[CONTRIBUTION FROM THE CANCER RESEARCH LABORATORY, UNIVERSITY OF FLORIDA]

Reaction of Thiaxanthydrol With Compounds Containing Active Hydrogen[1]

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Received September 30, 1955

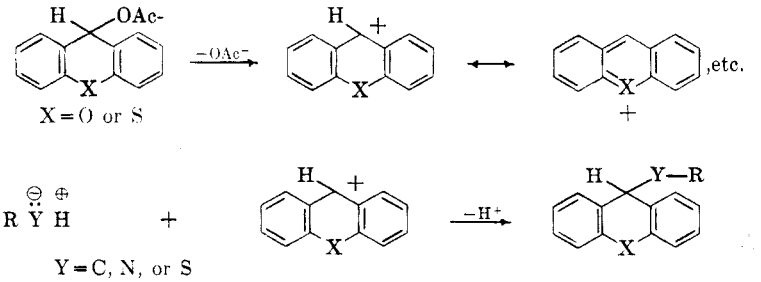
1. Thiaxanthydrol has been shown to react at room temperature in acetic acid-alcohol with many molecules containing hydrogen-substituted carbon, nitrogen, and sulfur atoms of high electron density. For example, derivatives were formed with 12 carbamates, 9 mercaptans, 6 β-diketones, 4 aromatic amines, hydrogen sulfide, hydrogen selenide, urea, pyrrole, 3-nitrobenzhydrazide, 4-phenethylurea, 9-methylcarbazole, and indole.

2. The reactions of xanthydrol have been extended. New derivatives were formed with 9 carbamates, 9 mercaptans, 4 β-diketones, 5 aromatic amines, 3 sulfonamides, hydrogen selenide, nitromethane, malononitrile, 3-nitrobenzhydrazide, 4-phenethylurea, and 9-methylcarbazole.

3. Some of the xanthyl and thiaxanthyl derivatives, particularly the carbamates, were shown to exhibit phosphorescence and/or fluorescence. The color reactions of thiaxanthydrol and xanthydrol with carbazole derivatives, indole derivatives, β-diketones, and barbituric acid were invesigated. Structures were assigned to many of the dyes.

The reaction of xanthydrol with urea under mild conditions to form an insoluble derivative is well known and has been used in many bioanalytical techniques.[3–5] Not as well known is the fact that since Fosse's initial research in 1906,[6] xanthydrol has been found to react similarly with many molecules containing hydrogen-substituted carbon and nitrogen atoms of high electron density.[7] In recent years, increasing attention has been directed toward bioanalytical techniques involving the reaction of xanthydrol with various natural products such as urea, arginine, asparagine, cysteine, glutamine, histidine, lysine, and tryptophan,[8] insulin, lysozyme, and ribonuclease,[9] and cytochrome.[10] We have extended these observations so that it can be stated that *thiaxanthydrol, as well as xanthydrol, will react with many molecules containing hydrogen-substituted carbon, nitrogen, and sulfur atoms of high electron density.*

Both xanthydrol and thiaxanthydrol react readily with acetic acid to form the acetate. The carbonium ion, which results, is stabilized by resonance of the positive charge. The carbonium ion then is attracted to the hydrogen-substituted carbon, nitrogen, or sulfur atom of high electron density in the donor molecule. 'Splitting off' of the active hydrogen atom to give acetic acid yields the final product.



This type of reaction has been shown to take place with other analogous carbonium ion type compounds. For example, Michler's hydrol reacts with aniline, nitroanilines, toluidines, naphthylamines, and urea;[11] 2,7-dibromo- and 2,7-diiodo-xanthydrol condense with urea, ureides, acetic acid, barbiturates, and primary and secondary alcohols;[12–14] 9-phenylxanthydrol has been shown to condense with aniline[15] and methanol and ethanol;[16] flavylium perchlorate attacks the *para* position of dimethylaniline;[17] (2-dimethylamino-5-pyridyl)car-

(1) Supported by grant CH-14 from the American Cancer Society on the recommendation of the Committee on Growth, National Research Council.

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(3) Allen and Luck, *J. Biol. Chem.*, **82**, 693 (1929).

(4) Jespersen and Larsen, *Arch. Pharm.*, **275**, 28 (1937).

(5) Fosse, *Compt. rend.*, **157**, 948 (1913).

(6) Fosse, *Compt. rend.*, **143**, 749 (1906).

(7) Wawzonek in Elderfield, *Heterocyclic Compounds*, John Wiley and Sons, Inc., N. Y., 1951, Vol. II, p. 419.

(8) Dickman and Westcott, *J. Biol. Chem.*, **210**, 481 (1954).

(9) Dickman, Kropf, and Proctor, *J. Biol. Chem.*, **310**, 491 (1954).

(10) Wescott and Dickman, *J. Biol. Chem.*, **210**, 499 (1954).

(11) Mohlau and Heinze, *Ber.*, **35**, 358 (1902).

