SYNTHESIS AND REACTIVITY OF THIOAURONES OVER THE PAST ONE HUNDRED YEARS

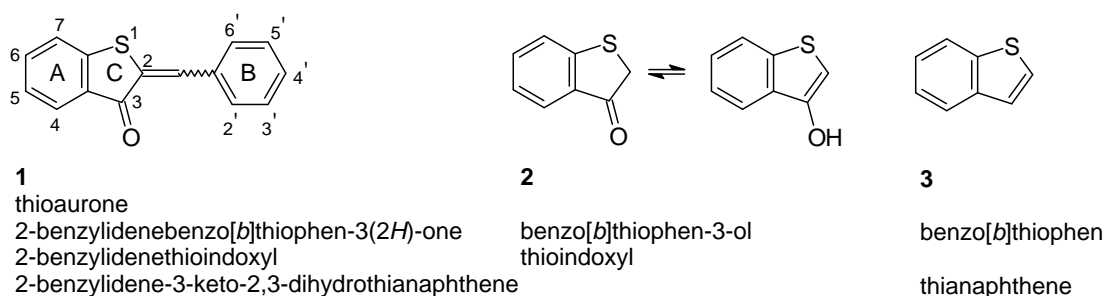**Marek T. Konieczny* and Wojciech Konieczny**

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Abstract – The synthesis and reactivity of 2-benzylidenebenzo[b]thiophen-3(2H)-ones (thioaurones) is comprehensively reviewed.

INTRODUCTION

The term thioaurone was introduced by O'Sullivan[1] as a trivial name for sulfur analogs of aurones, and referred to derivatives of 2-benzylidenebenzo[b]thiophen-3(2H)-one (**1**). Other names used for the compounds, and related systems are shown in Figure 1.

Figure 1

1
thioaurone
2-benzylidenebenzo[b]thiophen-3(2H)-one
2-benzylidenethioindoxyl
2-benzylidene-3-keto-2,3-dihydrothianaphthene

2
benzo[b]thiophen-3-ol
thioindoxyl

3
benzo[b]thiophen

thianaphthene

Even synthesis of thioaurones was achieved almost one century ago,[2,3] they are relatively little known, and are not covered by any review article, including the one devoted to thioflavonoid compounds.[4] Their synthesis was summarized in short by Lévai.[5] Meanwhile, they posses interesting properties and were extensively tested as thioindygo-like dyes,[6-19] and photochromic materials.[20-33] Recently, growing attention is given to their application in photoresponsive devices[30] and photoswitchable biomolecules.[31-33] Despite, the growing interest in aurones as potential medicinal agents[34] will probably result in similar interest in the thio analogs.

SYNTHESIS AND STRUCTURE OF THIOAURONES

The known derivatives of thioaurones are listed in Table 1. The list may miss some compounds, especially those described in the older literature, yet it certainly gives a good picture of the present status of the field. Thioaurones may exist as two isomers, *E* and *Z*, called in the older literature *cis* and *trans*, respectively (Figure 2).

Figure 2

1 *Z* (*trans*)   1 *E* (*cis*)

The isomer *Z* is thermodynamically more stable than the isomer *E*,[31] and for this reason it can be assumed that all thioaurones with undetermined stereochemistry of the double bond are most probably the *Z* isomers. The unstable *E* isomers can be prepared by irradiation of the *Z* form with sunlight[20] or UV/VIS light.[1,31-33] The equilibrium formed upon irradiation is unstable, and in darkness the isomer *Z* is formed again. For example, isomer *Z* of the compound (**130**) irradiated for 10 min. with 406 nm or 445 nm light gave a mixture containing 65 % of *E* and 35 % of *Z* isomer. The sample stored for a prolonged time in darkness gave a mixture of 98 % of *Z* and 2 % of *E*.[31]

130
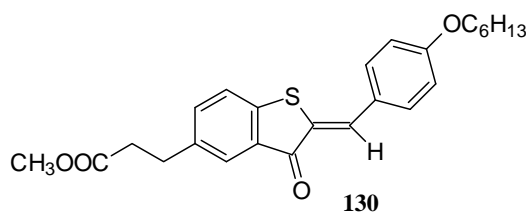
The two isomers can be distinguished base on NMR spectrum. The α hydrogen bonded to the exocyclic double bond is shifted in the unstable *E* isomer about 0.6 - 0.8 ppm upfield, with comparison to the corresponding *Z* isomer. At the same time, the protons 2' and 6' of the isomer *E* are shifted, under the influence of the carbonyl, about 0.4 ppm downfield.[1,31] The carbonyl group itself appears in the ^{13}C NMR spectrum of the isomer *E* about 5 ppm downfield in comparison to the *Z*.[1]

The oldest and probably still the most popular method of synthesis of thioaurones (**1**) depends on condensation of benzaldehydes with derivatives of benzothiophen-3-one (**2**) (Scheme 1).[2,3]

Table 1

List of thioaurones (**1**) published since 1908.

