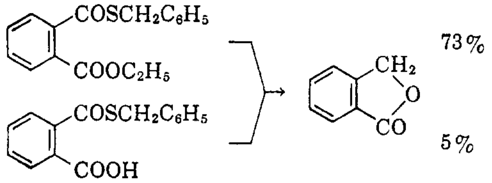


CLXXXI

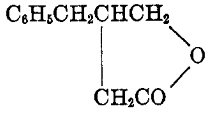
As the aldehyde CLXXXI in dioxane with Raney nickel at 25° gave a mixture of CLXXIX (40%) and CLXXX, the authors (211) conclude that the reductive cleavage of the thiol ester is a two-stage process: first the aldehyde is formed, which then is cleaved to CLXXIX and CLXXX.

Derivatives of dicarboxylic acids may give lactones on Raney nickel treatment at room temperature in ethanolic solution (346):

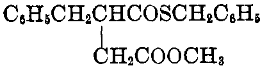




β-Benzyl-γ-butyrolactone (CLXXXII) is obtained under the same conditions either from CLXXXIII, CLXXXIV, or CLXXXV (347):

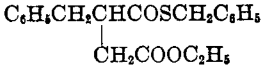


CLXXXII



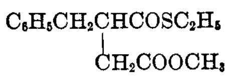
$C_6H_5CH_2CHCOSCH_2C_6H_5$, CH_2COOCH_3

CLXXXIII



$C_6H_5CH_2CHCOSCH_2C_6H_5$, $CH_2COOC_2H_5$

CLXXXV



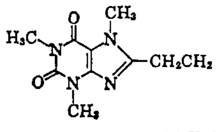
$C_6H_5CH_2CHCOSC_2H_5$, CH_2COOCH_3

CLXXXIV

Finally, aldehydes resulted from the treatment of thiol esters with Raney nickel at room temperature (345). Thus, the thiol esters $CH_3(CH_2)_nCOSR$ (*n* =

TABLE 52

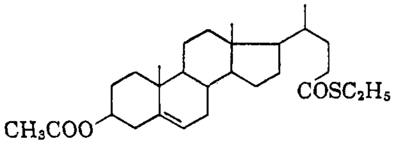
$RCOSCH_2C_6H_5 \rightarrow RCH_2OH$

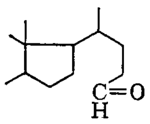
R	Yield, %	Reference
$C_2H_5OCOCH_2CH_2$	52	346
$4\text{-}HOOCC_6H_4$	27	346
$4\text{-}C_2H_5OCOC_6H_4$	74	346
$2\text{-}HOC_6H_4$	Trace	346
$2\text{-}CH_3OC_6H_4$	51	346
	55[a]	210

[a] Together with 8-ethylcaffeine.

6, 8, 10 or 16; R = C_2H_5 or $CH_2C_6H_5$) gave the corresponding aldehydes $CH_3(CH_2)_nCHO$, the ethyl esters in 10% higher yields than the benzyl esters.

Ethyl 3β-acetoxy-thiolchol-5-enate (CLXXXVI), when refluxed in acetone–water with Raney nickel (deactivated by refluxing in acetone) gave the aldehyde CLXXXVII in 52% yield (167):


CLXXXVI


CLXXXVII

When thiol esters of mono or dicarboxylic acids are desulfurized in acetone or tetrahydrofuran at 0–5° in the presence of 1,2-dianilinoethane, the aldehydes initially formed react immediately giving the imidazolidine derivatives CLXXXIX, thus being protected from reduction by Raney nickel (57); the N,N′-diphenyl-imidazolidines CLXXXIX are easily cleaved by acid with regeneration in good yield of the aldehydes. The results of these experiments are assembled in Tables 53 and 54.

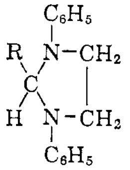
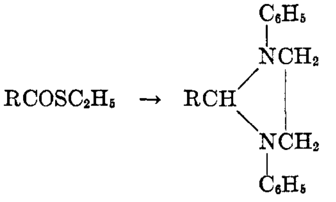

CLXXXIX

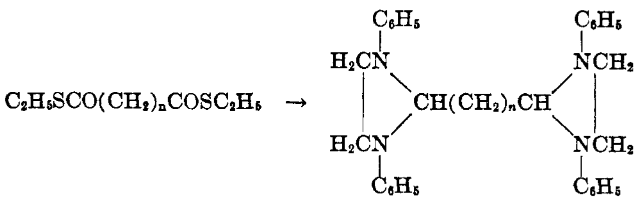
TABLE 53



R	Yield, %
CH_3	73
C_2H_5	80
$CH_3(CH_2)_{16}$	92
C_6H_5	51
$C_6H_5CH_2$	79
$C_6H_5CH_2CH_2$	84
$C_6H_5CH{=}CH$	45[a]
$1\text{-}C_{10}H_7CH_2$	66

[a] Main product is the derivative of hydrocinnamic aldehyde.

TABLE 54



n	2	3	4	6
Yield, %	48	70	77	66

VII. THIOPHENES

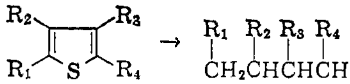
A. SIMPLE THIOPHENES

Desulfurization of thiophene derivatives, although first performed in 1949 by Papa, Schwenk, and Ginsberg (353) with nickel–aluminum alloy in alkaline solution, had its potentialities fully recognized as late as 1952–1954 when Gol'dfarb, Badger, and Buu-Hoï and their groups showed that it may be used as the last step in the synthesis of hydrocarbons, alcohols, amino alcohols, ethers, ketals, ketones, carboxylic, keto and amino acids. First from thiophene suitable derivatives are prepared which are then desulfurized and simultaneously hydrogenated.

1. Preparation of Hydrocarbons

Reactions furnishing hydrocarbons are summarized in Table 55; the thiophene derivatives were desulfurized with Raney nickel in ethanol, dioxane, or toluene.

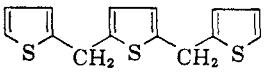
TABLE 55

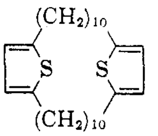


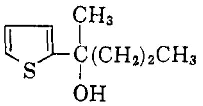
R_1	R_2	R_3	R_4	Yield, %	Reference
$CH_3(CH_2)_{15}$	H	H	H	74	481
$(C_6H_5)_3C$	H	H	H	—	206
$(C_6H_5)_2CH$	H	H	$CH(C_6H_5)_2$	51	202[a]
$C_6H_5(CH_3)_2C$	H	H	$C(CH_3)_2C_6H_5$	—	206
$CH_3(C_6H_5)_2C$	H	H	$C(C_6H_5)_2CH_3$	—	206
C_6H_5	C_6H_5	C_6H_5	C_6H_5	32[b]	27

[a] The corresponding sulfone reacts in the same way. [b] In xylene, together with 2.5% of $(C_6H_5CH_2)_2$.

2,5-Dithenylthiophene (CXC) on Raney nickel desulfurization gave 59% of tetradecane together with hydrocarbons of high molecular weight (190), and from the cyclic compound CXCI, cyclooctacosane was obtained (208). The unstable dehydration product of alcohol CXCII gave 4-methyloctane on Raney nickel desulfurization (481).


CXC


CXCI

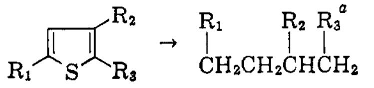

CXCII

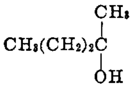
2. Preparation of Alcohols

Hydroxythiophenes and, in some instances, thiophene aldehydes and ketones are transformed into alcohols by Raney nickel in ethanol as may be seen from Tables 56 and 57.

Ketone CXCIII gave 5-decanol on Raney nickel desulfurization (203); 5,5′-diacetyl-2,2′-bithienyl

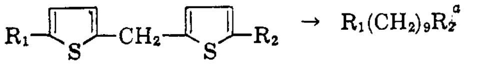
TABLE 56



R_1	R_2	R_3	Yield, %	Reference
 $CH_3(CH_2)_2\overset{CH_3}{\underset{OH}{C}}$	H	H	—	481
$CH_3(CH_2)_{14}CO$	H	H	90	481
$CH_3(CH_2)_8$	H	CHO	65	203
$(CH_3)_3C$	H	CHO	50	203
$CH_3(CH_2)_{17}$	H	$COCH_3$	81	481
$(CH_3)_3C$	CHO	CH_3	—	203
$(CH_3)_3C$	CHO	$C(CH_3)_3$	58	203

[a] Any carbonyl group present in the starting compounds is reduced to the hydroxy group.

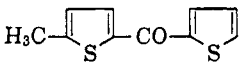
TABLE 57



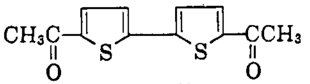
R_1	R_2	Yield, %	Reference
CHO	H	35	190
$HO(CH_2)_2$	H	76	199
CHO	CH_3	64	203
$HO(CH_2)_2$	CH_3	—	201
$HO(CH_2)_2$	$(CH_2)_2OH$	80	199

[a] Any carbonyl group present in the starting compound is reduced to the hydroxy group.

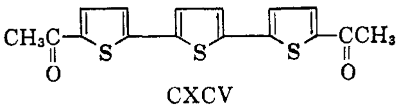
(CXCIV) gave dodecane-2,11-diol, which was oxidized directly to the diketone in 91% overall yield (481), and the terthienyl derivative CXCV yielded 80% of hexadecane-2,15-diol (480).



CXCIII



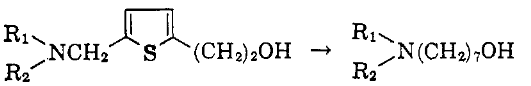
CXCIV



CXCV

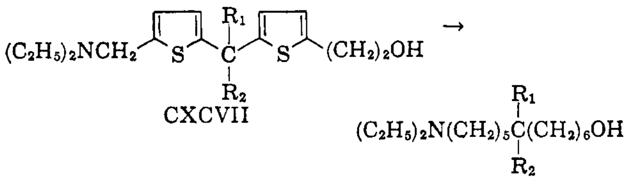
3. *Preparation of Amino Alcohols*

N,N-Disubstituted ω-aminoalcohols were prepared by desulfurization of compounds CXCVI and CXCVII (197) (yields are given in parentheses):



CXCVI

$R_1 = R_2 = C_2H_5$ (45%)
$R_1, R_2 = \cdot(CH_2)_5\cdot$ (50%)

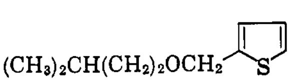


CXCVII

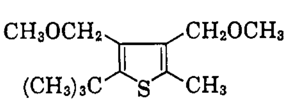
$R_1 = R_2 = H$ (46%)
$R_1 = CH_3$, $R_2 = C_2H_5$

4. *Preparation of Ethers and Ketals*

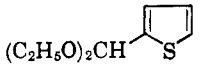
The following thiophene derivatives have been desulfurized with Raney nickel in ether to the corresponding saturated aliphatic ethers or ketals (yields and references are given below each formula):



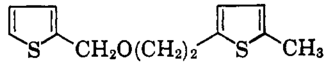
61% (204)



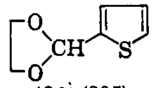
56% (204)



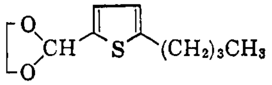
50% (204)



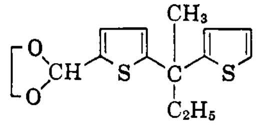
50% (204)



42% (205)

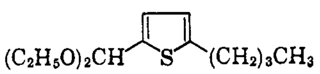


58% (205)



43% (205)

The diethylketal CXCVIII gave, on Raney nickel desulfurization, a mixture of the ketal CXCIX and the ether CC (204):



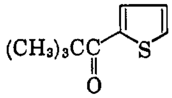
CXCVIII

→ $(C_2H_5O)_2CH(CH_2)_7CH_3$ CXCIX

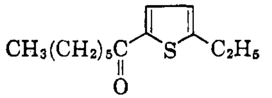
\+ $C_2H_5O(CH_2)_8CH_3$ CC

5. *Preparation of Ketones*

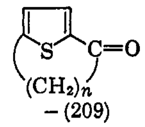
These listed ketones have been desulfurized with Raney nickel in ethanol–benzene, dioxane or acetone to the corresponding saturated aliphatic ketones (yields and references are given below each formula):



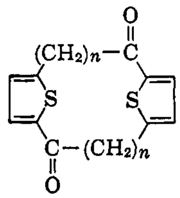
41% (205)



CCI 90% (33)

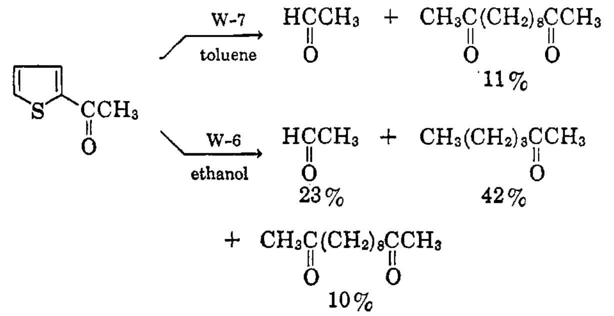


– (209)



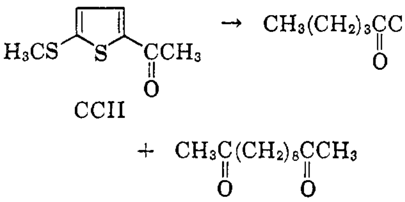
n = 5, 8, 9—(208)

When 2-acetylthiophene was refluxed with Raney nickel W-7 in toluene or with Raney nickel W-6 in ethanol, these products were obtained (33):



In these desulfurizations as well as in that of CCI the weight ratio compound : Raney nickel was only about 1:3. This may explain why, with the very active W-6 and W-7 preparations which caused even some carbon–carbon bond splitting, the keto-groups were not reduced, dimerization to dodecane-2,11-dione was observed and some starting material (deducted for yield calculations) remained unchanged.