(12) Bertrand, *Compt. rend.*, **225**, 1331 (1947).

(13) Bertrand, *Bull. soc. chim. France*, 428 (1948).

(14) Bertrand, *Bull. soc. chim. France*, 1078 (1948).

(15) Ullmann and Engi, *Ber.*, **37**, 2367 (1904).

(16) Bunzly and Decker, *Ber.*, **37**, 2931 (1904).

(17) Wizinger and Luthiger, *Helv. Chim. Acta*, **36**, 526 (1953).

binol similarly combines with dimethylaniline and 2-dimethylaminopyridine;[18] 2,6-dimethyl-4-pyryllium iodide reacts with mercaptans and secondary amines;[19,20] gramine reacts with mercaptans;[21] ethylthiomethanol attacks the α-position of β-naphthol.[21] Many more examples are available in the literature.

Fosse has reacted several carbamates with xanthydrol.[22,23] This reaction now has been extended and thiaxanthydrol, as well as xanthydrol, has been found to react readily with carbamates containing a free amino group, Table I. The thiaxanthene derivatives were found to melt at a lower temperature. Thiaxanthene carbamate crystals under ultraviolet light had a weak yellow fluorescence and a weak yellow phosphorescence.[24] By phosphorescence is meant a definite afterglow in the dark when the ultraviolet exciting source was turned off. The xanthene carbamates were non-fluorescent but had a fairly strong yellow phosphorescence.[24] Many of the other xanthene derivatives also showed a weak yellow phosphorescence. Although xanthydrol derivatives could not be prepared from negatively-substituted compounds, such as dichloro- and trichloro-acetamide, and picramide,[25] β-fluorourethan,[26] and β,β,β-trifluorourethan[27] reacted readily with both xanthydrol and thiaxanthydrol. In these carbamates the amino group is apparently not deactivated either because of its greater distance from the negative group than is the case in trichloroacetamide and picramide or because of the presence of the electron-repelling oxygen bridge.

Dickman and Westcott[8] have found that cysteine hydrochloride reacts with xanthydrol. We have extended this reaction and have found that both xanthydrol and thiaxanthydrol react readily in acetic acid at room temperature with aliphatic and aromatic mercaptans, Table II. The thiaxanthene derivatives were higher melting and superior for characterization of the mercaptans. A qualitative test for the SH group in the above derivatives with alcoholic lead acetate showed the absence of the free SH group (*no* copious yellow precipitate). Infrared spectra of these derivatives also showed the absence of the SH stretching frequency at 3.9 microns. Consequently in the aromatic mercaptans substitution of the xanthyl and thiaxanthyl groups takes place on the sulfur and not in the nucleus.

Several β-diketones have been shown to form derivatives with xanthydrol.[28] Thiaxanthydrol also readily forms derivatives with β-diketones, Table III.

If there are two active positions in the molecule, dixanthyl and dithiaxanthyl derivatives are formed, Table IV. For example, thiaxanthydrol, like xanthydrol, condenses with urea to form a disubstituted derivative. Hydrogen sulfide reacts with xanthydrol to form di-9,9′-xanthyl sulfide.[29] In the same way hydrogen sulfide and hydrogen selenide react with xanthydrol or thiaxanthydrol. Pyrrole has been shown to form 2,5-di-(9-xanthyl)pyrrole.[30] Thiaxanthydrol also forms a disubstituted pyrrole which is assumed to be the 2,5-derivative by analogy.

Xanthydrol has been shown to react very readily with all types of aromatic primary amines.[31] Thiaxanthydrol reacts as easily as xanthydrol, especially with negatively substituted aromatic amines, Table V. Several sulfa drugs were tried with xanthydrol and were found to give suitable derivatives. The question arises whether substitution in the negatively-substituted aromatic amines takes place on the amino nitrogen or in the nucleus. Adriani[31] has pointed out that in the N-xanthyl derivatives the carbon-nitrogen bond is easily split in acid solution thus forming a xanthydryl ion, while a xanthyl group substituted in the nucleus of an aromatic amine is stable to acid solution. A solution of any of the xanthyl- or thiaxanthyl-aromatic amino compounds, Table V, in hydrochloric acid gave the color of the respective xanthylium (yellow) or thiaxanthylium (tangerine) ion while solution in sulfuric acid gave the characteristic fluorescence of the xanthylium (green) and thiaxanthylium (orange) ions. The infrared spectra of these derivatives indicated the presence of only one N—H stretching frequency at 2.9 microns. This is characteristic of secondary amines. From these facts it is evident that substitution of the xanthyl and thiaxanthyl groups takes place on the amino nitrogen of the aromatic amines.

Various other types of compounds react with xanthydrol and thiaxanthydrol, Table VI. The reaction of xanthydrol with sulfonamides has been shown to take place readily.[32] In addition, we have found that xanthydrol, as compared to thiaxanthydrol, is much the superior reagent for condensation with sulfonamides or acid amides. Several sulfonamide derivatives of xanthydrol were prepared, Table VI. Under the same conditions thiaxanthydrol derivatives were not isolated. 3-Nitrobenzhydrazide and 4-phenethylurea formed derivatives with thiaxanthydrol as well as xanthydrol. Xanthydrol was also condensed with malononitrile and nitromethane, the latter in poor yield.