Cmpd no	Substituents in the ring A	Substituents in the ring B	References*	Cmpd no	Substituents in the ring A	Substituents in the ring B	References*
4	-	-	2 (A); 3 (A); 20 (*trans*, A); 23; 35 (*trans*, R); 37 (*trans*, R); 38 (B); 39 (B); 40 (A,R); 41 (F); 42 (F); 45 (D); 46 (E); 47 (C); 49 (P)	**97**	7-I	3'-OCH$_3$; 4'-OH	17 (A); 19 (A
5	-	2'-OH	3 (A); 22 (*trans*, P); 40 (A,R)	**98**	7-I	4'- N(CH$_3$)$_2$	18 (A)
6	-	3'-OH	3 (A)	**99**	7-I	4'- N(C$_2$H$_5$)$_2$	19 (A)
7	-	4'-OH	3 (A)	**100**	7-I	2'- NO$_2$	18 (A)
8	-	3'-OH; 4'-OH	3 (A)	**101**	7-I	3'- NO$_2$	18 (A)
9		2'-OCH$_3$	22 (trans, P)	**102**	7-I	4'- NO$_2$	18 (A)
10	-	4'-OCH$_3$	20 (*trans*, A); 22 (*trans*, P); 37 (*trans*, R); 39 (B); 40 (A, R); 42 (F); 47 (C); 48 (R)	**103**	4-CH$_3$	-	7 (A); 28 (*cis*, P)
11	-	2'-OCH$_3$; 5'-OCH$_3$	45 (D)	**104**	4-CH$_3$	4'-F	28 (*cis*, P)
12	-	4'-F	37 (*trans*, A, R); 47 (C)	**105**	4-CH$_3$	4'-Cl	28 (*cis*, P)
13		2'-Cl	21 (R); 22 (*trans*, P)	**106**	4-CH$_3$	4'-N(CH$_3$)$_2$	12 (P)
14	-	4'-Cl	22 (*trans*, P); 35 (*trans*, R); 37 (*trans*, R); 40 (A, R); 42 (F); 48 (R)	**107**	5- CH$_3$	-	1 (*cis* and *trans*, A); 2 (A); 6 (A); 7 (A); 28 (*cis*, P); 44 (*cis* and *trans*, R); 43 (B)
15	-	2'-Cl; 6'-Cl	21 (R); 22 (*trans*, P)	**108**	5- CH$_3$	3'-OH	6 (A)
16		2'-Cl; 4'-Cl	22 (*trans*, P)	**109**	5- CH$_3$	4'-OH	6(A); 28 (*cis*, P)
17	-	3'-Cl; 4'-Cl	40 (A, R)	**110**	5- CH$_3$	3'-OH; 4'-OH	6 (A)
18	-	4'- CH$_3$	35 (*trans*, R); 47 (C)	**111**	5- CH$_3$	4'-OCH$_3$	6 (A); 25 (P)
19	-	4'-CF$_3$	47 (C)	**112**	5- CH$_3$	3'-OCH$_3$; 4-OH	6 (A)
20	-	4'-N(CH$_3$)$_2$	20 (*trans*, A); 40 (A, R)	**113**	5- CH$_3$	3',4'-OCH$_2$O-	6 A)
21	-	2'-NO$_2$	22 (*trans*, P)	**114**	5- CH$_3$	2'- Cl	25 (A)
22	-	4'-NO$_2$	20 (*trans*, A); 22 (*trans*, P)	**115**	5- CH$_3$	4'- Cl	1 (*cis* and *trans*, A); 6 (A); 25 (P); 26 (A); 44 (*cis* and *trans*, R)
23	-	furyl-2	20 (*trans*, A); 40 (A, R); 47 (C)	**116**	5- CH$_3$	4'- CH$_3$	6 (A)
24	-	tienyl-2	47 (C)	**117**	5- CH$_3$	2'-NH$_2$	1 (*cis* and *trans*, F)
25	4-OCH$_3$	-	11 (A)	**118**	5- CH$_3$	3'-NH$_2$	6 (A)
26	4-OCH$_3$	4'-N(CH$_3$)$_2$	11 (A); 17 (P)	**119**	5- CH$_3$	4'-N(CH$_3$)$_2$	6 (A); 12 (P); 25 (P); 44 (*trans*, R)
27	4-OCH$_3$	4'-NO$_2$	11 (A)	**120**	5- CH$_3$	2'-NO$_2$	1 (*cis* and *trans*, A)
28	5-OCH$_3$	-	10 (A)	**121**	5- CH$_3$	3'-NO$_2$	6 (A)
29	5-OCH$_3$	4'-NO$_2$	10 (A)	**122**	5- CH$_3$	4'-NO$_2$	6 (A), 25 (P)
30	5-OCH$_3$	4'-N(CH$_3$)$_2$	12 (P)	**123**	5- CH$_3$; 7-NO$_2$	-	44 (*trans*, F)
31	5-OCH$_3$	4'-CH$_2$CH(NHBoc)COOCH$_3$	33 (*trans*, A)	**124**	6- CH$_3$	-	2 (A), 6 (A), 26
32	5-OCH$_3$	4'-CH$_2$CH(NHCHO)COOCH$_3$	33 (*cis* and *trans*, F)	**125**	6- CH$_3$	4'-N(CH$_3$)$_2$	22 (P)
33	5-OCH$_3$	4'-CH$_2$CH(NHCHO)COOH	33 (*trans*, F)	**126**	7- CH$_3$	-	7 (A), 8 (A)
34	5-OCH$_3$	4'-CH$_2$CH(NHCHO)CO-gramicidin	33 (*cis* and *trans*, F)	**127**	7- CH$_3$	4'-NO$_2$	7 (A)
35	6-OCH$_3$	-	11 (A)	**128**	7- CH$_3$	4'-N(CH$_3$)$_2$	7 (A); 12 (P)
36	6-OCH$_3$	4'-N(CH$_3$)$_2$	11 (A); 12 (P)	**129**	5-CHCHCOOCH$_3$	4'-OC$_6$H$_13$	31 (*trans*, A)
37	6-OCH$_3$	4'-NO$_2$	11 (A)	**130**	5-CH$_2$CH$_2$COOCH$_3$	4'-OC$_6$H$_13$	31 (*trans*, A)
38	7-OCH$_3$	-	11 (A)	**131**	5-CH$_2$CH$_2$CN	4'-OC$_6$H$_13$	31 (*trans*, A)
39	7-OCH$_3$	4'-N(CH$_3$)$_2$	11 (A); 12 (P)	**132**	5-CH$_2$CH$_2$CN	4'-OC$_4$H$_9$	31 (*trans*, A)
40	7-OCH$_3$	4'-NO$_2$	11 (A)	**133**	5-CH$_2$CH$_2$CN	4'-OC$_8$H$_17$	31 (*trans*, A)
41	6-OCH$_2$CH$_3$	-	20 (*trans*, A)	**134**	5-CH$_2$CH$_2$CN	3'-OC$_6$H$_13$	31 (*trans*, A)
42	6-OCH$_2$CH$_3$	4'-NO$_2$	20 (*trans*, A)	**135**	6-CH$_2$CH$_2$CN	4'-OC$_6$H$_13$	31 (*trans*, A)
43	6-OCH$_2$CH$_3$	4'-OCH$_3$	20 (*trans*, A)	**136**	4-CH$_2$CH$_2$CN	4'-OC$_6$H$_13$	31 (*trans*, A)
44	6-OCH$_2$CH$_3$	4'- N(CH$_3$)$_2$	20 (*trans*, A)	**137**	5-CH$_2$CH$_2$COOH	4'-OC$_6$H$_13$	31 (*trans*, F)