Dimerization was also observed when compound CCII was desulfurized with Raney nickel in ethanol and the reaction products oxidized with CrO_3 (198).



CCII

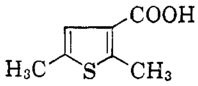
6. *Preparation of Carboxylic Acids*

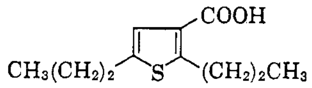
Thiophene-2-carboxylic acid derivatives have been desulfurized to the corresponding open chain mono-, di-, or polycarboxylic acids, either with Raney nickel in ethanol or with Raney Ni–Al alloy in aqueous alkali. The reactions are summarized in Table 58.

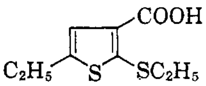
Thiophene-2-carboxylic acid itself, when treated with Raney Ni–Al alloy in D_2O to which sodium methoxide had been added, gave 59% of the deuteriated valeric acid CCIII (99):

$CHD_2CHDCHDCD_2COOH$ CCIII

The substituted thiophene-3-carboxylic acids CCIV, CCV, and CCVI were also transformed into the corresponding saturated aliphatic acids, the ethylthio group of CCVI being eliminated (references are given below each formula):

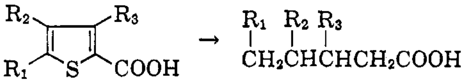

CCIV (428)


CCV (428)


CCVI (198)

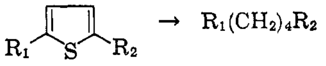
A great number of 2,5-disubstituted thiophenes carrying carboxyl groups in their side chains have been transformed into the corresponding aliphatic or arylaliphatic mono- or di-carboxylic acids. There, too, either Raney nickel in aqueous sodium carbonate or organic solvent or Raney Ni–Al alloy in aqueous alkali were used. The reactions are shown in Table 59.

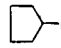
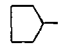
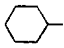
TABLE 58



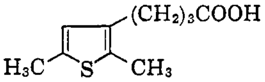
R_1	R_2	R_3	Yield, %	Reference
C_2H_5	H	H	—	231
$(CH_3)_3C$	H	H	71	430
$CH_3(CH_2)_9$	H	H	81	481
$CH_3(CH_2)_{17}$	H	H	—	481
$C_6H_5CH_2$	H	H	—	428
$C_6H_5(CH_2)_2$	H	H	—	427
$C_6H_5(CH_2)_3$	H	H	—	427
$C_6H_5(CH_2)_4$	H	H	—	427
$HOOC(CH_2)_3$	H	H	—	96
4-$HOOCC_6H_4CH_2$	H	H	—	96
4-$HOOCC_6H_4(CH_2)_2$	H	H	—	96
4-$HOOCC_6H_4(CH_2)_3$	H	H	—	427
4-$HOOCC_6H_4(CH_2)_4$	H	H	—	427
H	$CH(CH_3)_2$	H	—	412
H	H	$CH(CH_3)_2$	—	412
COOH	C_6H_5	C_6H_5	78	98
COOH	COOH	COOH	—	98

TABLE 59



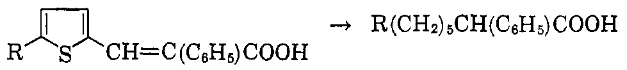
R_1	R_2	Yield, %	Reference
H	$CH(C_6H_5)COOH$	—	359
H	$CH_2CH(C_6H_5)COOH$	—	360
H	$CH(COOH)CH_2COOH$	—	358, 360
H	$CH_2CH(COOH)CH_2COOH$	69	178
H	$(CH_2)_3COOH$	73	33
C_2H_5	$(CH_2)_3COOH$	51	33
$(CH_3)_3C$	$(CH_2)_3COOH$	75	428
$(CH_3)_2CH(CH_2)_2$	$(CH_2)_3COOH$	—	429
$CH_3(CH_2)_6$	$(CH_2)_3COOH$	82	33
$CH_3(CH_2)_{10}$	$(CH_2)_3COOH$	99	33
$CH_3(CH_2)_2CH(C_2H_5)(CH_2)_4$	$(CH_2)_3COOH$	88	33
$CH_3(CH_2)_7CH(CH_3)CH_2$	$(CH_2)_3COOH$	—	429
$CH_3(CH_2)_{11}$	$(CH_2)_3COOH$	—	429
—$(CH_2)_3$	$(CH_2)_3COOH$	—	97
—$(CH_2)_3$	$(CH_2)_5COOH$	—	97
—$(CH_2)_3$	$(CH_2)_3COOH$	—	97
$C_6H_5CH_2$	$(CH_2)_3COOH$	—	428
$C_6H_5(CH_2)_2$	$(CH_2)_3COOH$	—	428
$HOOC(CH_2)_3$	$(CH_2)_3COOH$	—	95
$HOOC(CH_2)_5$	$(CH_2)_3COOH$	—	95
$HOOC(CH_2)_8$	$(CH_2)_3COOH$	—	95

Acid CCVII has been desulfurized in alkaline medium by Raney Ni-Al alloy (428) or by Raney nickel in aqueous sodium carbonate (32, 33), the latter procedure furnishing the saturated aliphatic acid in 93% yield.


CCVII

A double bond in the β-position to both the carboxy group and the thiophene ring is hydrogenated during desulfurization of those 2,5-disubstituted thiophene derivatives, as can be seen from Table 60.

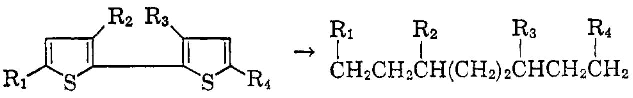
TABLE 60



R	Yield, %	Reference
H	75	93
C_2H_5	—	93
$C_6H_5(CH_2)_6$	74	94
$C_6H_5(CH_2)_7$	70	94
$C_6H_5(CH_2)_8$	63	94

Aliphatic acids have been obtained from substituted 2,2′-bithienyls (see Table 61) and 2,3′-bithienyls (480) (see Table 62).

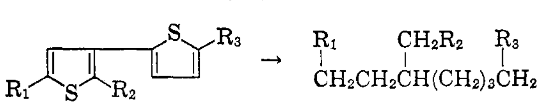
TABLE 61



R_1	R_2	R_3	R_4	Yield, %	Reference
H	H	H	COOH	85	480
COOH	H	H	COOH	67[a]	480
CH_3	COOH	COOH	CH_3	—	315

[a] Starting compound in form of ammonium salt.

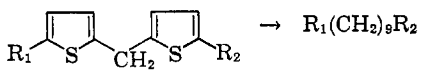
TABLE 62



R_1	R_2	R_3	Yield, %
COOH	H	H	79
H	COOH	H	80
H	H	COOH	74

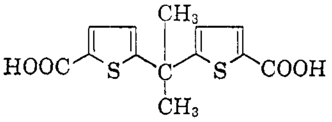
Carboxylic acids derived from dithienylmethane on treatment with Raney nickel in ethanol or aqueous sodium carbonate or with Raney Ni–Al alloy in alkaline solution gave the corresponding saturated aliphatic acids. The reactions are summarized in Table 63.

TABLE 63

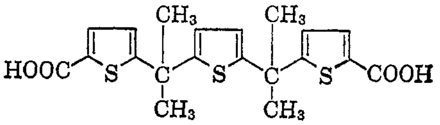


R_1	R_2	Yield, %	Reference
H	COOH	—	199
H	$(CH_2)_3COOH$	66	200
H	$(CH_2)_4COOH$	73	200
CH_3	COOH	69	201
COOH	COOH	—	96
COOH	$(CH_2)_6COOH$	—	95
$HOOC(CH_2)_4$	$(CH_2)_4COOH$	69	200

The diacids CCVIII and CCIX on Raney nickel desulfurization in sodium carbonate solution gave 6,6-dimethylundecanedioic acid (93% yield) (33) and 6,6,-11,11-tetramethylhexadecanedioic acid, respectively (98).



CCVIII

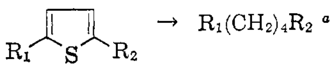


CCIX

7. *Preparation of Hydroxy, Methoxy and Keto Acids*

For the preparation of the corresponding saturated aliphatic hydroxy acids the substituted thiophenes shown in Table 64 have been desulfurized with Raney nickel in ethanol.

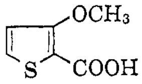
TABLE 64



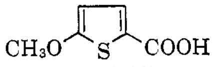
R_1	R_2	Yield, %	Reference
H	CH(OH)COOH	—[b]	219, 221
$CH_3(CH_2)_4$	$CO(CH_2)_7COOH$	61	217
$CH_3(CH_2)_3$	$CO(CH_2)_8COOH$	61	217
$CH_3(CH_2)_7$	$CO(CH_2)_4COOH$	83	217
$CH_3(CH_2)_6$	$CO(CH_2)_5COOH$	63	217
$CH_3(CH_2)_6CO$	$(CH_2)_7COOH$	70	217
$CH_3(CH_2)_7CO$	$(CH_2)_6COOH$	72	217

[a] Any keto group present in the starting compound is reduced to the hydroxy group. [b] Raney nickel in sodium bicarbonate or hydroxide.

Two methoxythiophenecarboxylic acids were desulfurized in aqueous sodium bicarbonate and gave the corresponding saturated aliphatic methoxycarboxylic acids (yields and references are given below each formula).



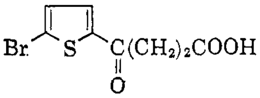
53% (220)



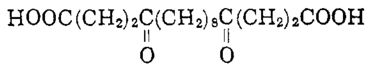
82% (403)

Saturated aliphatic keto acids were obtained by desulfurization of substituted thiophenes (see Table 65), either with Raney nickel in aqueous sodium carbonate or in ethanol, or with Raney Ni–Al alloy in alkali.

β-(5-Bromo-2-thenoyl)-propionic acid (CCX) was debrominated during desulfurization with Raney nickel in aqueous sodium carbonate, furnishing 4-oxoöctanoic acid in 25% yield (33). When the Raney nickel was deactivated by previous heating in water on



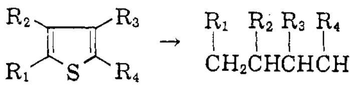
CCX



$$HOOC(CH_2)_2\underset{\Vert}{\underset{O}{C}}(CH_2)_8\underset{\Vert}{\underset{O}{C}}(CH_2)_2COOH$$

CCXI

TABLE 65

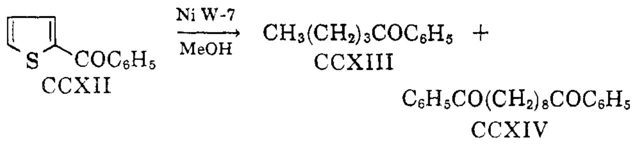


R_1	R_2	R_3	R_4	Yield, %	Reference
H	H	H	$CO(CH_2)_2COOH$	57	33
$CH_3(CH_2)_4$	H	H	$CO(CH_2)_7COOH$	84	217
$CH_3(CH_2)_3$	H	H	$CO(CH_2)_8COOH$	44–68	216, 217
$CH_3(CH_2)_7$	H	H	$CO(CH_2)_4COOH$	38	217
$CH_3(CH_2)_6$	H	H	$CO(CH_2)_5COOH$	38	217
$CH_3(CH_2)_8CO$	H	H	$(CH_2)_7COOH$	17–65	217
$CH_3(CH_2)_7CO$	H	H	$(CH_2)_8COOH$	28–51	217
CH_3	C_2H_5	$CO(CH_2)_2COOH$	CH_3	—	33

the steam-bath for 1 hour a product which seemed to be 4,13-dioxohexadecanedioic acid (CCXI) was isolated in 3.5% yield. Dimerization of a free radical intermediate resulting from elimination of bromine could in the authors' opinion (33) explain its formation.

Badger and Sasse, having obtained "dimeric" compounds during several desulfurizations (33), carried out a great number of those reactions under varying conditions in order to study this aspect of hydrogenolytic desulfurization in more detail (36). Some characteristic examples are assembled in Tables 66, 67, and 68. In almost all the cases varying quantities of unchanged starting material were recovered, which were deducted for yield calculations.

TABLE 66

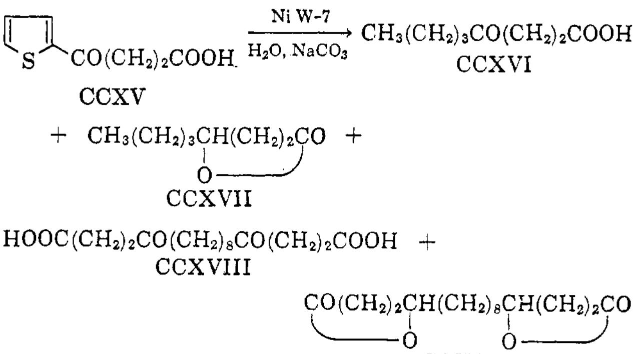


CCXII $\xrightarrow[\text{MeOH}]{\text{Ni W-7}}$ $CH_3(CH_2)_3COC_6H_5$ (CCXIII) + $C_6H_5CO(CH_2)_8COC_6H_5$ (CCXIV)

Concentration of CCXII, *M*	Reaction time, hr.	CCXIII, %	CCXIV, %
0.053	17	59	0.8
1.33	5	58	3.8
2.85	3	59	2.3
Saturated	~1[a]	60	1.0
1.11	5[b]	47	4.4

[a] Solution passed through column containing Raney Ni W-7. [b] Raney Ni W-7 deactivated by heating for 1 hr. at 90–95° in water.

