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Organic Photochemistry. V.[1] Dethioacetalization by Photolysis in the Presence of Molecular Oxygen[2]

Osamu Hoshino, Shohei Sawaki, and Bunsuke Umezawa

Faculty of Pharmaceutical Sciences, Science University of Tokyo[3]

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Photolysis (a 200 W high pressure mercury lamp) under oxygen stream of ethylene dithioacetals of 5,6-dimethoxy-α-indanone, α- and β-indanone, α-tetralone, 5α- and 5β-cholestan-3-ones, cholest-4-en-3-one, and cyclohexanone in an appropriate solvent (*n*-hexane, ethanol or benzene) was carried out to give the parent ketones. Ethylene dithioacetal of cholest-5-en-3-one on photolysis followed by $NaBH_4$ reduction gave cholest-4-en-3β-ol, showing photo-induced isomerization of the double bond.

Keywords——preparative TLC; 40% aq. $NaHSO_3$; Girard P; C-S bond; ethylene dithioacetal group; indanone; steroidal ketone

Because of synthetic usefulness[4] of dithioacetals many chemical means[4,5] for hydrolysis of the group have been devised. In spite of the fact[6] that a C-S bond in dithioacetals is sensitive to light, there had been no literature on the photochemical dethioacetalization until a recent communication by T.T. Takahashi *et al.*[7] has appeared. Having been engaged in an independent study on the dethioacetalization for some time, we now wish to report our own results concerning the matter.

An ethanolic solution of 5,6-dimethoxy-α-indanone ethylene dithioacetal (**1**) was irradiated at 0—5° by a high pressure mercury lamp (200 W) under oxygen stream for 10 min. The reaction mixture was treated with the Girard P reagent to give 5,6-dimethoxy-α-indanone[8] in 44% yield.

The photolysis of **1** under nitrogen stream gave complex mixtures including an α-indanone, while reaction under oxygen without irradiation resulted in complete recovery of **1**.

Therefore, it was presumed that **1*** in the excited state was allowed to react with molecular oxygen to afford the α-indanone, although the detailed mechanism is still an open question.[9]

Next, the similar photolysis of other ethylene dithioacetals (**2**—**4**) and cyclohexanone ethylene dithioacetal was carried out to give results shown in Table 1.

Thus it is evident that the group is not necessarily located in the benzylic or homobenzylic position for the photochemical dethioacetalization. In order to examine a scope of the reaction, the photolysis of some steroidal ethylene dithioacetals was tried.

The irradiation of 5α-cholestan-3-one ethylene dithioacetal (**5**)[10] in *n*-hexane followed by purification on preparative thin-layer chromatography (TLC) produced 5α-cholestan-3-

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2) A part of this work was presented at the 91th Annual Meeting of the Pharmaceutical Society of Japan, Fukuoka, 1971.
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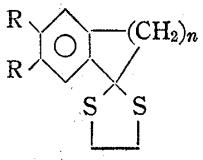
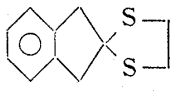
9) Reaction of **1** with singlet oxygen generated chemically was unfruitful.
10) L.F. Fieser, *J. Am. Chem. Soc.*, **76**, 1945 (1954).



1: n=2, R=OMe
2: n=2, R=H
4: n=3, R=H

Chart 1



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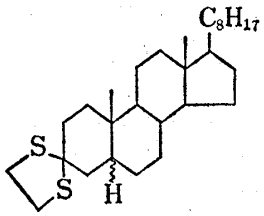
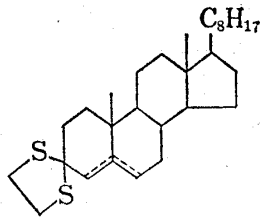


5 : 5α-H
6 : 5β-H



7 : Δ^4
8 : Δ^5

Chart 2

TABLE I. Yields of Ketones

Ethylene dithioacetal	(mmol)	Solvent[a] (ml)	Reaction time (min)	Method[b]	Yields[c] (%)
1	(0.5)	E (60)	10	A	5,6-Dimethoxy-α-indanone (44)[d]
2	(0.5)	B (60)	40	A	α-Indanone (37.4)[e,f]
2	(0.5)	H (60)	90	A	α-Indanone (60)[e,f]
3	(0.5)	H (60)	30	B	β-Indanone (21.5)[e,g]
4	(0.5)	H (60)	20	A	α-Tetralone (56)[e,h]
Cyclohexanone ethylene dithioacetal[i]	(1.1)	E (120)	120	C	Cyclohexanone (56.2)[j]

a) E: ethanol, B: benzene, H: *n*-hexane.
b) For the methods A, B, and C, see Experimental part.
c) Isolated yield.
d) mp 120.5—122° (MeOH) (lit.[9] 121—122°).
e) Isolated as an oil.
f) W. Baker, G.E. Coates, and F. Glockling, *J. Chem. Soc.*, **1951**, 1376 (mp 42°).
g) J.E. Horan and R.W. Schiessler, "Organic Syntheses," Col. Vol. 5, ed. by H.E. Baumgarten, John Wiley and Sons, N.Y., 1973, p. 647 (mp 57—58°).
h) G.D. Johnson, "Organic Syntheses," Col. Vol. 4, ed. by N. Rabjohn, John Wiley and Sons, N.Y. 1963, p. 900 (bp 135—137/15 mm).
i) H. Fuhrer and Hs.H. Günthard, *Helv. Chim. Acta*, **45**, 2036 (1962).
j) Yield based on 2,4-dinitrophenylhydrazone [mp 159—160° (EtOH)].