(18) Berezovskii, *Zhur. Obshchei Khim. (J. Gen. Chem.)*, **21**, 1903 (1951); *Chem. Abstr.*, **46**, 3282 (1952).
(19) Anker and Cook, *J. Chem. Soc.*, 117 (1946).
(20) King and Ozog, *J. Org. Chem.*, **20**, 448 (1955).
(21) Poppelsdorf and Holt, *J. Chem. Soc.*, 1124 (1954).
(22) Fosse, *Compt. rend.*, **145**, 813 (1907).
(23) Fosse, *Compt. rend.*, **158**, 1432 (1914).
(24) The ultraviolet light source was a General Electric 100 W PAR 38 Projector Flood Lamp. A Corning 5874 m 1092, 8-mm. thick filter was used.
(25) Phillips and Pitt, *J. Am. Chem. Soc.*, **65**, 1355 (1943).
(26) Sawicki and Ray, *J. Org. Chem.*, **18**, 1561 (1953).
(27) Oliverio and Sawicki, *J. Org. Chem.*, **20**, 363 (1955).
(28) Fosse and Robyn, *Compt. rend.*, **143**, 239 (1906).
(29) Fosse, *Compt. rend.*, **155**, 1019 (1912).
(30) Illari, *Gazz. chim. ital.*, **67**, 434 (1937).
(31) Adriani, *Rec. trav. chim. Belg.*, **35**, 180 (1916).
(32) Phillips and Frank, *J. Org. Chem.*, **9**, 9 (1944).

The condensation of carbazole with xanthydrol is alleged to form 9-(9-xanthyl)-carbazole.[33] Condensation of excess 9-methylcarbazole with xanthydrol or thiaxanthydrol, however, also gives a monosubstituted carbazole derivative. As 9-alkylated carbazoles are mainly attacked in the 3-position by electrophilic reagents,[34,35] xanthydrol and thiaxanthydrol would also be expected to attack the 3-position of 9-methylcarbazole. Consistent with this is the similarity of the ultraviolet absorption spectra of the new carbazole derivatives to that of 9-methylcarbazole, Fig. 1. No definite steric effect is noticeable as would be expected in a 1-substituted 9-methylcarbazole.

A hot solution of carbazole in acetic acid containing 1% concentrated hydrochloric acid has been shown to develop a deep indigo-blue color with xanthydrol,[36] while similar treatment of indole, skatole, and tryptophan caused the development of reddish-violet colors.[37] In the same fashion thiaxanthydrol gives brilliant color reactions with many active hydrogen compounds in acetic acid solution in the presence of a small amount of concentrated sulfuric acid. For dyes formed from carbazole and indole derivatives the sulfuric acid was necessary as a proton donor. In all cases it was necessary as an oxidizing agent.

For example, with 9-methylcarbazole and xanthydrol the following reaction scheme is postulated:

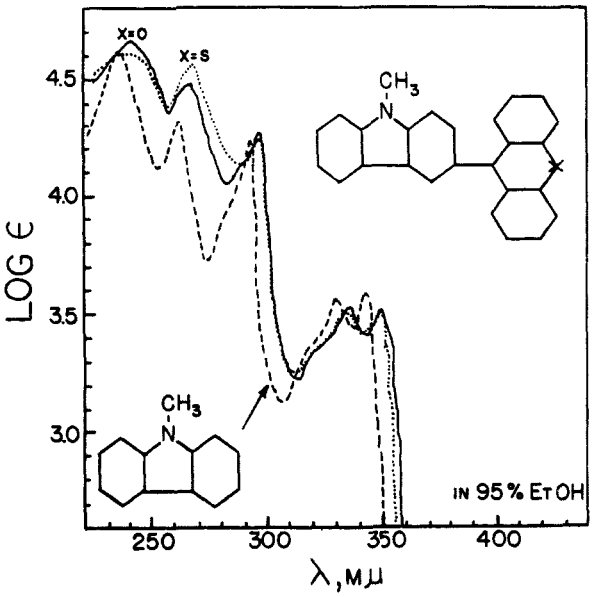
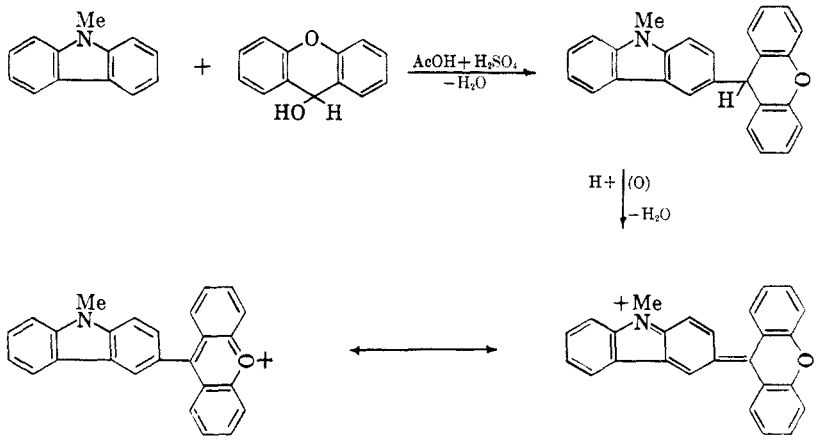