TABLE 67

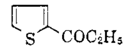
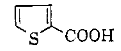
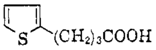
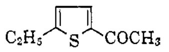
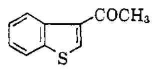
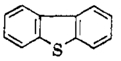


CCXV $\xrightarrow[\text{H}_2\text{O, NaCO}_3]{\text{Ni W-7}}$ $CH_3(CH_2)_3CO(CH_2)_2COOH$ (CCXVI) + CCXVII + $HOOC(CH_2)_2CO(CH_2)_8CO(CH_2)_2COOH$ (CCXVIII) + CCXIX

Concn. of of CCXV, *M*	Reaction time, hr.	CCXVI, %	CCXVII, %	CCXVIII, %	CCXIX, %
0.029	3[a]	15	58	4	0
0.045	6.5	0	71	0	0.5
0.2	2	0	80	0	1.9

[a] Raney Ni W-7 deactivated by heating for 1 hr. at 90–95° in water.

TABLE 68

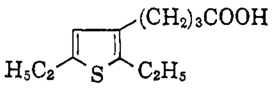
Starting compound	Reaction products and yields, %
	$CH_3(CH_2)_3COC_2H_5$ + $C_2H_5CO(CH_2)_8COC_2H_5$ 71% 1.2%
	$CH_3(CH_2)_3COOH$ + $HOOC(CH_2)_8COOH$ 72% 4.9%
	$CH_3(CH_2)_6COOH$ + $HOOC(CH_2)_{14}COOH$ 80% 0.4%
	$CH_3(CH_2)_5COCH_3$ 69%
	$C_6H_5CH(CH_3)COCH_3$ 85%
	$C_6H_5 \cdot C_6H_5$[a] 98%

[a] No starting compound was recovered.

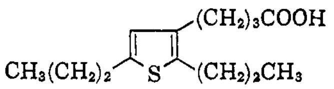
The yield of "dimeric" products increases at first with increasing concentration of the thiophene derivatives, in the authors' opinion because at higher concentrations more molecules are adsorbed per unit area of the nickel and the mean distance between the free radical intermediates is thus diminished. At still higher concentrations, however, the yield of "dimeric" product decreases. This is explained by admitting that more molecules than can be desulfurized are adsorbed, the interaction between the intermediate radicals being hindered and recombination therefore being lower. On the other hand, low hydrogen content, characteristic of deactivated Raney nickel, favors dimerization (36). Recombination occurs invariably in the 5-position, which is explained by assuming intermediate formation of 1,4-diradicals where the substituent R hinders the recombination sterically: $R—\dot{C}H=CH—CH=\dot{C}H$. This favors the view that dimerization occurs at the nickel surface, since steric effects should not be important in solution unless R is a very bulky group (36).

It should be mentioned at this point that Raney nickel desulfurization of thiophene derivatives failed in some instances to give the corresponding saturated aliphatic compounds. Thus, compounds CCXX and CCXXI could not be desulfurized (429), CCXXII did not react completely with Raney nickel even after a long time of reflux (203), the same happening with CCXXIII (205).

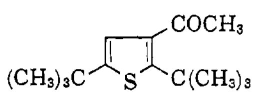
Models of these compounds show that, as already has been pointed out (429), steric hindrance may be



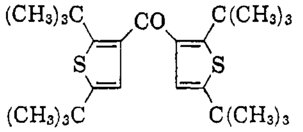
CCXX



CCXXI



CCXXII



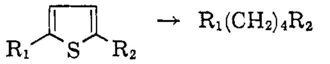
CCXXIII

responsible for this behavior. The models of CCXXII and CCXXIII cannot even be constructed: the substituents at $C_{(2)}$ and $C_{(3)}$ do not fit into their places because of the bulky *tert*-butyl groups. In all four compounds the substituent at $C_{(3)}$ bends the group at $C_{(2)}$ down in such a way that the sulfur atom becomes sterically hindered.

8. *Preparation of Amino Acids*

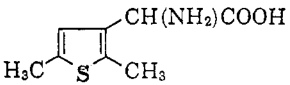
Aliphatic amino acids may be obtained by desulfurization of 2,5-disubstituted thienyl amino acids with Raney nickel in aqueous solution of sodium carbonate or ammonium hydroxide. The reactions are summarized in Table 69.

TABLE 69



R_1	R_2	Yield, %	Reference
H	$CH(NH_2)COOH$	59	191, 194
H	$CH(NH_2)CH_2COOH$	79	195
H	$CH(NH_2)(CH_2)_2COOH$	73	192
H	$CH(NH_2)(CH_2)_3COOH$	53	192
H	$CH(NH_2)(CH_2)_4COOH$	40	192
CH_3	$CH(NH_2)COOH$	53, 57	191, 194
C_2H_5	$CH(NH_2)COOH$	41	191, 194
CH_3	$CH(NH_2)CH_2COOH$	Low	195
C_2H_5	$CH(NH_2)CH_2COOH$	Very low	195
$CH_3CH(NH_2)$	$(CH_2)_4COOH$	40	196
$C_2H_5CH(NH_2)$	$(CH_2)_3COOH$	50	196
$C_2H_5CH(NH_2)$	$(CH_2)_5COOH$	24	196
$HOOC(CH_2)_3$	$CH(NH_2)COOH$	83	193
$HOOC(CH_2)_4$	$CH(NH_2)COOH$	—	193

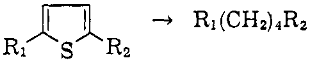
Similarly, amino acid CCXXIV gave the corresponding aliphatic compound in 51% yield (194).



CCXXIV

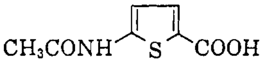
Acetamino acids derived from thiophene were desulfurized by Raney nickel in aqueous ammonia to the corresponding aliphatic acetamino acids, as can be seen from Table 70.

TABLE 70

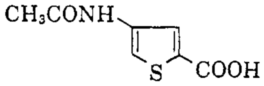


R_1	R_2	Yield, %	Reference
C_2H_5	$\cdot CHCH_2COOH$ $NHCOCH_3$	78	195
$CH_3CH\cdot$ CH_3CONH	$(CH_2)_5COOH$	44	196
$CH_3CONHCH_2$	$(CH_2)_3COOH$	84	166
$CH_3CONHCH_2$	$(CH_2)_4COOH$	72	166
$CH_3CONHCH_2$	$(CH_2)_5COOH$	65	166
$CH_3CONHCH_2$	$(CH_2)_2CH(CH_3)CH_2COOH$	62	166

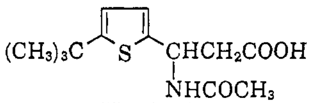
In some instances hydrolytic cleavage of the N-acetyl group occurred when the reaction was performed with Raney nickel in aqueous ammonia or with Raney Ni-Al alloy in dilute alkali. Thus, the following compounds gave the corresponding saturated aliphatic amino acids instead of their acetyl derivatives (yields and references are given below each formula):



– (93, 207)

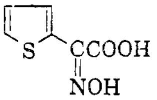


– (93)

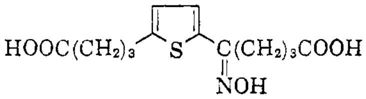


55% (195)

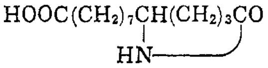
Aliphatic amino acids also may be obtained by hydrogenolytic desulfurization of oximes derived from thienyl ketones. Raney nickel in aqueous ammonia was used in the desulfurization of CCXXV (194), which gave 50% of α-aminocaproic acid, and of CCXXVI (193), which yielded a mixture of the expected δ-aminobrassylic acid and its lactam CCXXVII.



CCXXV



CCXXVI

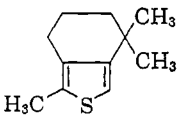


CCXXVII

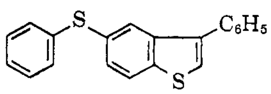
B. THIOPHENES WITH CONDENSED RINGS

The first to desulfurize thianaphthene derivatives were Blicke and Sheets (67, 68) in 1948. In the last few years various substituted thianaphthenes have been desulfurized to the corresponding phenyl-substituted aliphatic products. Most of these reactions, which are summarized in Table 71, were undertaken in order to prove the structure of the sulfur compounds.

Compound CCXXVIII on Raney nickel desulfurization in Carbitol gave 75% of sulfur-free product, half of which was ethyl-2,3,3-trimethylcyclohexane and the remainder a cyclic olefin $C_{11}H_{22}$ of unknown

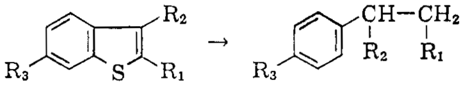


CCXXVIII



CCXXIX

TABLE 71

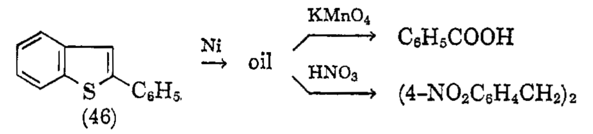


R_1	R_2	R_3	Yield, %	Reference
H	$C(CH_3)_3$	H	85[a]	122
$4\text{-}CH_3OC_6H_4$	H	H	—	46
$HOOCCH(CH_3)$	H	H	—	406
C_6H_5CONH $HOOC\overset{\vert}{C}{=}CH$	H	H	—[b]	379
COOH	CH_3	H	—	402
NH_2CO	CH_3	H	85	402
CH_3	COOH	H	—	402
CH_3CONH	CH_3	H	—	402
CH_3	$NHCOCH_3$	H	—	402
COOH	H	CH_3O	97	356
C_6H_5	H	CH_3O	—	46

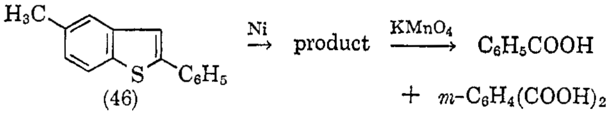
[a] A small quantity of $CH_2{=}C(C_6H_5)C(CH_3)_3$ also was obtained. [b] The double bond in R_1 was hydrogenated too.

structure (62); thianaphthene CCXXIX gave 1,1-diphenylethane (131).

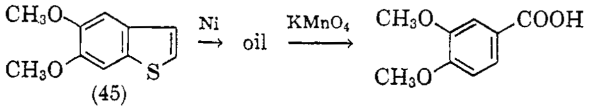
In some instances the products of desulfurization were oils which for characterization were oxidized by potassium permanganate or nitrated with fuming nitric acid to solid products (references are given below each thianaphthene derivative):



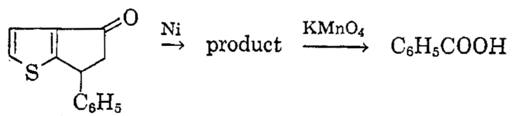
(46)



(46)



(45)

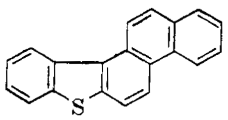


(3)

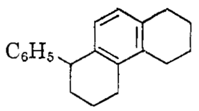
Some benzo- and naphthothianaphthenes have also been desulfurized with Raney nickel to yield the corresponding substituted naphthalenes or phenanthrenes (see Table 72).

Dibenzo- and dinaphthothiophenes have been desulfurized with Raney nickel in methanol or ethanol to give the corresponding aromatic hydrocarbons, as can be seen from Table 73.

The transformation of compound CCXXX into CCXXXI was the first example of hydrogenation accompanying desulfurization observed in the phenanthrene series, and was ascribed to the great activity of the W-4 type Raney nickel used (138):

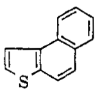
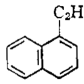
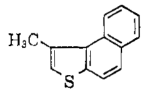
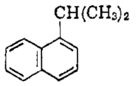
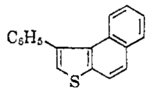
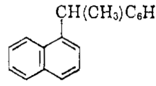
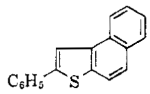
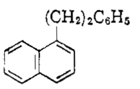
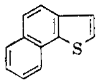
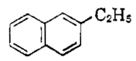
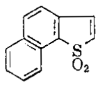
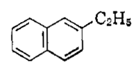
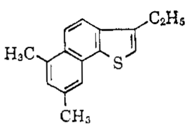
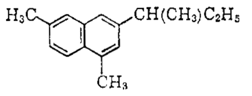
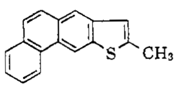
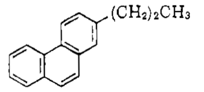


CCXXX



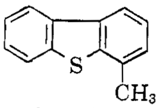
CCXXXI

TABLE 72

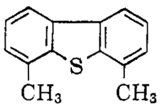
Starting compound	Reaction product	Yield, %	Reference
		—[a]	45
		78	131
		75	131
		—	131
		—	103
		—	137
		—	106
		—	105

[a] In boiling ethylene glycol; not desulfurized in boiling ethanol.