#				#			
45	6-OCH$_2$CH$_3$	furyl-2	20 (*trans*, A)	138	5-CH$_2$CH$_2$COOH	4'-OC$_8$H$_{17}$	31 (*trans*, F)
46	6-Cl	-	20 (*trans*, A)	139	5-CH$_2$CH$_2$COOH	3'-OC$_6$H$_{13}$	31 (*trans*, F)
47	6-Cl	4'-NO$_2$	20 (*trans*, A)	140	6-CH$_2$CH$_2$COOH	4'-OC$_6$H$_{13}$	31 (*trans*, F)
48	6-Cl	4'-OCH$_3$	20 (*trans*, A)	141	4-CH$_2$CH$_2$COOH	4'-OC$_6$H$_{13}$	31 (*trans*, F)
49	6-Cl	4'- N(CH$_3$)$_2$	20 (*trans*, A)	142	5-(CH$_2$)$_5$CH$_3$	4'-OH	29 (*trans*, A)
50	6-Cl	furyl-2	20 (*trans*, A)	143	5-(CH$_2$)$_5$CH$_3$	4'-OCH$_2$COOC$_2$H$_5$	29 (*trans*, F)
51	7-Cl	-	8 (A)	144	5-(CH$_2$)$_5$CH$_3$	4'-OCH$_2$COOH	29 (*trans*, F)
52	7-Cl	4'- NO$_2$	8 (A)	145	5-(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_5$CH$_3$	29 (*trans*, F)
53	7-Cl	4'- N(CH$_3$)$_2$	8 (A); 12 (P)	146	5-(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_4$Br	29 (*trans*, F)
54	4-Br	-	16 (A)	147	5-(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_4$N$^+$(CH$_3$)$_3$ Br$^-$	29 (*trans*, F)
55	4-Br	4'- N(CH$_3$)$_2$	16 (A)	148	5-(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_{10}$Br	29 (*trans*, F)
56	4-Br	4'- NO$_2$	16 (A)	149	5-(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_{10}$N$^+$(CH$_3$)$_3$ Br$^-$	29 (*trans*, F)
57	5-Br	-	9 (A, R)	150	5-(CH$_2$)$_5$CH$_3$	4'-N(CH$_3$)$_2$	29 (*trans*, F)
58	5-Br	4'- NO$_2$	9 (A, R)	151	7-COOH	4'-CH$_2$NHCOOC(CH$_3$)$_3$	32 (A)
59	5-Br	4'- N(CH$_3$)$_2$	9 (A, R); 17 (P)	152	7-COOH	4'-OCH$_2$COOH	32 (*cis and trans*, F)
60	5-Br	4'-OH	31 (*trans*, A)	153	7-COOCH$_3$	4'-OCH$_2$COOH	32 (*cis and trans*, A)
61	5-Br	4'-OC$_6$H$_{13}$	31 (*trans*, F)	154	7-COOCH$_3$	4'-COOCH$_3$	32 (*cis and trans*, A)
62	6-Br	-	15 (A)	155	7-COOCH$_3$	4'-OCH$_2$COOC(CH$_3$)$_3$	32 (A)
63	6-Br	4'- N(CH$_3$)$_2$	15 (A)	156	7-COOCH$_3$	4'-CH$_2$NHCOOC(CH$_3$)$_3$	32 (A)
64	6-Br	4'- NO$_2$	15 (A)	157	7-COOCH$_3$	4'-CH$_2$NH$_2$ x HCl	32 (*cis and trans*, F)
65	7-Br	-	14 (A)	158	7-COpiperidine	4'-OCH$_2$COOC(CH$_3$)$_3$	32 (A)
66	7-Br	4'- N(CH$_3$)$_2$	14 (A)	159	7-COpiperidine	4'-OCH$_2$COOH	32 (F)
67	7-Br	4'- NO$_2$	14 (A)	160	7-CO (*S*) Lys (Cbz) OCH$_3$	4'-CH$_2$NHCOOC(CH$_3$)$_3$	32 (F)
68	4-I	-	19 (A)	161	7-COO(CH$_2$)$_5$CH$_3$	4'-OCH$_3$	29 (*trans*, F)
69	4-I	2'-OH	19 (A)	162	7-COO(CH$_2$)$_5$CH$_3$	4'-OC$_2$H$_5$	29 (*trans*, F)
70	4-I	4'- OCH$_3$	19 (A)	163	7-COO(CH$_2$)$_5$CH$_3$	4'-O(CH$_2$)$_5$CH$_3$	29 (*trans*, F)
71	4-I	3'- OCH$_3$; 4-OH	19 (A)	164	7-COOC$_2$H$_5$	4'-O(CH$_2$)$_5$CH$_3$	29 (*trans*, F)
72	4-I	4'- N(CH$_3$)$_2$	19 (A)	165	5-NO$_2$	-	24 (*trans*, A)
73	4-I	4'- N(C$_2$H$_5$)$_2$	19 (A)	166	5-NO$_2$	4'-OH	27 (*trans*, A)
74	4-I	2'- NO$_2$	19 (A)	167	5-NO$_2$	2'-OCH$_3$	24 (*trans*, A)
75	4-I	3'- NO$_2$	19 (A)	168	5-NO$_2$	4'-OCH$_3$	24 (*trans*, A)
76	4-I	4'- NO$_2$	19 (A)	169	5-NO$_2$	2'-Cl	24 (*trans*, A)
77	5-I	2'-OH	13 (A); 19 (A)	170	5-NO$_2$	4'-Cl	24 (*trans*, A)
78	5-I	3'-OH	22 (*trans*, P)	171	5-NO$_2$	4'-N(CH$_3$)$_2$	24 (*trans*, A)
79	5-I	4'-OH	13 (A)	172	5-NO$_2$	2'-NO$_2$	24 (*trans*, A)
80	5-I	3'- OCH$_3$	13 (A)	173	5-NO$_2$	4'-NO$_2$	24 (*trans*, A)
81	5-I	4'- OCH$_3$	13 (A)	174	5-NO$_2$	4'-F	27 (*trans*, A)
82	5-I	2'- NO$_2$	18 (A)	175	5-NO$_2$	4'-CH$_3$	27 (*trans*, A)
83	5-I	3'- NO$_2$	18 (A)	176	5-NO$_2$	4'-NH$_2$	27 (*trans*, A)
84	6-I	-	18 (A)	177	5-NO$_2$	4'-NO$_2$	27 (*trans*, A)
85	6-I	2'-OH	19 (A)	178	5-NH$_2$	-	27 (*trans*, A)
86	6-I	4'-OCH$_3$	19 (A)	179	5-NH$_2$	4'-OH	27 (*trans*, A)
87	6-I	3'- OCH$_3$; 4-OH	19 (A)	180	5-NH$_2$	4'-F	27 (*trans*, A)
88	6-I	4'- N(CH$_3$)$_2$	18 (A)	181	5-NH$_2$	4'-CH$_3$	27 (*trans*, A)
89	6-I	4'- N(C$_2$H$_5$)$_2$	18 (A)	182	5-NH$_2$	4'-NH$_2$	27 (*trans*, A)
90	6-I	2'- NO$_2$	18 (A)	183	5-NH$_2$	4'-NO$_2$	27 (*trans*, A)
91	6-I	3'- NO$_2$	18 (A)	184	benzo[*e*]	-	20 (*trans*, A)
92	6-I	4'- NO$_2$	18 (A)	185	benzo[e]	4'-OCH$_3$	20 (trans, A)
93	7-I	-	17 (A); 18 (A)	186	benzo[e]	4'-NO$_2$	20 (trans, A)
94	7-I	2'-OH	19 (A)	187	benzo[*e*]	4'-N(CH$_3$)$_2$	20 (*trans*, A)
95	7-I	3'-OH	17 (A)	188	benzo[*e*]	furyl-2	20 (*trans*, A)
96	7-I	4'-OCH$_3$	17 (A); 19 (A)	189	benzo[*f*]	4'-N(CH$_3$)$_2$	12 (A)