FIG. 1.—ULTRAVIOLET ABSORPTION SPECTRA. 9-Methylcarbazole (—); 3-(9-Xanthyl)-9-methylcarbazole (———), and 3-(10′-Thiaxanthyl)-9-methylcarbazole (•••••).



The color reactions (see experimental section for general procedure and wave length maxima) of carbazole, tryptophan, barbituric acid, and 1,3-indandione with xanthydrol and thiaxanthydrol are shown in Table VII. In the same fashion the following color reactions were obtained with xanthydrol in the order, —compound, color, time for development of color,— 9-methylcarbazole (dark blue-5 min.), 9-ethylcarbazole (dark blue-5 min.), carbazole (blue-5 min.), 3-carbethoxyamino-9-methylcarbazole (blue-2 hrs.), 2-acetylamino-9-methylcarbazole (blue-2 hrs.), 3-acetylamino-9-methylcarbazole (blue-2 hrs.), 3-trifluoroacetylamino-9-methylcarbazole (blue-2 hrs.), indole (purple-5 min.), gramine (dark red-5 min.), 1,2,3,4-tetrahydrocarbazole (dark blue-30 min.), 5,10-dihydroindeno[1,2-*b*]indole (green-blue-30 min.), 5 methyl-5,10-dihydroindeno[1,2-*b*]indole (green-5 min.), and tryptophan (violet-30 min.). With thiaxanthydrol the following useful color reactions are obtained—carbazole (blue-30 min.), 9-methylcarbazole (blue-2 hrs.), 9-ethylcarbazole (blue-2 hrs.), indole (blue-30 min.), gramine (red-30 min.), tryptophan (violet-30 min.), and 1,2,3,4-tetrahydrocarbazole (unstable purple-2 hrs.). Xanthydrol and thiaxanthydrol give only yellow colors after two hours with 2-aminocarbazole, 2-amino-9-methylcarbazole, 3-amino-9-methylcarbazole, 9-acetylcarbazole, 9-carbethoxycarbazole, 2-nitro-9-carbethoxycarbazole, 2-acetyl-

(33) Illari, *Gazz. chim. ital.*, **68**, 103 (1938).
(34) Sawicki, *J. Am. Chem. Soc.*, **76**, 664 (1954).
(35) Buu Hoï and Royer, *J. Org. Chem.*, **16**, 1198 (1951).
(36) Arreguine, *Rev. Univ. Nacl. Cordoba (Arg.)*, **31**, 1706 (1944); *Chem. Abstr.*, **39**, 3222 (1945).
(37) Arreguine, *Rev. Asoc. Bioquim. Argentina*, **12**, 3 (1945); *Chem. Abstr.*, **39**, 3223 (1945).

amino-9-mesylcarbazole, and 2-amino-9-mesylcarbazole. With 2-nitrocarbazole, 2-nitro-9-methylcarbazole, 2-nitro-9-ethylcarbazole, and 3-nitro-9-methylcarbazole reddish to violet colors are obtained with xanthydrol in 3 to 4 hours. An acyl group in the 9-position of carbazole, as well as an amino or nitro group in the 2- or 3-positions of carbazole or 9-methylcarbazole, interferes with the formation of the blue color. In all the color reactions xanthydrol is superior to thiaxanthydrol in respect to stability of reagent, clarity of color, and speed of reaction.

3-(9-Xanthyl)-9-methyl carbazole and the thiaxanthyl analog produce the blue color with solid acids also. When melted with acids such as *p*-toluenesulfonic acid, citric acid, salicylic acid, *p*-nitrobenzoic acid, and *m*-toluic acid a dark blue color is obtained which remains when the mixture solidifies. On the other hand with nicotinic acid both carbazole derivatives form a dark blue melt which becomes white on solidification. This reversible color change can be repeated indefinitely and is probably a redox reaction.

3-(9-Xanthyl)-9-methylcarbazole treated with acetic acid containing a small amount of sulfuric acid produces a blue dye with a wave length maximum at approximately 600 mμ as does 9-methylcarbazole in the color reaction. Indole by the general color reaction gives a violet dye as does 3-(9-xanthyl)indole in acetic acid solution containing a drop of sulfuric acid. 1,3-Indandione treated by the general color reaction and diluted with acetic acid furnishes a violet dye with wave length maxima at 430, 450, and 538 mμ. This violet dye must be 2-(9-xanthylidene)indan-1,3-dione[38] for this latter compound has a parallel curve in acetic acid with wave length maxima at 430, 450, and 539 mμ. The structure of the xanthydrol-tryptophan dye has been discussed by Dickman and Westcott.[8] These authors reported a wave length maximum within the range of 510 to 520 mμ in acetic acid-hydrochloric acid. This checks with our value of 523 mμ in acetic acid-sulfuric acid, Table VII.