During the treatment with Raney nickel in boiling ethanol 1-methyldibenzothiophene (CCXXXII) (104) and 1,8-dimethyldibenzothiophene (CCXXXIII) (104, 309) remained essentially unaltered, supposedly because of steric hindrance (104). However, other 1- and 1,8-substituted dibenzothiophenes have been desulfurized with good yields and, apparently, under the same conditions (see Table 73); this discrepancy as yet remains to be explained.



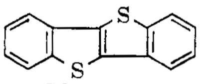
CCXXXII



CCXXXIII

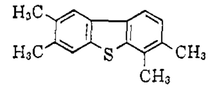
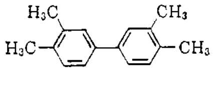
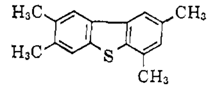
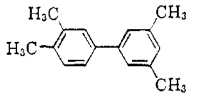
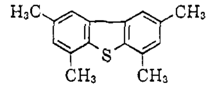
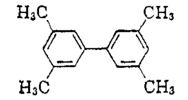
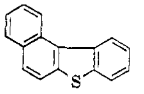
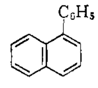
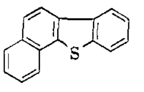
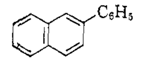
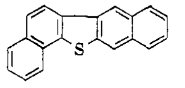
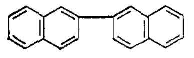
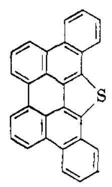
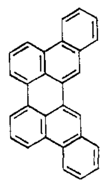
Finally, compounds containing two or three thiophene nuclei have been desulfurized successfully with Raney nickel in ethanol, as can be seen from Table 74.

The desulfurization of thianaphtheno[3,2-b]thianaphthene (CCXXXIV) with various types of active and deactivated Raney nickel gave varying amounts of bibenzyl, *trans*-stilbene and 2-phenylthianaphthene



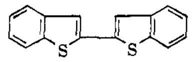
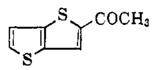
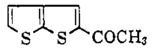
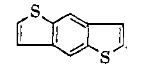
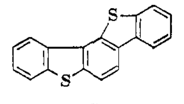
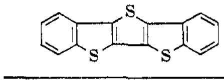
CCXXXIV

TABLE 73

Starting compound	Reaction product	Yield, %	Reference
		—	106
		91	106
		95	106
		—	287
		57	287, 308
		—[a]	16
		3.7[b]	27

[a] In xylene. [b] In mesitylene.

TABLE 74

Starting compound	Reaction product	Yield, %	Reference
	$C_6H_5(CH_2)_4C_6H_5$	—	185
	$CH_3(CH_2)_5COCH_3$	64	112
	$C_2H_5CH(CH_3)(CH_2)_2$-$CH(OH)CH_3$	—	112
	p-$C_6H_4(C_2H_5)_2$	~61	132
	m-$C_6H_4(C_6H_5)_2$	53	139
	$C_6H_5(CH_2)_4C_6H_5$	81[a]	352

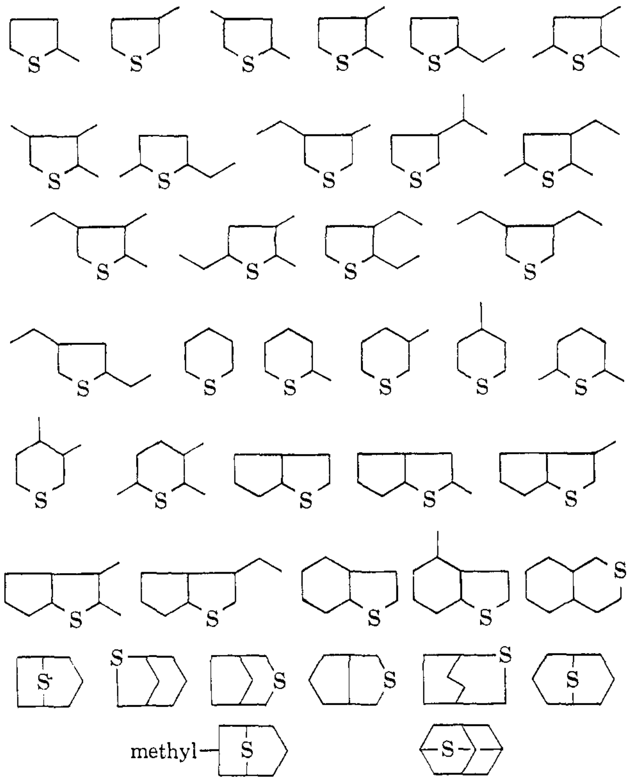
[a] Yield of crude product.

(31); no 1,2,3,4-tetraphenylcyclobutane, previously reported as reaction product (44), could be isolated. The results suggest that the sulfur compound is chemisorbed in a more or less perpendicular fashion on the nickel, and that the desulfurization of thiophenes proceeds by removal of the sulfur to give a diradical, with subsequent hydrogenation to the observed product (31).

VIII. HETEROCYCLES OTHER THAN THIOPHENE

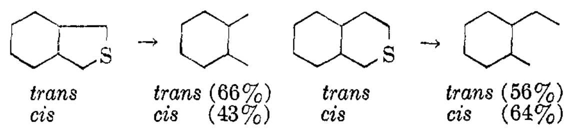
A. COMPOUNDS WITH SULFUR AS THE ONLY HETERO ATOM

Many thiacycloalkanes, together with some thiophene derivatives, have been isolated from petroleum fractions and their structures characterized by desulfurization to the corresponding aliphatic and cycloaliphatic hydrocarbons (60, 61, 63):

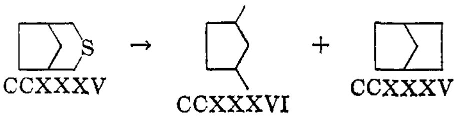


In some instances the proof of structure was inconclusive since the obtained hydrocarbon could have been formed from more than one possible sulfide.

It was shown (65) that hydrocarbons produced by desulfurization of cyclic sulfides retain the stereochemical identity of the starting compounds (yields are given in parentheses):

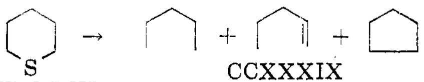


Ring closure was observed in two cases. 3-Thiabicyclo[3.2.1]octane (CCXXXV) gave with Raney nickel in alcohol 1.4% of bicyclo[2.2.1]heptane (CCXXXVII) besides 76% of the expected 1,3-dimethyl-



CCXXXV CCXXXVI CCXXXVII

pentane (CCXXXVI) (64), and thiacyclohexane (CCXXXVIII) yielded the products shown, as well as some starting material:



CCXXXVIII CCXXXIX

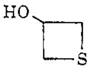
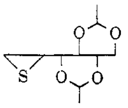
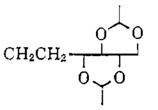
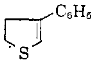
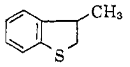
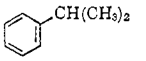
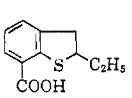
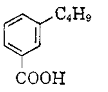
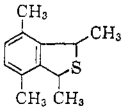
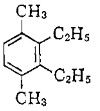
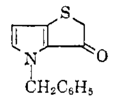
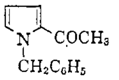
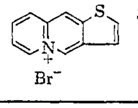
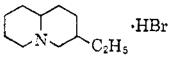
(total yield of hydrocarbons, 49%)

With Raney nickel previously refluxed with ethanol desulfurization of CCXXXVIII led practically to the same result except that the yield of CCXXXIX was increased (64). The formation of CCXXIX may be explained by assuming disproportionation of intermediate pentyl radicals to pentane and pentene.

Pentamethylenesulfone did not react when refluxed with Raney nickel in ethanol for four hours (64).

Other cyclic sulfides which have been desulfurized with Raney nickel are assembled in Table 75.

TABLE 75

Starting compound	Reaction product	Yield, %	Reference
	$CH_3CH(OH)CH_3$ [a]	—	2
		92	126
	$CH_3CH_2CH(C_6H_5)CH_3$	65	482
		84	291
		74	357
		—	130
		—	281
 [b]		13	339

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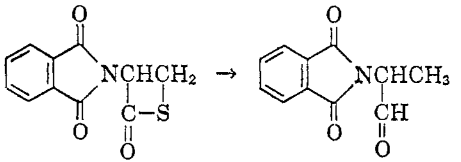
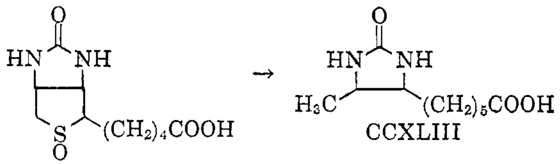
[a] Product was oxidized and the resulting acetone isolated as 2,4-dinitrophenylhydrazone. [b] In the presence of H_2 (2 atm.).

The thiolactone CCXL on desulfurization gave the aldehyde CCXLI together with a considerable amount of the corresponding alcohol (172), and a concentrate from *Aspergillus niger* which showed biotin-activity (CCXLII) gave 5-dethiobiotin (CCXLIII) (479):

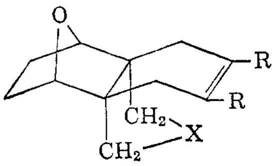


CCXL CCXLI



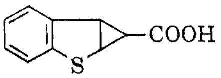
CCXLII CCXLIII

Desulfurization of the cyclic sulfides CCXLIVa ($R = H$, CH_3 or C_6H_5) mixed with the corresponding cyclic oxides CCXLIVb was either incomplete or accompanied by hydrogenation of the double bond (422).

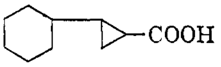


CCXLIV (a, X = S; b, X = O)

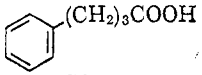
When treated with Raney nickel, the crude sulfide CCXLV was thought to give impure 2-cyclohexylcyclopropanecarboxylic acid CCXLVI (28), but the constitution of the main product was shown later to be



CCXLV



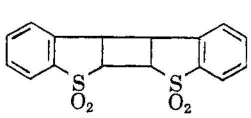
CCXLVI



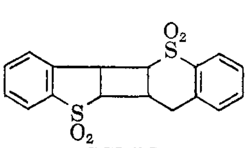
CCXLVII

CCXLVII (34), the cyclopropane ring being cleaved under the conditions of desulfurization.

The photodimerization product of thianaphthene sulfone was desulfurized (136) to ethylbenzene in 16% yield; the attempted decision between the two possible structures CCXLVIII and CCXLIX was therefore



CCXLVIII

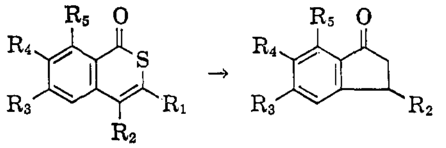


CCXLIX

not possible due to the hydrogenolysis of C–C bonds.

For the conversion of 1,2-dihydro-1-keto-2-thianaphthalenes, especially 1,2-dihydro-1-keto-3-carboxy-6,7-methylenedioxy-2-thianaphthalene (CCL, R_3, R_4 = O—CH_2—O), into indanones by the action of Raney nickel (89, 144), see Table 76.

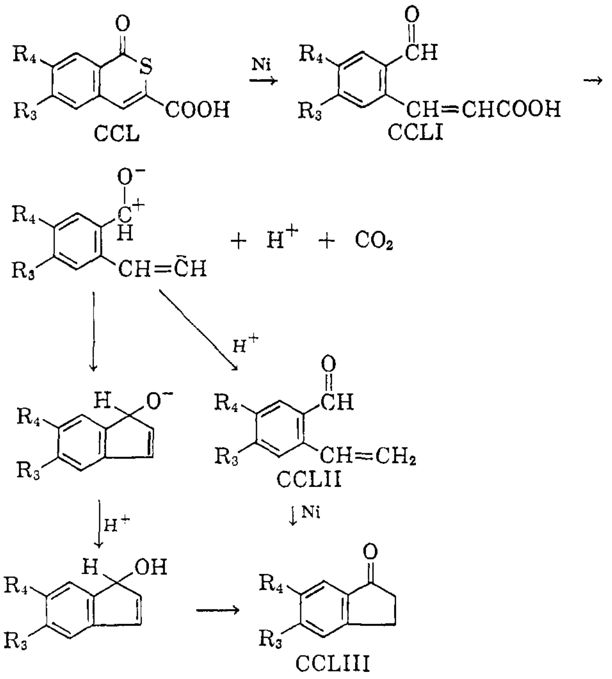
TABLE 76



R_1	R_2	R_3	R_4	R_5	Yield, %
H	H	H	H	H	46
COOH	H	H	H	H	62
COOH	CH_3	H	H	H	84
COOH	H	OCH_3	OCH_3	H	14[a]
COOH	H	H	OCH_3	OCH_3	59
COOH	H	$\cdot OCH_2O\cdot$		H	41

[a] The product contained some 2-vinyl-4,5-dimethoxybenzaldehyde.