* Explanation of the symbols in the parentheses:

A. Prepared by condensation of benzaldehyde with benzo[*b*]thiophen-3(2*H*)-one (**2**) (Scheme 1) or with 3-acetoxybenzo[*b*]thiophene (Scheme 2)

B. Prepared by rearrangement of thioflavanone-1-oxide (Schemes 5 and 6)

C. Prepared by cyclization of lithium derivatives of thiosalicylic acid S-methyl ethers (Scheme 3)

D. Prepared by cyclization of α-phenylthiocinnamates (Scheme 4)

E. Prepared by cyclization of chalcones (Scheme 10)

F. Synthetic method other than above (Schemes 11 and 12)

P. Description of properties, without synthesis

R. Description of reactivity

Stereochemistry of the double bond is given only if described in the original paper. For the *E* izomer denotation *cis*, and for the *Z* izomer denotation *trans* are used, to avoid confusion with the letters used above.

Scheme 1
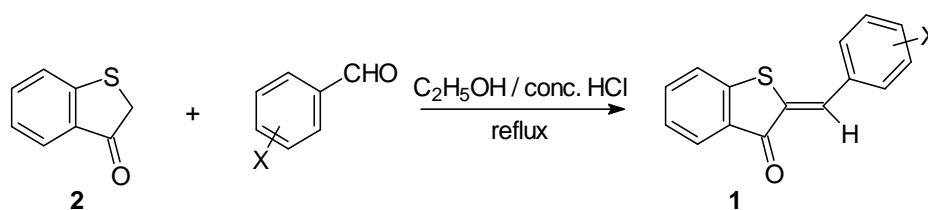
Usually, the reaction is performed in alcohols in the presence of concentrated hydrochloric acid, however the Knoevenagel reaction conditions (benzene, catalytic amount of piperidine) were also used.[29,31,32] In case of certain (eg. COOCH$_3$) substituents the reaction was very capricious, and careful adjustment of the condensation conditions was needed.[32] Mostoslawskii has modified the method and as the starting material introduced the acyl derivative of the enol form of **2** (Scheme 2).[20,24,27]