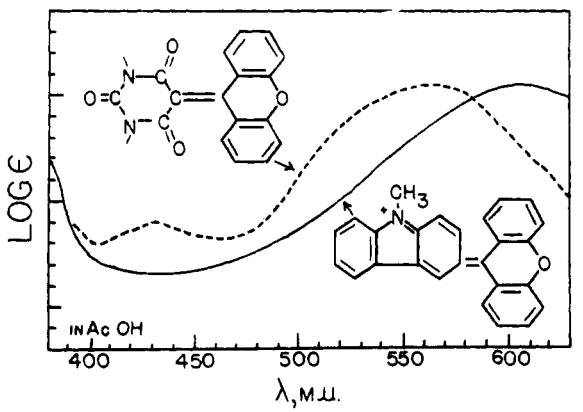


FIG. 2.—VISIBLE ABSORPTION SPECTRA. Qualitative curves for barbituric acid (---) and 9-methylcarbazole (————) treated with xanthydrol in the general color reaction and appropriately diluted with acetic acid.

(38) Schonberg, Mustafa, and Sobhy, *J. Am. Chem. Soc.*, **75**, 3377 (1953).

Thus, it would seem that the dyes formed in the reaction between xanthydrol or thiaxanthydrol and compounds containing active hydrogen attached to a carbon atom involve a C=C grouping at the *meso* position of thiaxanthene and xanthene as shown in Fig. 2. The structure assigned to the barbituric acid-xanthydrol color product, Fig. 2, is consistent with the fact that 5,5-disubstituted barbiturates do not give the color reaction.

It is likely that many substances related to xanthydrol and thiaxanthydrol in respect to forming stabilized carbonium ions in acid media could be found that would even react with alcohols, aliphatic ketones, carboxylic acids and other types of active hydrogen-containing compounds. It is apparent that many new color reactions and qualitative or quantitative techniques of value in bioanalysis thus could be developed.

EXPERIMENTAL[39]

Xanthydrol[40] and thiaxanthydrol[41] were easily prepared by excellent procedures in the literature.

General procedure for the preparation of xanthydrol and thiaxanthydrol derivatives. β-Fluoroethyl N-9-xanthylcarbamate. To a test tube containing 1 g. (0.005 mole) of xanthydrol dissolved in a mixture of 1.5 ml. of glacial acetic acid and 1.5 ml. of ethanol was added 0.54 g. (0.005 mole) of fluorourethan[26] dissolved in an equal volume of the same solvent. The resulting mixture completely solidified after standing at room temperature three days. The solid material was collected on a small Hirsch funnel, washed several times with small portions of ice-cold methanol, and recrystallized from heptane to give 1 g. (71%) of long white needles, m.p. 183–184°. No attempts were made to obtain optimal yields.

Carbamates, Table I. The general procedure was used. Although in some cases reaction took place within a few minutes, the mixtures all were allowed to stand for three days. The crystallizing solvents were usually pentane, hexane, or heptane. Yields ranged from 60–80%.

Mercaptan derivatives, Table II. The general procedure was used for these derivatives except that the reaction took place quickly; after an hour excess water was added to the mixture. The carboxylic acid derivatives were crystallized from water or aqueous alcohol. The remainder of the compounds were crystallized from pentane or hexane. Yields ranged from 80–95%. In all cases the thiaxanthyl derivatives had a higher melting point.

β-Diketone derivatives, Table III. The general procedure was used. The crystallizing solvent was hexane or heptane. Yields ranged from 60 to 80%.

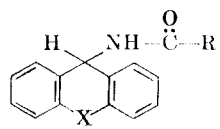
Dixanthyl and dithiaxanthyl compounds, Table IV. For the preparation of the sulfides and selenides the procedure of Fosse[29] was followed. Hydrogen sulfide or hydrogen selenide was passed through an aqueous acetic acid solution of xanthydrol or thiaxanthydrol for 20 minutes and then the mixture was allowed to stand overnight. For the sulfides the crystallizing solvent was acetic acid; for the selenides the crystallizing solvent was hexane-heptane (1:1). Yields ranged from 10–30%.

(39) All melting points and boiling points are uncorrected. Analyses are by Peninsular ChemResearch, Inc., Gainesville, Florida.

(40) Holleman in Gilman, *Org. Syntheses,* Coll. Vol. I, 2nd Ed., 554 (1941).

(41) Oehlschlaeger and MacGregor, *J. Am. Chem. Soc.*, **72**, 5332 (1950).