The pathway shown was suggested based on the observation that under desulfurization conditions 2-formylcinnamic acid (CCLI, $R_3 = R_4 = H$) is transformed easily into 1-indanone (CCLIII, $R_3 = R_4 = H$) and 2-vinyl-4,5-methylenedioxybenzaldehyde (CCLII, R_3, R_4 = O—CH_2—O) gives the corresponding indanone (CCLIII) (89, 144):



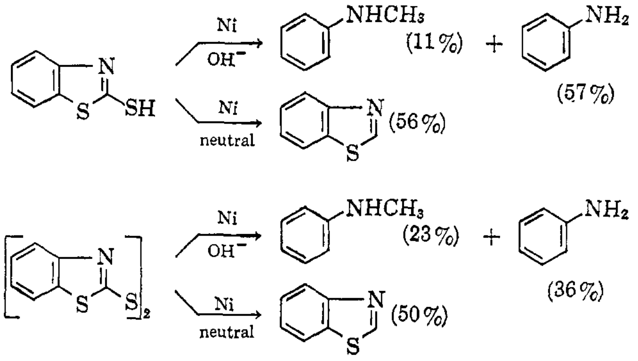
During the desulfurization of thioindigoid dyes (287) with Raney nickel alloy in sodium hydroxide or Raney nickel in ethanol, the carbon skeleton remained essentially intact (see Table 77). With Raney nickel in ethanol all the keto groups present were reduced to methylene groups, whereas with Raney nickel alloy in sodium hydroxide, at least one oxygen remained in the molecule.

Sulfur heterocycles with two or more sulfur atoms have been desulfurized too, as shown in Table 78.

B. COMPOUNDS WITH SULFUR AND OTHER HETERO ATOMS

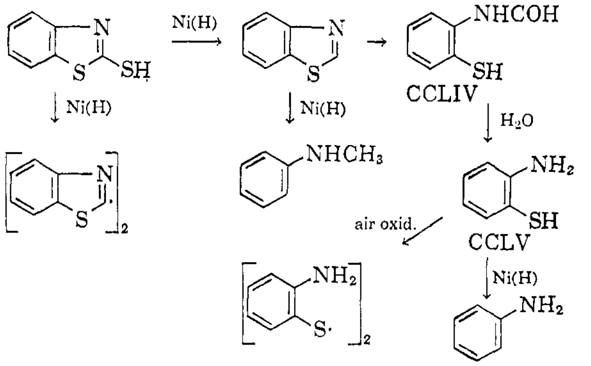
Some derivatives of phenoxathiin and phenothiazine have been desulfurized with Raney nickel (see Table 79).

Desulfurization of thiazoles was shown (278) to give different products in neutral or alkaline medium (yields are given in parentheses):



A more detailed study of these reactions was undertaken using methanol, which does not alkylate amines in the presence of Raney nickel (29); the results are summarized in Table 80.

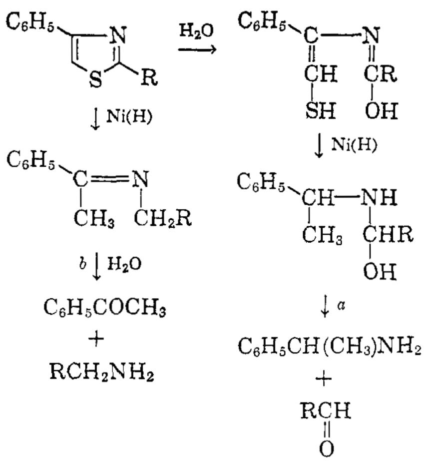
The authors (29) proposed a mechanism for the desulfurization of 2-mercaptobenzothiazole:



With very active Raney nickel (W-6 and W-7) desulfurization is the faster and therefore the only reaction. With less active preparations (W-5 and dehydrogenated W-7) the known hydrolytic fission of the thiazole ring by alkali occurs to some extent before desulfurization and leads through intermediate CCLIV to *o*-aminothiophenol CCLV, partly isolated as its disulfide and partly desulfurized to aniline.

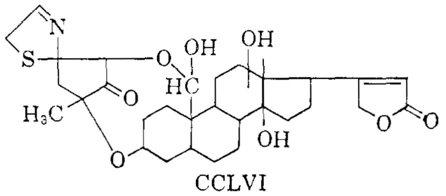
During desulfurization of simple substituted thiazoles competition of the hydrolytic reaction is stronger, its extent depending on the alkalinity of the medium.

This mechanism has been suggested (29):

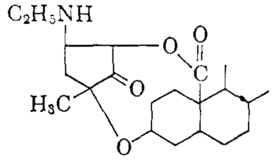


[a] Disproportionation during subsequent distillation. [b] Fission with acid during work-up.

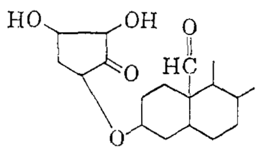
Uscharin (CCLVI), a component of African arrow poisons, on desulfurization with Raney nickel in absolute dioxane, gave uscharamine (CCLVII) in 68% yield (258), together with calactin (CCLVIII), calotropagenin (CCLIX), and other compounds. The model compound 2,4,5-trimethyl-2-ethyl-3-thiazoline (CCLX) was desulfurized in anhydrous dioxane, yielding di-2-butylamine, methyl ethyl ketone, 2-pentanol and ammonia:



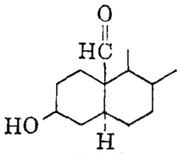
CCLVI



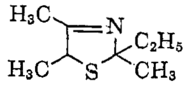
CCLVII



CCLVIII



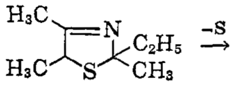
CCLIX

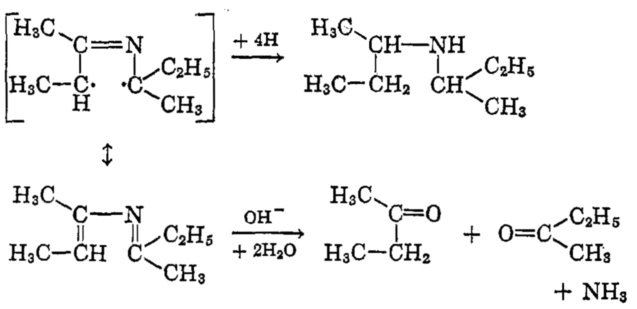


CCLX

$$\rightarrow \underset{(16\%)}{[C_2H_5CH(CH_3)]_2NH} + \underset{(15\%)}{CH_3COC_2H_5} + \underset{(7\%)}{CH_3CH(OH)C_2H_5} + NH_3$$

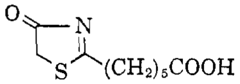
The following reaction mechanism was proposed:





When dioxane–water (3 : 1) was used as solvent only the last three compounds, supposedly formed by hydrolysis of the radical resulting from desulfurization, were found (258).

Raney nickel desulfurization also was used in the determination of the structure of other biologically interesting thiazoline derivatives. Thus, the antibiotic acidomycin (CCLXI) gave a compound $C_9H_{17}O_3N$, probably CCLXII; the methyl ester behaved similarly (332). In bacitracin-A, a naturally occurring antibiotic polypeptide, the presence of a thiazoline ring was deduced from the result of desulfurization with Raney nickel, among other evidence (340, 462).

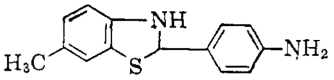


CCLXI

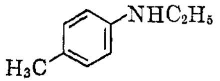
$CH_3CONH(CH_2)_6COOH$

CCLXII

"Dehydrothio-*p*-toluidine" (CCLXIII) on desulfurization in ethanol gave 4-methyl-N-ethylaniline (CCLXIV) (288), thus providing an example of alkylation of amines with alcohols in the presence of Raney nickel.



CCLXIII

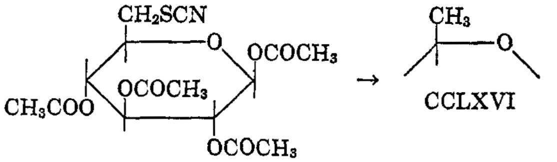


CCLXIV

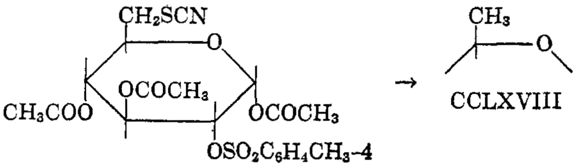
Many thiazolidines and other sulfur and nitrogen-containing heterocycles have been desulfurized, mainly to clarify their structures. The reactions are summarized in Table 81.

IX. MISCELLANEOUS COMPOUNDS

Thiocyanates undergo hydrogenolytic desulfurization when refluxed with Raney nickel in ethanol. Thus, the 6-rhodano derivative of 1,2,3,4-tetraacetyl-β,D-gluco-

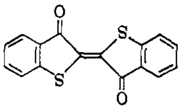
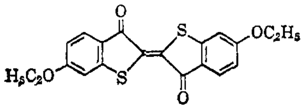
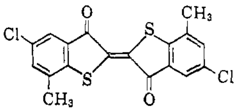
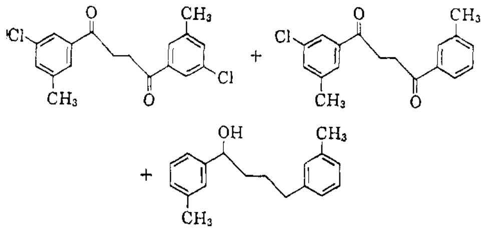
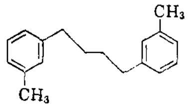
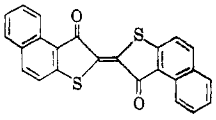
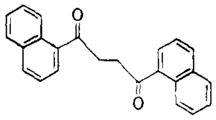
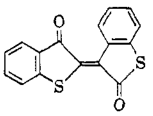
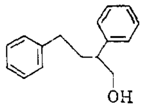
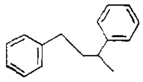
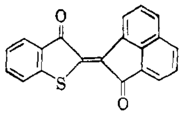
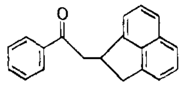
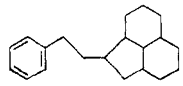
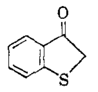
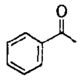
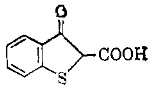
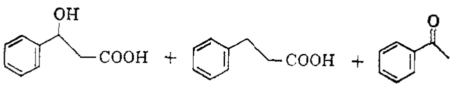


CCLXV CCLXVI



CCLXVII CCLXVIII

TABLE 77

Starting compound	Raney nickel	Reaction products
	In EtOH	
	In EtOH	
	Alloy in NaOH[a]	
	In EtOH	
	Alloy in NaOH	 + yellow liquid [b]
	In EtOH	Colorless liquid[b]
	Alloy in NaOH	
	In EtOH	
	Alloy in NaOH	
	In EtOH	
	Alloy in NaOH	
	Alloy in NaOH	

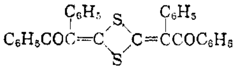
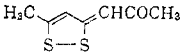
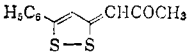
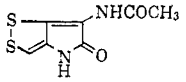
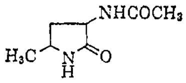
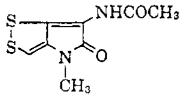
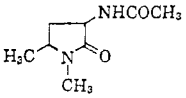
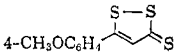
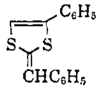
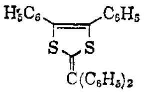
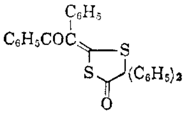
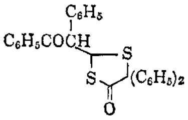
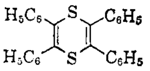
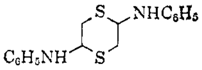
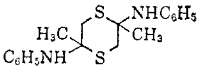
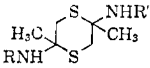
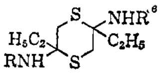
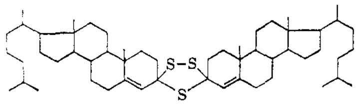
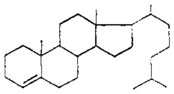
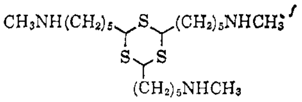
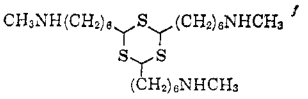
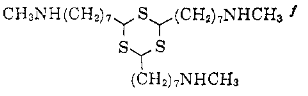
[a] Dye previously vatted with glucose or sodium hydrosulfite. [b] Both liquids analyzed for 1,4-di-(1-tetrahydronaphthyl)-butane.

pyranose (CCLXV) gave the β-D-quinovose derivative CCLXVI in 93% yield, and from 1,3,4-triacetyl-2-p-toluenesulfonyl-6-thiocyano-β-D-glucopyranose (CCLXVII) 45% of CCLXVIII was obtained (418).

Isothiuronium tosylates were desulfurized with Raney nickel as shown in Table 82.