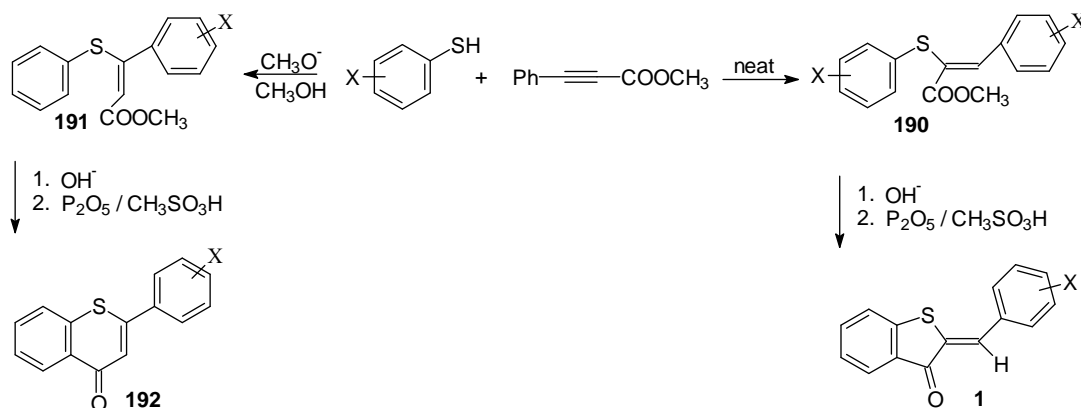
Scheme 2
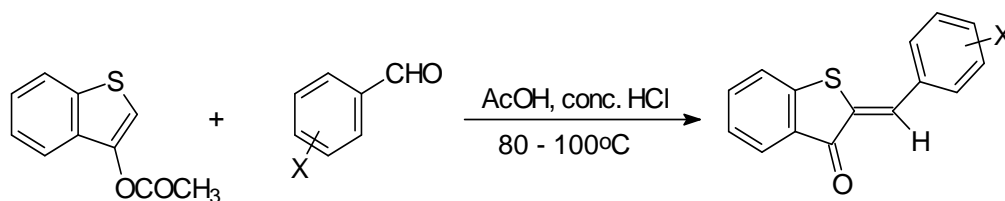
Cabiddu *et al*. described an elegant method in which thioaurones are formed from **2** generated *in situ* by lithiation of S-methyl ethers of thiosalicylate in the presence of benzaldehydes (Scheme 3).[47]

Scheme 3
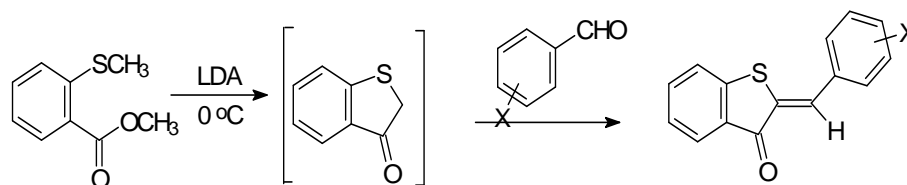
Another interesting, and seemingly universal synthesis of thioaurones was published by Wadsworth and Detty.[45] The key step of the method depends on radical, stereoselective addition of arylthiols to phenylpropiolates leading to α-phenylthiocinnamates (**190**), and those, after hydrolysis, were cyclized to **1**. Interestingly, related ionic addition results in β adducts (**191**), which can be cyclized to thioflavones (**192**) (Scheme 4).
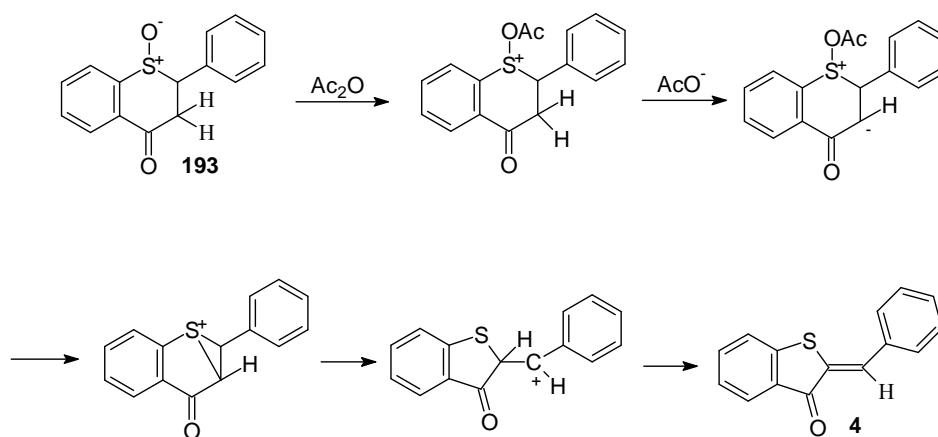
Scheme 4

The first transformation of thioflavanones oxide into thioaurone was reported by Still, who found that irradiation of 6-methylthioflavanone-1-oxide gave thioaurone (**107**) (Scheme 5).[43]
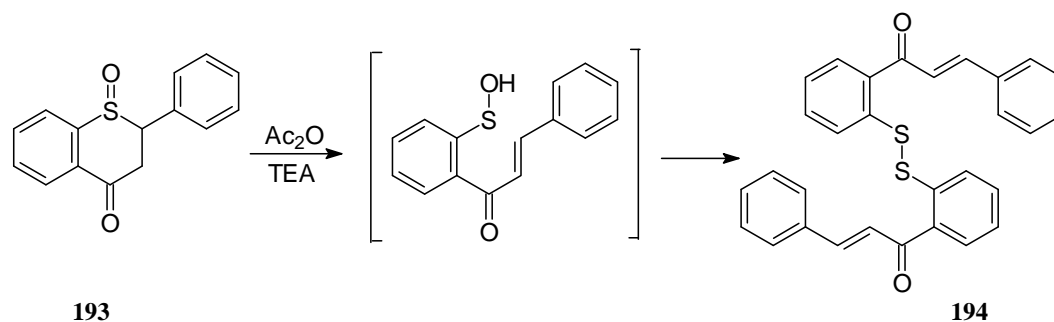
Scheme 5