TABLE I

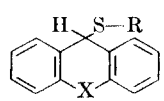


XANTHYL- AND THIAXANTHYL- CARBAMATES

R	M.p., °C. X = O	Formula	Analyses Calc'd C	H	N	Found C	H	N	M.p., °C. X = S	Formula	Analyses Calc'd C	H	Found C	H
CH_3O—	192–193[a]								155–156	$C_{15}H_{13}NO_2S$	66.4	4.8	66.3	4.9
F_3CCH_2O—	166–167	$C_{16}H_{12}F_3NO_3$	59.4	3.7	4.3	59.3	3.8	4.2	126–128	$C_{16}H_{12}F_3NO_2S$	56.6	3.5	56.7	3.6
$ClCH_2CH_2O$—	171–172	$C_{16}H_{14}ClNO_3$	63.3	4.6		63.4	4.8		114–116	$C_{16}H_{14}ClNO_2S$	60.1	4.4	60.2	4.4
FCH_2CH_2CO—	183–184	$C_{16}H_{14}FNO_3$	66.9	4.9	4.9	67.1	5.0	4.8	161–162	$C_{16}H_{14}FNO_2S$[d]	63.4	4.6	63.6	4.8
C_2H_5O—	170–171[b]	$C_{16}H_{15}NO_3$							170–171	$C_{16}H_{15}NO_2S$[e]	67.4	5.3	67.3	5.2
C_2H_5S—	173–174	$C_{16}H_{15}NO_2S$	67.4	5.3	4.9	67.5	5.1	4.8	147–149	$C_{16}H_{15}NOS_2$	63.8	5.0	63.5	5.1
CH_2=$CHCH_2O$—	147–148	$C_{17}H_{15}NO_3$	72.6	5.3		72.8	5.5		106–107	$C_{17}H_{15}NO_2S$	68.7	5.1	68.6	5.1
n-C_3H_7O—	144–145	$C_{17}H_{17}NO_3$	72.1	6.0		72.2	6.1		123–124.5	$C_{17}H_{17}NO_2S$	68.2	5.7	68.1	5.9
n-C_4H_9O—	140–141	$C_{18}H_{19}NO_3$	72.7	6.4		72.9	6.3		91–92	$C_{18}H_{19}NO_2S$	69.0	6.1	68.8	6.1
i-C_6H_9O—	145–146[c]	$C_{18}H_{19}NO_3$							118–119	$C_{18}H_{19}NO_2S$	69.0	6.1	68.9	6.1
n-$C_5H_{11}O$—	146–147	$C_{19}H_{21}NO_3$	73.3	6.8		73.4	6.8		83.5–85	$C_{19}H_{21}NO_2S$	69.7	6.4	69.7	6.6
n-$C_6H_{13}O$—	120	$C_{20}H_{23}NO_3$	73.8	7.1		73.5	7.0		80–81	$C_{20}H_{23}NO_2S$	70.4	6.7	70.3	6.6

[a] Lit. m.p. 193°.[23] [b] Lit. m.p. 168–169°.[22] [c] Lit. m.p. 148°.[23] [d] N, Calc'd 4.6. Found: 4.7. [e] N, Calc'd 4.9. Found, 5.0.

TABLE II

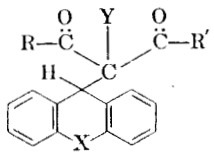


MERCAPTAN DERIVATIVES OF XANTHYDROL AND THIAXANTHYDROL

R	M.p., °C. X = O	Formula	Analyses Calc'd C	H	Found C	H	M.p., °C. X = S	Formula	Analyses Calc'd C	H	Found C	H
HOOC—CH_2—	131–132	$C_{15}H_{12}O_3S$	66.2	4.4	66.2	4.5	165–167	$C_{15}H_{12}O_2S_2$	62.5	4.2	62.6	4.2
CH_3CH_2—	63–65	$C_{15}H_{14}OS$	74.4	5.8	74.5	5.9	135–136	$C_{15}H_{14}S_2$	69.8	5.4	70.0	5.4
HOOC—$(CH_2)_2$—	84–85	$C_{16}H_{14}O_3S$	67.1	4.9	67.1	5.0	132–133	$C_{16}H_{14}O_2S_2$	63.6	4.6	63.7	4.7
HOOC—CH_2CH(COOH)—	207–208[a]	$C_{17}H_{14}O_5S$	61.8	4.2	61.9	4.3	234–235 dec	$C_{17}H_{14}O_4S_2$	59.0	4.0	59.0	4.1
$CH_3(CH_2)_4$—							104–105	$C_{18}H_{20}S_2$	72.0	6.7	72.2	6.7
p-O_2N—C_6H_4—	133–135	$C_{19}H_{13}NO_3S$	68.1	3.9	68.3	3.9	164–166	$C_{19}H_{13}NO_2S_2$	65.0	3.7	65.1	3.8
C_6H_5—	77–78	$C_{19}H_{14}OS$	78.6	4.8	78.8	4.9	152–153	$C_{19}H_{14}S_2$	74.5	4.6	74.6	4.6
$CH_3(CH_2)_7$—	37–38	$C_{21}H_{26}OS$	77.3	8.0	77.3	8.1	64–65	$C_{21}H_{26}S_2$	73.7	7.6	73.8	7.7
β-Naphthyl	137–138	$C_{23}H_{16}OS$	81.2	4.7	81.1	4.8	217–218[b]	$C_{23}H_{16}S_2$	77.5	5.6	77.3	5.7

[a] Melts with decomposition and effervescence. [b] Resolidifies after melting.