Besides the sulfoxides and sulfones already mentioned in the earlier discussion and in Table 55, Table 72, and Table 79, a variety of other sulfones have been submitted to hydrogenolytic desulfurization

TABLE 78

Starting compound	Reaction product	Yield, %	Reference
	$C_6H_5COCH(C_6H_5)CH_3 + C_6H_5CH(OH)CH(C_6H_5)CH_3$	—	486
	$CH_3(CH_2)_4COCH_3$	—	52
	$C_6H_5(CH_2)_4COCH_3$	—	52
		55	164
		70	110
	$4\text{-}CH_3OC_6H_4(CH_2)_6C_6H_4OCH_3\text{-}4$	39–48[a]	317
	$C_6H_5C_2H_5$[b] + $C_6H_5(CH_2)_4C_6H_5$[c]		299
	$C_6H_5(CH_2)_2C_6H_5$[d]	23	299
	$C_6H_5COCH(C_6H_5)CH_3 + C_2H_5OCOCH(C_6H_5)_2 + CH_2(C_6H_5)_2$	—	485
	$C_6H_5COCH(C_6H_5)CH_3 + C_2H_5OCOCH(C_6H_5)_2$	—	485
	$C_6H_5(CH_2)_2C_6H_5$	78	299
	$C_6H_5NHC_2H_5$	—	267
	$C_6H_5NHCH(CH_3)_2$	60	24
	$4\text{-}CH_3C_6H_4NHCH(CH_3)_2$	75	24
	$4\text{-}CH_3C_6H_4NHCH(CH_3)C_2H_5$	65	26
		—	85
	$CH_3(CH_2)_5N(CH_3)C_2H_5$[g]	41	314
	$CH_3(CH_2)_6N(CH_3)C_2H_5$[h]	49	314
	$CH_3(CH_2)_7N(CH_3)C_2H_5$[g]	52	314

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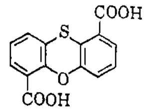
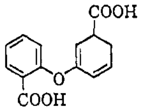
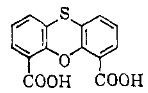
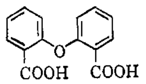
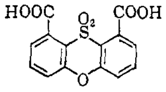
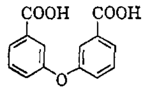
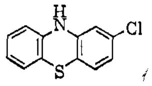
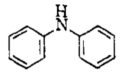
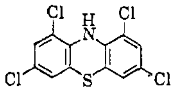
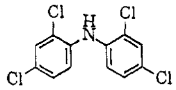
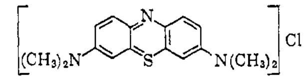
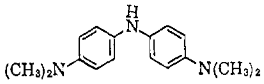
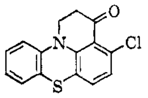
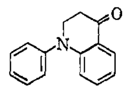
[a] Raney nickel previously heated at 100° *in vacuo* for 1 hr. [b] Azeotrope with solvent EtOH; obtained as sole product in 32% yield when reaction was carried out in propylene glycol. [c] Yield 3%. [d] 1,1-Diphenylethane was possibly also present but was not isolated. [e] R = 4-$CH_3C_6H_4$. [f] As hydrochloride. [g] As picrolonate. [h] As picrate.

TABLE 79

Starting compound	Reaction product	Yield, %	Reference
		15[a]	187
		11[b]	187
		17	187
		41	286
		26	405
		9–28	278
		—	286

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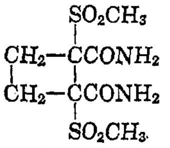
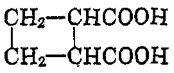
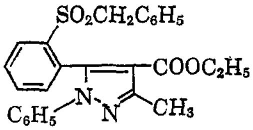
[a] Unchanged starting compound was recovered. [b] Benzoic and salicylic acids also were isolated.



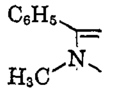
CCLXIX



CCLXX



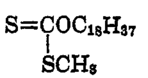
CCLXXI



CCLXXII

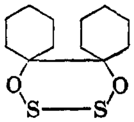
whereby the hydrogen is substituted for the sulfone group. The cyclobutane derivative CCLXIX in aqueous solution gave 50–60% yield of *cis*-cyclobutane-1,2-dicarboxylic acid (CCLXX) (227), and the sulfone CCLXXI yielded the pyrazole derivative CCLXXII (48).

Cleavage of the carbon–oxygen bond occurs when xanthates are treated with Raney nickel; octadecyl-S-methyl xanthate (CCLXXIII) thus gave 50–65% of octadecanol and a white waxy residue probably containing octadecyl methyl ether (454).

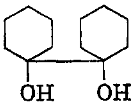


$S{=}C(OC_{18}H_{37})SCH_3$

CCLXXIII

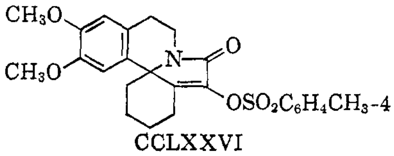


CCLXXIV

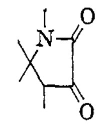


CCLXXV

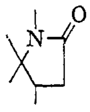
Some compounds whose sulfur is linked to atoms other than carbon have been desulfurized successfully. From 4,5-bis-pentamethylene-3,6-dioxa-*o*-dithiane (CCLXXIV), with Raney nickel in benzene, cyclohexanone pinacol (CCLXXV) was obtained in 81% yield (145). The enol tosylate of 15,16-dimethoxyerythrinane-7,8-dione (CCLXXVI) gave, with Raney nickel in ethanolic sodium hydroxide, 15,16-dimethoxyerythrinane-7,8-dione (CCLXXVII) together with 15,16-dimethoxyerythrinan-8-one (CCLXXVIII) (335), and triphenylphosphine sulfide (CCLXXIX), when treated with Raney nickel in methanol, gave 29% of triphenylphosphine (264).



CCLXXVI



CCLXXVII



CCLXXVIII

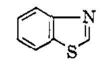
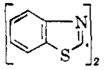
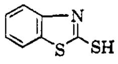
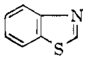
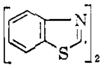
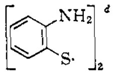
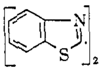
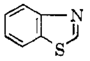
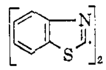
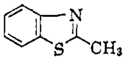
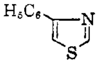
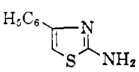
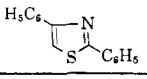
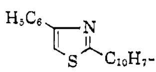
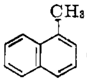
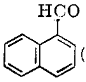
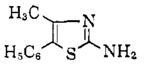
$(C_6H_5)_3P{=}S$

CCLXXIX

X. DEGASSED RANEY NICKEL

The behavior of sulfur compounds in the presence of Raney nickel degassed by heating *in vacuo* at 100° (Raney Ni 100) and 200° (Raney Ni 200) has been studied by Hauptmann, Wladislaw, and Camargo (248, 249, 251). Later the degassing temperature was raised to 500° (Raney Ni 500) (247, 252). Furthermore,

TABLE 80

Starting Compound	Ni/solvent	Reaction products and yields, %
	W-7/MeOH	$C_6H_5NHCH_3$[a] (72%)
	W-5/MeOH + NaOH	$C_6H_5NHCH_3$[a] (7%) + $C_6H_5NH_2$[a] (25%)
	W-6/MeOH	$C_6H_5NHCH_3$[a] (87%)
	Dehydr. W-7/xylene[b]	 (0.8%)[c]
	W-5/MeOH	 (55%) +  (0.1%)
	W-5/MeOH + NaOH	 (10%)[d] +  (7%) + $C_6H_5NHCH_3$[a] (27%) + $C_6H_5NH_2$[a] (10%)
	Dehydr. W-7/MeOH[b]	 (35%) +  (6%) + $C_6H_5NHCH_3$[a] (19%) + $C_6H_5NH_2$[a] (7%)
	W-6/MeOH	$C_6H_5NHC_2H_5$[a] (90%)
	W-7/MeOH	$C_6H_5NHC_2H_5$[a] (80%)
	W-7/MeOH	$C_6H_5CH(CH_3)NH_2$ (35%)[c]
	W-6/MeOH	$C_6H_5CH(CH_3)NH_2$ (31%) + $C_6H_5COCH_3$ (12%) + CH_3NH_2[c]
	W-7/MeOH	$C_6H_5CH(CH_3)NH_2$ (59%) + CH_3NH_2 + NH_3
	W-6/MeOH	$C_6H_5CH(CH_3)NH_2$ (47%) + $C_6H_5COCH_3$ (33%)
	W-7/MeOH	$C_6H_5CH(CH_3)NH_2$ (21%) + C_6H_5CHO (37%)
	W-6/MeOH	$C_6H_5CH(CH_3)NH_2$ (24%) + C_6H_5CHO (74%)[c]
	W-7/MeOH	 (14%) +  (37%) + $C_6H_5CH(CH_3)NH_2$ (20%) + $C_6H_5COCH_3$ (9%)
	W-7/MeOH	$C_6H_5CH_2CH(CH_3)NH_2$ (23%) + $C_6H_5CH_2COCH_3$ (5%)[c]
	W-6/MeOH	$C_6H_5CH_2CH(CH_3)NH_2$ (47%) + $C_6H_5CH_2COCH_3$ (20%)[c]

[a] Isolated as *p*-toluenesulfonamide. [b] W-7 partially degassed at 100° *in vacuo*. [c] Unchanged starting compound was recovered. [d] By air oxidation of unchanged starting material. [e] Isolated as picrate.

nickel powder obtained by reducing nickel oxide with hydrogen at 320° (247) or by decomposing nickel oxalate at 350° (246) has been employed; the former was degassed at 200° *in vacuo* before being used, the latter was used without pretreatment.

W-7 Raney nickel heated *in vacuo* (12 mm.) at 100° (W-7-J) (30, 35) and nickel prepared by reduction of the oxide at 500° (30) also have been used recently.

With exception of Raney Ni 100 and W-7-J these nickel preparations contain but small or negligible amounts of hydrogen (245, 252), so that very little or no hydrogenolysis is observed during the reaction with sulfur compounds.

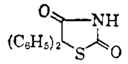
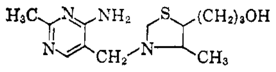
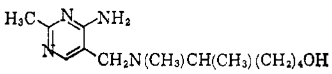
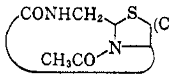
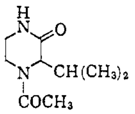
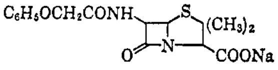
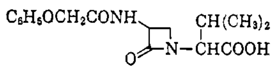
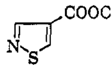
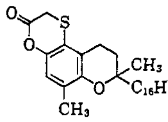
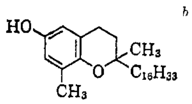
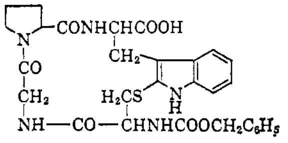
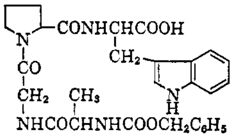
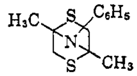
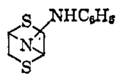
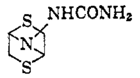
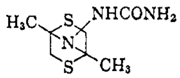
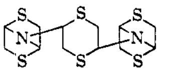
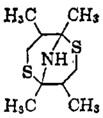
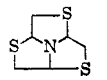
A. THIOLS

When treated with Raney Ni 200 at 140°, aromatic thiols form sulfides, whereas desulfurization is complete at 220° (see Table 83). Mixtures of two different thiols at 140° yield simple thioethers together with the mixed one.

B. SULFIDES

Symmetric aromatic sulfides were not affected at 64° by W-7-J Raney nickel, neither at 140° by Raney Ni 200 (see Table 84), but 1,1′-dinaphthyl sulfide was essentially desulfurized by W-7-J at 140°. Unsymmetric sulfides underwent partial disproportionation when heated at 140° with Raney Ni 200, giving two symmetric sulfides. When the starting sulfide contained benzyl groups linked to sulfur, frequently dibenzyl derivatives were formed already at 140°; bis-(4-methoxyphenyl) sulfide gave the corresponding biaryl, also at 140°. At 220° biaryls were obtained. A mixture of diphenyl and 2,2′-dinaphthyl sulfides, when heated at 220° with Raney Ni 200, gave two symmetric biaryls and the corresponding unsymmetric hydrocarbon.

TABLE 81

Starting compound	Reaction product	Yield, %	Reference
	$(C_6H_5)_2CHCONH_2$	68	133
		34	80
		56	263
		33–50	297, 392
	$NH_2CH_2CH(CH_3)COOCH_3$[a]	5	1
	 [b]	—	215
		—	471
	$(CH_3)_2CHN(C_6H_5)CH(CH_3)_2$	61	24
	$C_8H_{10}N_2$[c]	—	267
	$NH_2CONHN(C_2H_5)_2$	—	267
	$NH_2CONHN[CH(CH_3)_2]_2$	—	25
	$N(C_2H_5)_3$	—	230
	$[CH_3CH(CH_3)CH(CH_3)_3]_2NH$[d]	—	442
	$N(C_2H_5)$[e]	70	441

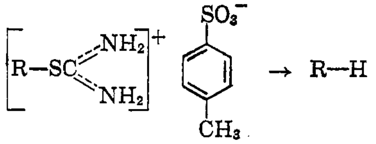
[a] As 3,5-dinitrobenzamide. [b] After treatment with KOH, then HCl. $C_{16}H_{33} = (CH_2)_3CH(CH_3)(CH_2)_3CH(CH_3)(CH_2)_3CH(CH_3)_2$. [c] This unstable product was obtained instead of diethylphenylhydrazine. [d] Isolated half as hydrochloride, half as picrate. [e] Isolated as picrate.

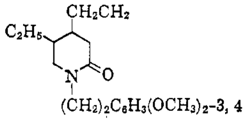
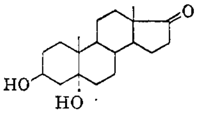
No dimerization of radicals was observed when aliphatic sulfides were treated with Raney Ni 500; instead, disproportionation into paraffin and olefin took place.