107 (14 %)
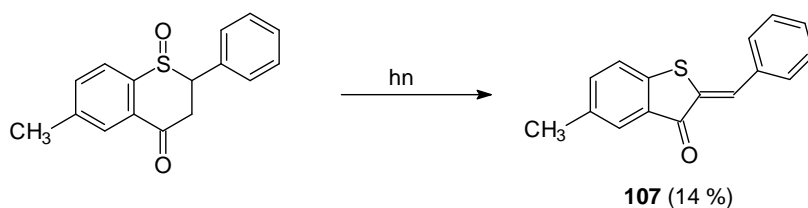
Similar transformation was described by Samogyi, who found that thioflavanone-1-oxide (**193**) and its derivatives are transformed in reaction with acetyl anhydride - sodium acetate, with good yields, into related thioaurones, a mechanism of the reaction was proposed (Scheme 6).[39]
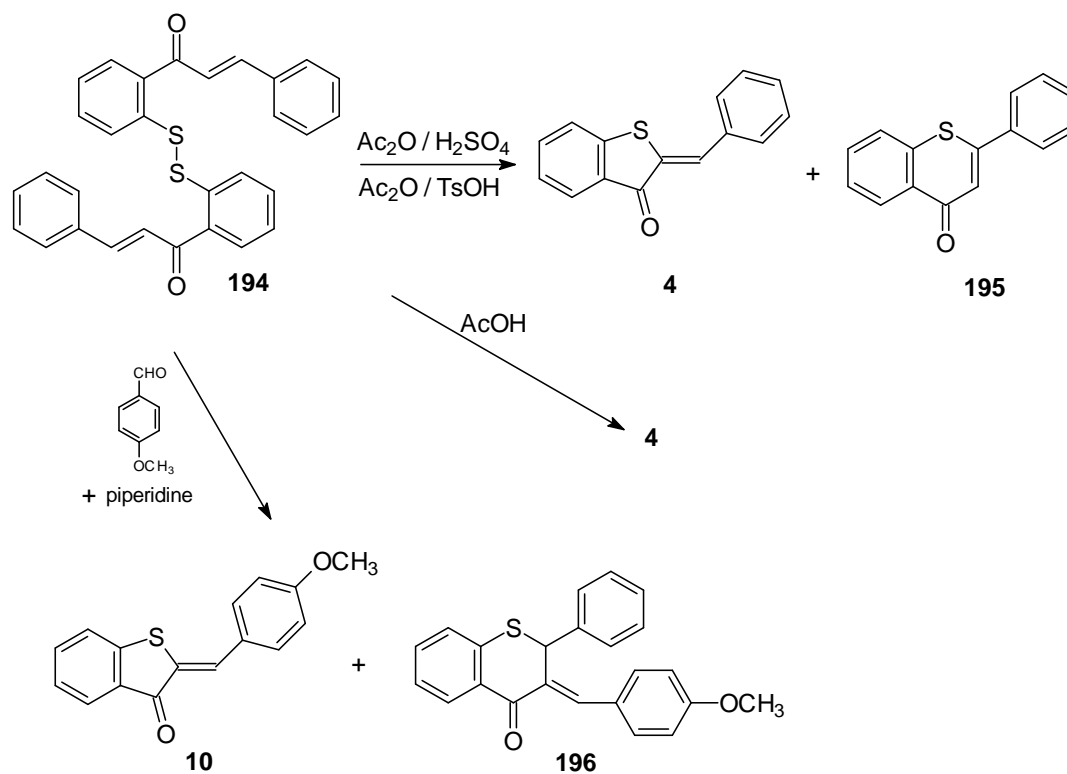
Scheme 6

When the oxide (**193**) was treated with acetic anhydride in the presence of triethylamine, or with diisopropylcarbodiimide the reaction lead to disulfide (**194**) (Scheme 7).[39]

Scheme 7

**193**   **194**

The disulfide (**194**) in turn, was transformed into various product - including thioaurones, depending on the reaction condition (Scheme 8).[39]

Scheme 8

194   **4**   **195**

10   **196**

It was suggested that the 4'-methoxythioaurone (**10**) was, most probably, produced from initially formed thioaurone (**4**) as heating of the former with *p*-anisaldehyde in piperidine resulted in "transaldehydation" to **10** (Scheme 9).[39]

Scheme 9
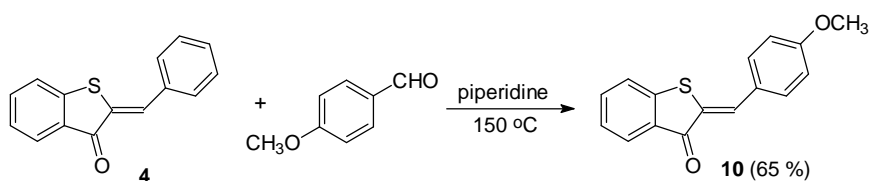

A specific method of synthesis of tioaurones was discovered by Taylor and Dean, who designed a new synthesis of thioflavones, and found that surprisingly, the result of final cyclization of chalcone (**197**) depends on the acid used (Scheme 10).[46]