TABLE III

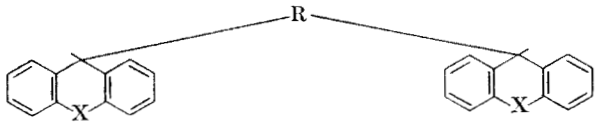


SOME β-DIKETONES OF XANTHYDROL AND THIAXANTHYDROL

R	R′	Y	M.p., °C. X = O	Formula	Analyses Calc'd C	Calc'd H	Found C	Found H	M.p., °C. X = S	Formula	Analyses Calc'd C	Calc'd H	Found C	Found H
CH_3	CH_3	H	152–153	$C_{18}H_{16}O_3$	77.1	5.7	77.3	5.8	165–166	$C_{18}H_{16}O_2S$	73.0	5.4	72.8	5.3
CH_3	OC_2H_5	H	87–89[a]	$C_{19}H_{18}O_4$					117–118	$C_{19}H_{18}O_3S$	69.9	5.5	70.1	5.6
α-Thienyl	CF_3	H	133–134	$C_{21}H_{13}F_3O_3S$	62.7	3.2	62.7	3.3	143–144	$C_{21}H_{13}F_3O_2S_2$	60.3	3.1	60.4	3.2
C_6H_5	CH_3	H	171–172[a]	$C_{23}H_{18}O_3$					150–152	$C_{23}H_{18}O_2S$	77.1	5.0	77.3	5.1
	o-C_6H_4	NO_2	157–158[b]	$C_{22}H_{13}NO_5$	71.2	3.5	70.9	3.3	188–189	$C_{22}H_{13}NO_4S$	68.2	3.4	68.1	3.3
	o-C_6H_4	H	143–145 dec	$C_{22}H_{14}O_3$	81.0	4.3	81.3	4.5	141–142	$C_{22}H_{14}O_2S$	77.2	4.1	77.3	4.1

[a] Lit. value.[28] [b] M.p. 166–167°.[43]

TABLE IV

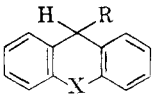


DIXANTHYL AND DITHIAXANTHYL DERIVATIVES

R	M.p., °C. X = 0	Formula	Analyses Calc'd C	Calc'd H	Found C	Found H	M.p., °C. X = S	Formula	Analyses Calc'd C	Calc'd H	Found C	Found H
S	179–180 dec	$C_{26}H_{18}O_2S$	79.2	4.6	79.0	4.6	184–185 dec	$C_{26}H_{18}S_3$	73.2	4.2	73.4	4.3
Se	145–146 dec	$C_{26}H_{18}O_2Se$	70.7	4.1	70.6	4.0	~190[b]	$C_{26}H_{18}S_2Se$	66.0	3.8	66.1	3.9
—NHCONH—	274 dec[c]						283–285	$C_{27}H_{20}N_2OS_2$[d]				
	198–201[e]						238–239	$C_{30}H_{21}NS_2$	78.4	4.6	78.6	4.7

[a] This compound was prepared by Fosse[29] but no melting point was reported. [b] In bath at 190°. Decomposes to red solid. [c] Lit. m.p. 220° dec.[22] [d] N, Calc'd, 6.2. Found, 6.1. [e] Lit. m.p. 200° dec.[30]

TABLE V

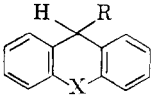


AROMATIC AMINE DERIVATIVES OF XANTHYDROL AND THIAXANTHYDROL

R	X	M.P., °C.	Formula	Analyses Calc'd N	Analyses Found N
2-Cl-4-NO_2—C_6H_3NH—	S	170–172	$C_{19}H_{13}ClN_2O_2S$	7.6	7.5
2-NO_2—C_6H_4—NH—	O	201–202[a]			
2-NO_2—C_6H_4—NH	S	150–151	$C_{19}H_{14}N_2O_2S$	8.4	8.2
2-NO_2—4-CH_3O—C_6H_3—NH	O	164–165	$C_{20}H_{16}N_2O_4$	8.0	7.9
2-NO_2—4-CH_3O—C_6H_3—NH	S	165–167	$C_{20}H_{16}N_2O_3S$	7.7	7.6
N^4-Sulfadiazine	O	246–247	$C_{23}H_{18}N_4O_3S$	9.8	10.2
N^4-Sulfapyridine	O	241–242	$C_{24}H_{19}N_3O_3S$	13.0	13.3
3-NO_2—2-Dibenzofuryl—NH—	O	230–231	$C_{25}H_{16}N_2O_4$	6.9	6.8
3-NO_2—4-Xenylamino	O	181–182	$C_{25}H_{18}N_2O_3$	7.1	7.0
3-NO_2—4-Xenylamino	S	170–171	$C_{25}H_{18}N_2O_2S$	6.8	6.8