C. DISULFIDES

With the exception of bis-(4-nitrophenyl) disulfide (252), aromatic disulfides gave sulfides when heated at 140° with nickel degassed at 200 or 500°. Mixtures of two different disulfides gave at 140° one unsymmetric and two symmetric sulfides. Addition of 4,4′-dinitrobiphenyl or *m*-dinitrobenzene to the reaction mixture completely inhibited the transformation of diphenyl disulfide into diphenyl sulfide (242, 252). Poisoning of the nickel surface by preferential adsorption of the nitro compound was assumed as explanation and the observation was considered evidence for the importance of adsorption of the sulfur compound at

TABLE 82



R	Yield, %	Reference
$C_6H_5CH_2CH_2$	95	432
	59	432
	61	440

[a] With Raney nickel previously boiled in acetone.

TABLE 83

Starting compounds	Reaction temp., °C.	Reaction products and yields, %	Reference
C_6H_5SH	140	$(C_6H_5)_2S$ (79)	252
C_6H_5SH + 1-$C_{10}H_7SH$	140	$(C_6H_5)_2S$ (42) + 1-$C_{10}H_7SC_6H_5$ (28) + (1-$C_{10}H_7)_2S$ (52) + $C_{10}H_8$ (6)	252
C_6H_5SH + 2-$C_{10}H_7SH$	140	$(C_6H_5)_2S$ (41) + 2-$C_{10}H_7SC_6H_5$ (33) + (2-$C_{10}H_7)_2S$ (52) + $C_{10}H_8$ (16)	241
C_6H_5SH	220	$(C_6H_5)_2$ (23)	247

the nickel surface as the initial step of the desulfurization reaction. At 220° the disulfides yielded mainly biaryls, besides small amounts of higher condensation products. Again, mixtures of disulfides formed three hydrocarbons at 220°. Dioctyl disulfide at 180° yielded a mixture of octane and octene, disproportionation of octyl radicals being admitted as explanation of this result; analogous behavior was shown by dicyclohexyl disulfide. The reactions are summarized in Table 85.

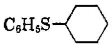
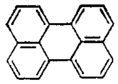
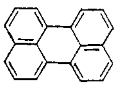
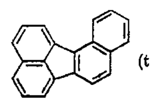
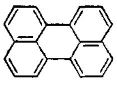
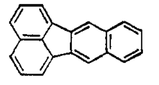
D. THIOKETALS

When heated at 140° with Raney Ni 100 or Raney Ni 200 in xylene, benzaldehyde thioketals gave stilbenes; if the mercaptals were derived from aromatic thiols, sulfides (248) (see Table 86) were obtained simultaneously and were the only reaction products isolated when formaldehyde diaryldithioketals were employed. Dibenzyldithioketals gave dibenzyl instead of dibenzyl sulfide.

E. THIOL ESTERS

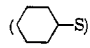
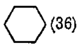
When heated at 140° with Raney Ni 100, thioben-

TABLE 84

Starting compounds	Type of nickel	Reaction temp., °C.	Reaction products and yields, %	Reference
$(C_8H_{17})_2S$	Raney Ni 500	180[a]	1-C_8H_{16} (25%) + C_8H_{18} (20%)	242
$(C_6H_{13})_2S$	Red. Ni/H_2	220–230[a]	C_6H_{14} (0.8)[b]	30
$(C_6H_5CH_2CH_2)_2S$	Raney Ni 500	220[a]	$C_6H_5CH_2CH_3$ (49%) + $C_6H_5CH{=}CH_2$ (31)[c]	242
$C_6H_5SC_5H_{11}$	Raney Ni 500	220[a]	C_5H_{10} (67) + C_5H_{12} (6) + C_6H_6 (74) + $(C_6H_5)_2$ (5)[d]	242
	Raney Ni 500	220[a]	C_6H_6 (100)[e] + C_6H_{12} (62) + $(C_6H_5)_2$ (2)	242
2-$CH_3C_6H_4CH(C_6H_5)SCH_2C_6H_5$	Raney Ni 200	140	[2-$CH_3C_6H_4CH(C_6H_5)]_2$ + $C_6H_5CH_3$	54
4-$CH_3C_6H_4SC_2H_5$	Raney Ni 200	220	4-$CH_3C_6H_4C_2H_5$ (21) + (4-$CH_3C_6H_4)_2$ (10)	247
2-$C_{10}H_7SC_2H_5$	Raney Ni 200	140–145[a]	(2-$C_{10}H_7)_2S$ (60) + $C_{10}H_8$ (7)	252
$C_6H_5SCH_2C_6H_5$	Raney Ni 200	140	$(C_6H_5)_2S$ (49)[f]	252
	Raney Ni 200	140–145[a]	$(C_6H_5)_2S$ (79) + $(C_6H_5CH_2)_2$ (10)	252
$(C_6H_5)_2S$	Raney Ni 200	220	$(C_6H_5)_2$ (62)	247
	Raney Ni 500	220	$(C_6H_5)_2$ (75) + 4-$C_6H_5C_6H_4C_6H_5$ (6)[g]	247
	Red. Ni 200	220	$(C_6H_5)_2$ (61)	247
	Oxal. Ni[h]	220	$(C_6H_5)_2$ (72)	246
(4-$CH_3OC_6H_4)_2S$	Raney Ni 200	140	(4-$CH_3OC_6H_4)_2$ (50)	252
1-$C_{10}H_7SC_6H_5$	Raney Ni 200	140–145[a]	$(C_6H_5)_2S$ (20) + (1-$C_{10}H_7)_2S$	252
(1-$C_{10}H_7)_2S$	W 7-J	64	 (trace)[i]	30
	W 7-J	140	(1-$C_{10}H_7)_2$(15) + (2-$C_{10}H_7)_2$(0.4) + $C_{10}H_8$ (61) +  (0.2) +  (trace)	30
	W 7-J	220	(1-$C_{10}H_7)_2$(20) + (2-$C_{10}H_7)_2$(0.8) +  + 	30
$(C_6H_5)_2S$ + (2-$C_{10}H_7)_2S$	Raney Ni 200	220[a]	$(C_6H_5)_2$ (63) + 2-$C_{10}H_7C_6H_5$ (25) + (2-$C_{10}H_7)_2$ (63) + C_6H_6 (7)	247

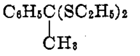
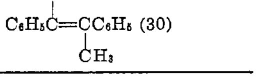
[a] Without solvent. [b] 89% of starting compound was recovered. [c] Styrene was partly polymerized. [d] A trace of amylbenzene also was isolated. [e] The high yield of benzene may be due to dehydrogenation of cyclohexene. [f] 49% of starting compound was recovered. [g] 6% of starting compound was recovered. [h] Nickel powder obtained by decomposing nickel oxalate. [i] 99.9% of starting compound was recovered.

TABLE 85

Starting compounds	Type of nickel	Reaction temp., °C.	Reaction products and yields, %	Reference
$(C_8H_{17}S)_2$	Raney Ni 500	140[a]	$(C_8H_{17})_2S$ (20)[b]	242
	Raney Ni 500	180[a]	C_8H_{18} (36) + C_8H_{16} (45)	319
	Raney Ni 500	220[a]	 (36) +  (37)	242
$(C_6H_5S)_2$	Raney Ni 200	140	$(C_6H_5)_2S$ (82)	248
	Raney Ni 500	140	$(C_6H_5)_2S$ (87)	247
	Red. Ni 200	140	$(C_6H_5)_2S$ (84)	247
	Oxal. Ni[c]	140	$(C_6H_5)_2S$ (87)	246
	Raney Ni 200	180[a]	$(C_6H_5)_2$ (54) + 4-$C_6H_5C_6H_4C_6H_5$ (0.2) + C_6H_6 (18)	247
	Raney Ni 200	220	$(C_6H_5)_2$ (65)	247
	Raney Ni 500	220	$(C_6H_5)_2$ (78) + 4-$C_6H_5C_6H_4C_6H_5$ (0.02)	247
	Red. Ni 200	220	$(C_6H_5)_2$ (85)	247
	Oxal. Ni[c]	220	$(C_6H_5)_2$ (73)	246
(2-$CH_3C_6H_4S)_2$	Raney Ni 200	140	(2-$CH_3C_6H_4)_2S$ (24)[d]	250
	Raney Ni 200	220	(2-$CH_3C_6H_4)_2S$ (11) + (2-$CH_3C_6H_4)_2$ (15)	246
(3-$CH_3C_6H_4S)_2$	Raney Ni 200	140	(3-$CH_3C_6H_4)_2S$ (75)	247
	Raney Ni 200	220	(3-$CH_3C_6H_4)_2$ (58)	247
(4-$CH_3C_6H_4S)_2$	Raney Ni 200	140	(4-$CH_3C_6H_4)_2S$ (84)	252
(4-$ClC_6H_4S)_2$	Raney Ni 200	140	(4-$ClC_6H_4)_2S$ (73)	252
(4-$CH_3OC_6H_4S)_2$	Raney Ni 200	140	(4-$CH_3OC_6H_4)_2S$ (73)[e]	252
(4-$NH_2C_6H_4S)_2$	Raney Ni 200	140	(4-$NH_2C_6H_4)_2S$ (57)	252
(4-$(CH_3)_2NC_6H_4S)_2$	Raney Ni 200	140	(4-$(CH_3)_2NC_6H_4)_2S$ (68)	252
(4-$CH_3CONHC_6H_4S)_2$	Raney Ni 200	140	(4-$CH_3CONHC_6H_4)_2S$ (53)	252
(1-$C_{10}H_7S)_2$	Raney Ni 200	140	(1-$C_{10}H_7)_2S$ (81)	252
(2-$C_{10}H_7S)_2$	Raney Ni 200	220[a]	(2-$C_{10}H_7)_2$ (68) + $C_{10}H_8$ (19)	247
	Raney Ni 500	220[a]	(2-$C_{10}H_7)_2$ (81) + $C_{10}H_8$ (8)	247
	Red. Ni 200	220	(2-$C_{10}H_7)_2$ (90)	247
$(C_6H_5S)_2$ + (1-$C_{10}H_7S)_2$	Raney Ni 200	140	$(C_6H_5)_2S$ (65) + 1-$C_{10}H_7SC_6H_5$ (31) + (1-$C_{10}H_7)_2S$ (69)	252
2$(C_6H_5S)_2$ + (2-$C_{10}H_7S)_2$	Raney Ni 500	140	$(C_6H_5)_2S$ (51) + 2-$C_{10}H_7SC_6H_5$ (43) + (2-$C_{10}H_7)_2S$ (40) + $C_{10}H_8$ (10)	319
$(C_6H_5S)_2$ + (2-$C_{10}H_7S)_2$	Raney Ni 200	220[a]	$(C_6H_5)_2$ (>9) + 2-$C_{10}H_7C_6H_5$ (23) + (2-$C_{10}H_7)_2$ (32) + $C_{10}H_8$ + C_6H_6 (11)	247

[a] Without solvent. [b] 13% of starting compound was recovered. [c] Nickel powder obtained by decomposing nickel oxalate. [d] Considerable amount of starting compound was recovered. [e] 3% of 4,4′-dimethoxybiphenyl was also formed.

TABLE 86

Starting compound	Type of Ni	Reaction products and yields, %
$CH_2(SC_6H_5)_2$	Raney Ni 100	$(C_6H_5)_2$ (9)
	Raney Ni 200	$(C_6H_5)_2S$ (71)
$CH_2(SC_6H_4CH_3\text{-}4)_2$	Raney Ni 200	(4-$CH_3C_6H_4)_2S$ (71)
$CH_2(SC_{10}H_7\text{-}2)_2$	Raney Ni 200	(2-$C_{10}H_7)_2S$ (69)
$C_6H_5CH(SC_2H_5)_2$	Raney Ni 100	$C_6H_5CH{=}CHC_6H_5$ (34)
	Raney Ni 200	$C_6H_5CH{=}CHC_6H_5$ (69)
$C_6H_5CH(SCH_2C_6H_5)_2$	Raney Ni 100	$C_6H_5CH{=}CHC_6H_5$ (37)
	Raney Ni 200	$C_6H_5CH{=}CHC_6H_5$ + $C_6H_5CH_2CH_2C_6H_5$
$C_6H_5CH(SC_6H_5)_2$	Raney Ni 200	$(C_6H_5)_2S$(88) + $C_6H_5CH{=}CHC_6H_5$ (60)
 $C_6H_5C(CH_3)(SC_2H_5)_2$	Raney Ni 200	 $C_6H_5C(CH_3){=}C(CH_3)C_6H_5$ (30)

zoates or phenyl thioesters yielded biphenyl, whereas sulfides were formed at the same temperature when Raney nickel degassed at 200° was employed. In these reactions carbon monoxide was split off. Phenyl 4-nitrothiobenzoate did not react with Raney Ni 200 at 140° (252). Desulfurization is essentially complete at 220°. Unsymmetric thioesters and mixtures of two different thioesters gave one unsymmetrical and two symmetrical products. The reactions are summarized in Table 87.

F. MISCELLANEOUS COMPOUNDS

Nitriles resulted from the treatment in absence of solvent of thiocyanates (319) with Raney nickel degassed at 200 or 500°, in the case of *n*-pentyl thiocyanate together with a mixture of pentane and pentene (yields are given in parentheses):

$$C_5H_{11}SCN \xrightarrow[180^\circ]{\text{Raney Ni 500}} C_5H_{11}CN\ (23) + C_5H_{12}\ (13) + C_5H_{10}\ (9)$$

$$C_6H_5SCN \xrightarrow[220^\circ]{\text{Raney Ni 500}} C_6H_5CN\ (22)$$

4,5-Bis-pentamethylene-3,6-dioxa-*o*-dithiane (CCLXXIV, p. 390) in benzene solution on treatment with Raney nickel degassed at 200° yielded 25% of cyclohexanone together with 35% of cyclohexanone pinacol (CCLXXV, p. 390) (145).