Scheme 10
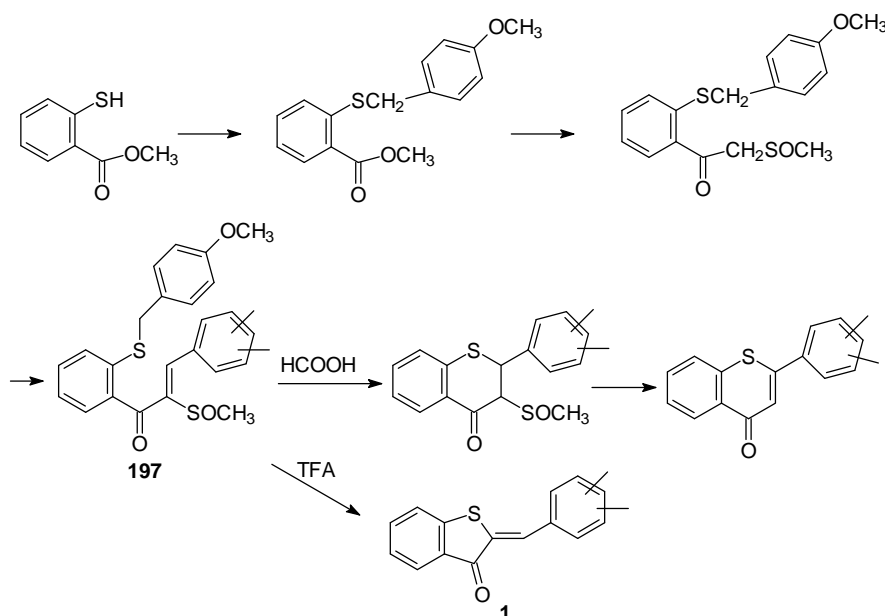
Another synthesis of thioaurones starting with thiosalicylic acid was described by Awad and Abdul-Malik (Scheme 11).[42]
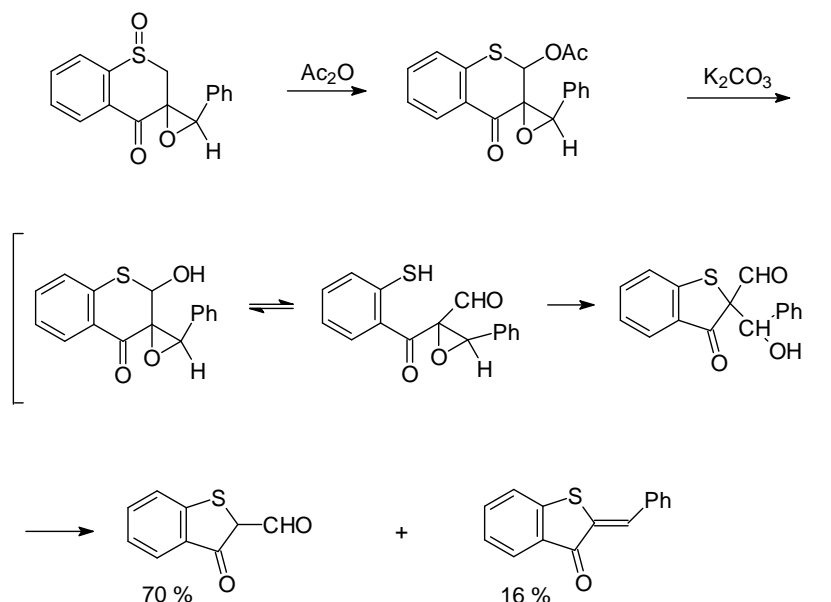
Scheme 11
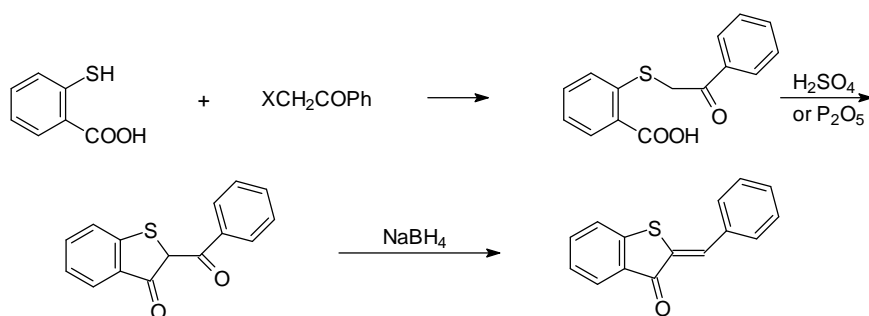
Finally, formation of thioaurone was described by Hofmann *et al.*, but the reaction does not seem to have a preparative value (Scheme 12).[41]

Scheme 12

REACTIVITY OF THIOAURONES

Relatively little is known about reactivity of thioaurones. The only exception are the oxidation reactions, which were studied in details by O'Sullivan and coworkers. They succeeded in selective, preparatively useful synthesis of several products of oxidation of thioaurone, the results are presented in Figure 3 and Table 2.[44]

Table 2

Products of oxidation of thioaurone (**107**) [ref. 44]