[a] Lit. m.p. 197–199°.[44]

TABLE VI



MISCELLANEOUS DERIVATIVES

R	X	M.p., °C.	Formula	Analyses Calc'd C	Calc'd H	Calc'd N	Found C	Found H	Found N
NO_2CH_2—	O	94–96	$C_{14}H_{11}NO_3$						
$(CN)_2CH$—	O	186–188	$C_{16}H_{10}N_2O$			11.4			11.3
3,4-Cl_2—C_6H_3—SO_2NH—	O	186–187	$C_{19}H_{13}Cl_2NO_3S$	56.2	3.2		56.1	3.1	
4-Br—C_6H_4—SO_2NH—	O	216–217	$C_{19}H_{14}BrNO_3S$	54.8	3.4		54.9	3.3	
3-NO_2—C_6H_4—SO_2NH—	O	206–207	$C_{19}H_{14}N_2O_5S$			7.3			7.3
3-NO_2—C_6H_4—CONH—NH—	O	191–192	$C_{20}H_{15}N_3O_4$			11.6			11.5
3-NO_2—C_6H_4—CONH—NH—	S	194–195	$C_{20}H_{15}N_3O_3S$			11.1			11.3
4-C_2H_5O—C_6H_4—NHCO—NH—	O	245	$C_{22}H_{20}N_2O_3$			7.8			7.6
4-C_2H_5O—C_6H_4—NHCO—NH—	S	232–233	$C_{22}H_{20}N_2O_2S$	70.2	5.3		70.6	5.5	
3-(9-Methylcarbazole)-	O	193–195	$C_{26}H_{19}NO$	86.4	5.3		86.5	5.4	
3-(9-Methylcarbazole)-	S	162–163	$C_{26}H_{19}NS$	82.8	5.0		82.6	5.3	
3-Indole	S	155–156	$C_{21}H_{15}NS$	80.5	4.8		81.0	4.7	

The urea and pyrrole derivatives were prepared by the standard procedure. The urea derivative was crystallized from dimethylformamide in 40–50% yield and the pyrrole derivatives from Methyl Cellosolve[42] in 70–75% yield.

Amine derivatives, Table V. The general procedure was used except that the amine was first dissolved in the minimum amount of acetic acid. For example, approximately 300 ml. of acetic acid was necessary to dissolve 0.46 g. of 3-amino-2-nitrodibenzofuran. The mixtures were allowed to stand for over a week. Heptane and aqueous Methyl Cellosolve were the crystallizing solvent. Yields ranged from 30–50%.

Miscellaneous derivatives, Table VI. The general procedure was used for these compounds except in the preparation of the carbazole derivatives where 0.01 mole of a 9-methylcarbazole derivative was reacted with 0.005 mole of xanthydrol or thiaxanthrol. The urea derivatives and the 9-methylcarbazole derivatives were crystallized from Methyl Cellosolve, the nitromethane derivative was crystallized from pentane, and the remainder were crystallized from benzene or alcohol. Most of the reaction mixtures solidified within one or two hours but were allowed to stand overnight. In the case of the nitromethane derivative water was added to the reaction mixture after three days. The yields ranged from 70–80% except for the nitromethane derivative and the 3-nitrobenzhydrazide derivative of thiaxanthydrol which were obtained in 10% yield.

TABLE VII

COLOR REACTIONS IN ACETIC ACID[a]

Compound	Color ($\lambda_{max.}$ in mμ) Xanthydrol	Thiaxanthydrol
Carbazole	Blue (585)	Blue (520, 607)
Tryptophan	Violet (523)	Violet (557)
Barbituric acid	Violet (430, 560)	Blue (595)
1,3-Indandione	Violet (430, 450, 538)	

[a] Reaction solution contains 1% H_2SO_4.

General color reaction. To a solution of 1 to 5 mg. of the compound to be tested in 1 ml. of acetic acid was added 1 ml. of a 1% acetic acid solution of xanthydrol or thiaxanthydrol. After standing 5–10 minutes 1 drop of concentrated sulfuric acid was added and the mixture was shaken. The color was read at appropriate times.

GAINESVILLE, FLORIDA

(42) Trade name for 2-methoxyethanol.

(43) Vanags and Geita, *Latvijas PSR Zinatnu Akad. Vestis,* 149 (1952); *Chem. Abstr.,* **49,** 307 (1955).

(44) Shriner and Wolf, *J. Am. Chem. Soc.,* **73,** 891 (1951).