XI. SELENIUM COMPOUNDS

Organic selenium compounds are not as readily available as their corresponding sulfur analogs. This probably is why only a few investigators have studied their behavior in the presence of Raney nickel.

As can be seen from Table 88, deselenization was accomplished by refluxing a great variety of selenium

TABLE 87

Starting compounds	Type of nickel	Reaction temp., °C.	Reaction products and yields, %	Reference
$CH_3COSC_6H_5$	Raney Ni 100	140	$(C_6H_5)_2$ (28)	249
	Raney Ni 200	220	$(C_6H_5)_2$ (47) + $C_6H_5CH_3$ (10)	247
$C_5H_{11}COSC_6H_5$	Raney Ni 500	220[a]	C_5H_{10} (69)[b] + C_6H_6 (25) + $(C_6H_5)_2$ (13) + $C_5H_{11}C_6H_5$ (9)	242
$C_6H_5COSC_2H_5$	Raney Ni 100	140	$(C_6H_5)_2$ (29)	249
	Raney Ni 200	140	$(C_2H_5)_2S$ (15) + $C_6H_5SC_2H_5$ (36) + $(C_6H_5)_2S$ (16)	252
$C_6H_5COSCH_2C_6H_5$	Raney Ni 200	140	$(C_6H_5)_2S$ + $C_6H_5SCH_2C_6H_5$ (45) + $(C_6H_5CH_2)_2$ (8)	249
$C_6H_5COSC_6H_5$	Raney Ni 100	140	$(C_6H_5)_2$ (46)	249
	Raney Ni 200	140	$(C_6H_5)_2S$ (71)	249
	Raney Ni 500	140	$(C_6H_5)_2S$ (74)	247
	Red. Ni 200	140	$(C_6H_5)_2S$ (76)[c]	247
	Oxal. Ni[d]	140	$(C_6H_5)_2S$ (78)	246
	Raney Ni 200	180[a]	$(C_6H_5)_2S$ (36) + $(C_6H_5)_2$ (37)	247
	Raney Ni 200	220	$(C_6H_5)_2$ (56)	247
	Raney Ni 500	220	$(C_6H_5)_2$ (57)	247
	Red. Ni 200	220	$(C_6H_5)_2S$ (18) + $(C_6H_5)_2$ (58)	247
4-$CH_3OC_6H_4COSC_6H_5$	Raney Ni 200	140	4-$CH_3OC_6H_5SC_6H_5$ (63)[e]	252
$C_6H_5COSC_{10}H_7$-1	Raney Ni 200	140	$(C_6H_5)_2S$ (23) + 1-$C_{10}H_7SC_6H_5$ (53) + (1-$C_{10}H_7)_2S$ (20)	249
$C_6H_5COSC_{10}H_7$-2	Raney Ni 200	140	$(C_6H_5)_2S$ (20) + 2-$C_{10}H_7SC_6H_5$ (42) + (2-$C_{10}H_7)_2S$ (39)	249
	Raney Ni 200	220[a]	$(C_6H_5)_2$ + 2-$C_{10}H_7C_6H_5$ (18) + (2-$C_{10}H_7)_2$ (50) + $C_{10}H_8$	247
1-$C_{10}H_7COSC_2H_5$	Raney Ni 200	140	1-$C_{10}H_7SC_2H_5$ (42) + (1-$C_{10}H_7)_2S$ (17)	252
	Raney Ni 200	140[a]	1-$C_{10}H_7SC_2H_5$ (12) + (1-$C_{10}H_7)_2S$ (32) + $C_{10}H_8$ (12)	252
2-$C_{10}H_7COSC_2H_5$	Raney Ni 200	140[a]	2-$C_{10}H_7SC_2H_5$ (27) + (2-$C_{10}H_7)_2S$ (24) + $C_{10}H_8$ (7)	252
$C_6H_5COSC_6H_5$ + 1-$C_{10}H_7COSC_{10}H_7$-1	Raney Ni 200	140	$(C_6H_5)_2S$ (27) + 1-$C_{10}H_7SC_6H_5$ (17) + (1-$C_{10}H_7)_2S$ (39)	252

[a] Without solvent. [b] Impure pentene containing $Ni(CO)_4$. [c] 7% of starting compound was recovered. [d] Nickel powder obtained by decomposition of nickel oxalate. [e] Some starting compound was recovered.

compounds in a mixture of ethanol and benzene; in ethanol alone diphenyl diselenide remained unchanged (472).

The behavior of selenium compounds in the presence of degassed Raney nickel was shown to be very similar to that of their sulfur analogs; however, selenium is eliminated at a lower temperature than is sulfur. The reactions are shown in Table 89.

Bis-(2-nitrophenyl) triselenide (CCLXXX, X = Se) (377) and the corresponding selenenyl sulfide (CCLXXX, X = S) (376) were also treated with Raney nickel degassed at 200° in benzene.

2-$NO_2C_6H_4SeXSeC_6H_4NO_2$-2 (2-$NO_2C_6H_4Se)_2$
CCLXXX (X = Se or S) CCLXXXI

In both compounds the central atom X was removed easily with the formation of bis-(2-nitrophenyl) diselenide (CCLXXXI) in good yield, in spite of nitro groups being present in the molecule.

XII. CONCLUSIONS AND MECHANISM

From the results gathered some general conclusions concerning the course of hydrogenolytic desulfurization can be drawn.

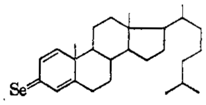
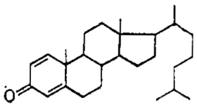
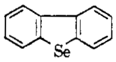
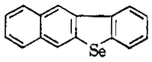
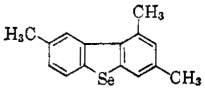
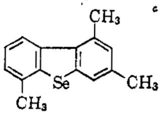
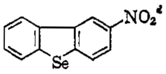
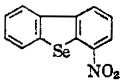
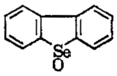
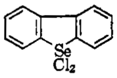
If active nickel preparations are used in sufficient amount and in a suitable solvent, most frequently ethanol, the substitution of hydrogen for sulfur is the only or at least the main reaction. Very few side reactions have been observed, the most frequent being substitution of hydrogen for geminal or, in some special cases, for vicinal oxygen or nitrogen. With very active nickel preparations carbonyl groups or olefinic double bonds are sometimes hydrogenated. Carbon–carbon bond scission is very infrequent, dehalogenation occurs in some cases under desulfurization conditions, and from cyclic monothioketals sulfur is removed with regeneration of the corresponding carbonyl compound.

If less active or deactivated Raney nickel preparations are used, especially in solvents such as benzene or acetone, side reactions become competitive with desulfurization and various "abnormal" products are formed. Among those reactions, substitution of oxygen-containing groups for those containing sulfur, "dimerization" and formation of double bonds are the most important.

As to the mechanism of hydrogenolytic desulfurization of bivalent sulfur derivatives, there seems to be general agreement that adsorption on the nickel surface essentially through the sulfur atom (31, 36, 73, 74, 248, 249) is the first step. Maxted (322) and Lüttringhaus (318) have pointed out how this absorption could be accomplished.

As for the next steps of desulfurization, it was the idea first suggested by Kenner, Lythgoe, and Todd (293) and supported with evidence some years later by Hauptmann and Wladislaw (248, 249) and by Bonner (73, 74) that radicals are the intermediates in the desulfurization reaction. Romo, Rosenkranz, and Djerassi (385) were the first to postulate an inter-

TABLE 88

Starting compound	Reaction product	Yield, %	Reference
$(2\text{-}C_6H_5C_6H_4Se)_2$	$(C_6H_5)_2$	76	472
$(4\text{-}C_2H_5OC_6H_4)_2Se$	$C_6H_5OC_2H_5$	79	472
	 [a]	15	173
$2\text{-}C_6H_5C_6H_4SeCN$	$(C_6H_5)_2$	84	472
$4\text{-}NH_2C_6H_4SeCN$	$C_6H_5NH_2$	79	472
$4\text{-}(CH_3)_2NC_6H_4SeCN$	$C_6H_5N(CH_3)_2$	14	472
$(4\text{-}CH_3OC_6H_4)_2SeO_2$	$C_6H_5OCH_3$	25	472
$2\text{-}C_6H_5C_6H_4SeO_2H$	$(C_6H_5)_2$	62	472
$(4\text{-}C_2H_5OC_6H_4)_2SeCl_2$	$C_6H_5OC_2H_5$	43	472
	$(C_6H_5)_2$	87	472
 [b]	$2\text{-}C_{10}H_7C_6H_5$	—	92
 or  [c]	$3\text{-}CH_3C_6H_4C_6H_3(CH_3)_2\text{-}2,4$	78	90
 [d]	$3\text{-}C_6H_6C_6H_4NH_2$	47	473
 [d]	$3\text{-}C_6H_5C_6H_4NH_2$	63	473
	$(C_6H_5)_2$	72	472
	$(C_6H_5)_2$	72	472

[a] Together with products of hydrogenation. [b] Starting compound distilled with a mixture of zinc and Raney Ni-Al alloy. [c] Starting compound had one of these structures. [d] Under a 50-lb. pressure of hydrogen.

TABLE 89

Starting compound	Type of nickel	Reaction temp., °C.	Reaction products and yields, %	Reference
$(C_6H_5)_2Se$	Raney Ni 200	180[a]	$(C_6H_5)_2$ (77)	243
$(2\text{-}CH_3C_6H_4)_2Se$	Raney Ni 200	180[a]	$(2\text{-}CH_3C_6H_4)_2$ (52)	243
$(C_6H_5Se)_2$	Raney Ni 200	80	$(C_6H_5)_2Se$ (89)	243
	Red. Ni 200	80	$(C_6H_5)_2Se$ (88)	244
	Raney Ni 200	140	$(C_6H_5)_2Se$ (21) + $(C_6H_5)_2$ (31)	243
	Raney Ni 200	180[a]	$(C_6H_5)_2$ (72)	243
	Raney Ni 500	220	$(C_6H_5)_2$ (78)	244
$(2\text{-}CH_3C_6H_4Se)_2$	Raney Ni 200	140	$(2\text{-}CH_3C_6H_4)_2Se$ (67)	243
$C_6H_5COSeC_6H_5$	Raney Ni 200	80	$(C_6H_5)_2Se$ (54)	243
	Raney Ni 200	140	$(C_6H_5)_2Se$ (42) + $(C_6H_5)_2$ (15)	243
	Raney Ni 200	180[a]	$(C_6H_5)_2$ (51)	243

[a] Without solvent.

mediate 1,4-diradical. Carbanions seem to be excluded because of the steric course of the reaction, and carbonium ions are held to be the least likely intermediates; however, an SNi mechanism with hydride ions attacking the sulfur-bearing carbon atom has been considered as possible (434).

Evidence for intermediate radical formation is supplied mainly by these observations:

1. The stereochemical course of hydrogenolytic desulfurization, which leads to racemization (73, 74, 434, 464).

2. The formation of mixtures of paraffins and olefins from saturated aliphatic sulfur compounds (64, 154, 242, 319, 464), disproportionation to those mixtures being the characteristic way of stabilization of alkyl radicals (419).

3. "Dimerization" (29, 33, 36, 248, 249, 252) and cyclization (64, 350, 351), as well as terphenyl formation (247), which are best understood on the basis of a homolytic mechanism. Terphenyl formation from benzene derivatives has always been considered characteristic for the occurrence of phenyl radicals (18, 143).

4. The formation of carbon monoxide when thioesters are treated with degassed Raney nickel (249, 252); this is a typical way of reaction of acyl radicals (47, 234, 458).

5. The formation of cyclohexanone when 4,5-bis-pentamethylene-3,6-dioxa-*o*-dithiane in benzene solution is treated with Raney nickel degassed at 200°. The ketone formation is best explained by admitting a Criegee scission (127) of a 1,4-diradical in the 2,3-position (128).

Some doubts have been raised as for the intermediate role of arylthio (thiyl) radicals, since their formation under conditions similar to those of desulfurization but in absence of a metal surface (394) has been shown to be unlikely (177). However the intermediate formation of "short life" alkyl and arylthio radicals has frequently been assumed (295, 296, 313).

There are some observations which seem to indicate that hydrogen may take part in the splitting of carbon–sulfur bonds (30, 247). The very fact that hydrogenolytic desulfurization occurs under conditions at which no reaction is observed with degassed Raney nickel, if not due to modification of the adsorption qualities of the nickel surface during degassing, seems to point in this direction. However, at higher temperatures all carbon–sulfur bonds are split in the presence of degassed nickel preparations and even of those obtained from nickel oxalate which had never been in contact with hydrogen (246).

The desulfurization of sulfones seems to proceed through another mechanism. Adsorption on the nickel surface is accomplished through an oxygen atom, and for the substitution of hydrogen for the sulfone group attack from the rear (73), possibly through an ionic mechanism (464), has been postulated.

There is one side reaction for which an ionic mechanism, nucleophilic attack by water or alcohol molecules or hydroxyl ions, has been suggested, namely, the introduction of oxygen-containing groups during desulfurization of monothioketals (154). If this side reaction too occurs in the adsorbed state, it seems rather difficult to get direct insight into the details of its mechanism.

XIII. REFERENCES

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