TABLE II. Yields of Steroidal Ketones

Ethylene dithioacetal	(mmol)	Solvent[a] (ml)	Reaction time (min)	Method[b]	Yields[c] (%)
5[d]	(0.5)	H (60)	90	D	5α-Cholestan-3-one (30.7)[e]
6[f]	(0.5)	H (60)	60	D	5β-Cholestan-3-one (50)[g,h,i]
7[d]	(0.5)	H (60)	60	D	Cholest-4-en-3-one (44.9)[g,j]
8[k]	(0.5)	H (60)	60	E	Cholest-4-en-3β-ol (22)[l,m]

a) H: *n*-hexane.
b) For the methods D and E. see Experimental part.
c) Isolated yield.
d) Ref. 10.
e) mp 127—128.5° (EtOH) (lit.[11] 129—130°).
f) D.A. Lightner, C Djerassi, K. Takeda, K. Kuriyama, and T. Komeno, *Tetrahedron*, **21**, 1581 (1965).
g) Isolated as an oil.
h) Starting material (**6**) was recovered in 38% yield.
i) E.W. Warnhoff and P. NaNonggai, *J. Org Chem.*, **27**, 1186 (1962) (mp 59.5—61.5°).
j) L.F. Fieser, "Organic Syntheses." Col. Vol. 4, ed. by N. Rabjohn, John Wiley and Sons, N.Y., 1963, p. 195 (mp 81—82°).
k) J.F. Eastham and G.B. Miles, *J. Org. Chem.*, **25**, 826 (1960).
l) Starting material (**8**) was recovered in 4.8% yield.
m) mp 117—120° (EtOH-H_2O) (lit.[13] 132°).

one[11] in 30.7% yield. The same treatment of other ethylene dithioacetals (**6**—**8**) furnished the corresponding ketones except for the case of cholest-5-en-3-one. The results are given in Table II.

As to ethylene dithioacetals (**6**—**7**) the similar results as noted in the literature[7] were obtained. Since partial isomerization of cholest-5-en-3-one to 4-en-3-one was observed on silica gel, the reaction mixture from **8** was immediately reduced with sodium borohydride. Separation of the reaction mixture, however, afforded no cholesterol but cholest-4-en-3β-ol,[12,13] showing that the isomerization took place efficiently during the photolysis.

In conclusion, the dethioacetalization was photochemically effected in the presence of molecular oxygen to supply the parent ketones.

Experimental[14]

Ethylene Dithioacetals——Thioacetalization with ethanedithiol of ketones was carried out according to Fieser's method.[10] Melting points and microanalytical data are given in Table III.

Table III. Ethylene Thioacetals (**1**—**4**)

Compound	mp (°C) (Recrystn. solv.)	Formula	Analysis (%) Calcd. C	H	S	Found C	H	S
1	96.5— 97 (MeOH)	$C_{13}H_{16}O_2S_2$	58.20	6.01	23.86	57.95	6.15	23.84
2	46 — 47 (petrol. ether)	$C_{11}H_{12}S_2$	63.45	5.81	30.78	63.37	5.53	30.53
3	103 —104 (MeOH)	$C_{11}H_{12}S_2$	63.45	5.81	—	63.21	5.90	—
4	59 (MeOH)	$C_{12}H_{14}S_2$	64.85	6.35	28.80	64.25	6.47	28.55

General Procedure for Photolysis——A solution of the ethylene dithioacetal in an appropriate solvent was irradiated at 0—5° under oxygen stream by a high pressure mercury lamp. Work-up of the reaction mixture was carried out according to the method A, B, C, D or E.

Method A: The mixture was condensed to a volume of *ca.* 10 ml at reduced pressure. To the condensate were added AcOH (1 ml) and the Girard P (120 mg) and the whole was refluxed for 1 hr. Usual work-up gave an oil, which was identical with an authentic sample by comparison of each IR spectrum ($CHCl_3$) and GLC.

Method B: The mixture was treated with 40% aq. $NaHSO_3$. Usual work-up of the aqueous layer gave an oil, which was identical with an authentic sample by the same analysis as noted in method A.

Method C: The mixture was converted into a 2,4-dinitrophenylhydrazone without removal of the solvent. The hydrazone was identical with an authentic sample by comparison of each mixed mp and IR spectrum (KBr).

Method D: Removal of the solvent at reduced pressure gave an oil, which was separated on preparative TLC. The product was identical with the corresponding authentic specimen by comparison of each IR spectrum ($CHCl_3$).

Method E: To the mixture were added EtOH (30 ml) and $NaBH_4$ (170 mg) and the whole was stirred at room temperature for 1 hr. Usual work-up followed by separation on preparative TLC gave **8** and cholest-4-en-3β-ol.[13] The product was identical with an authentic specimen by comparison of each mixed mp and IR spectrum (KBr).

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11) W.F. Bruce, "Organic Syntheses," Col. Vol. 2, ed. by A.H. Blatt, John Wiley and Sons, N.Y., 1943, p. 139.
12) Further purification of the product was not attempted.
13) R. Schoenheimer and E.A. Evans, Jr., *J. Biol. Chem.*, **114**, 567 (1936) [*Chem. Abstr.*, **30**, 6385 (1936)].
14) All melting points were uncorrected using a Büchi melting point measuring apparatus. Irradiation was carried out with a high pressure mercury lamp (Osawa UV-HT; 200 W) without filter. Infrared (IR) spectra were taken on a Hitachi 215 spectrometer and gas–liquid chromatography (GLC) was run on a Shimadzu GC-4APF gas chromatograph with 1.5% OV-17 as stationary phase. Preparative TLC was performed on silica gel GF_{254} using benzene–MeOH (100: 1) as a developing solvent.