Entry	Substrate	Reaction condition*	Product (yield)
1	**107Z**	H_2O_2 / AcOH; 17 h	**198** (84 %)
2	**107Z**	H_2O_2 / AcOH; 110 h	**198** (8 %) + **199** (60 %)
3	**107Z**	*m*CPBA, dioxane; 15 s	**198** (37 %) + **199** (35 %)
4	**107Z**	*m*CPBA, AcOEt; reflux; 15 min	**199** (86 %)
5	**107Z**	$Ba(ClO_3)_2$ / HCl; 5 min	**198** (54 %)
6	**107Z**	HNO_3; 10 min	**107Z** (22 %) + **198** (37 %) + **123** (10 %)
7	**107Z**	H_2O_2 / Triton B; 45 s	**200** (89 %)
8	**107E**	H_2O_2 / Triton B; 45 s	**200** (48 %) + **201** (44 %)
9	**107Z**	*t*BuOOH / Triton B; 20 s	**200** (85 %)
10	**107Z**	NaOCl, pH 13; 5 min	**200** (88 %)
11	**107Z**	NaOCl / AcOH, pH 4; 10 s	**198** (81 %)
12	**107Z**	NaOCl / AcOH, pH 6; 5 s	**202** (42 %) + **203** (0.4 %)
13	**107Z**	NaOCl, pH 8; 3 min	**202** (14 %) + **203** (25 %)
14	**199**	H_2O_2 / Triton B; 3 min	**204** (83 %)

* All reactions were done at room temperature, except when specified otherwise.

Figure 3

107 Z   **107 E**   **198**

199   **200**   **201**

**202**   **203**   **204**

123
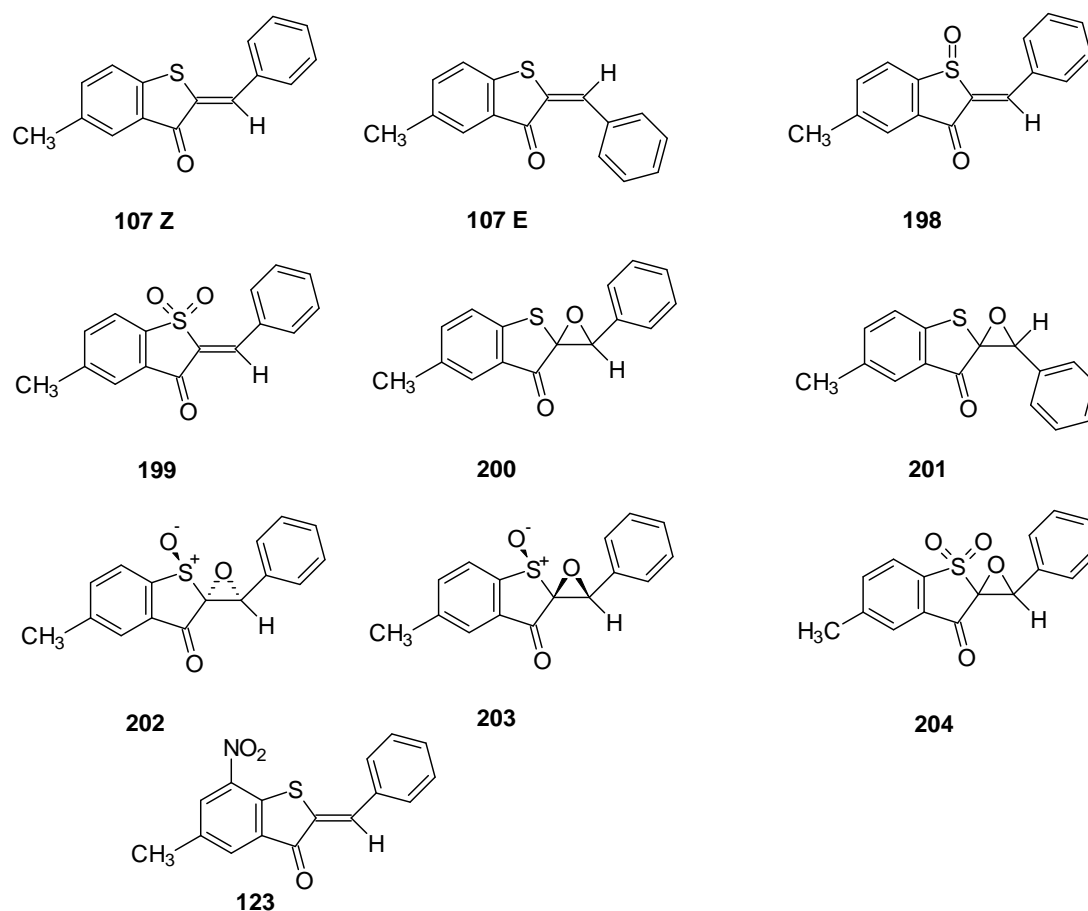
Similar results were obtained for 4'-chloro-5-methylthioaurone (**115**), however attempted epoxidation of 4'-dimethylamino derivative (**119**) failed, due, probably, to disadvantageous polarization of the molecule (Figure 4).[44]

Figure 4

119
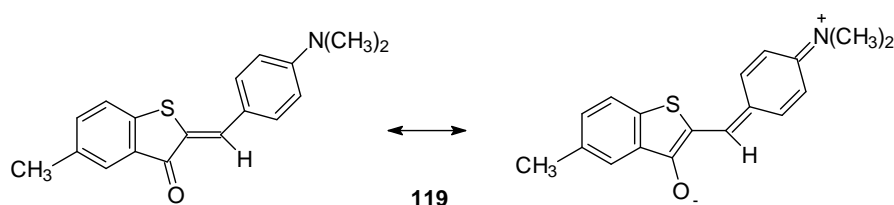
Adam *et al*. studied oxidation of thioaurones (**4**, **14** and **18**) with dimethyloxirane, and found that small excess of the reagent results in mixture of sulfoxide (**205**) and sulfone (**206**), while a large excess lead to formation of sulfone (**206**) alone (Scheme 13).[35] In this case, spiroepoxides were not formed, even with methyl(trifluoromethyl)oxirane as the oxidant.[35]

Scheme 13

4 (X=H); 14 (X =Cl);   205   206
18 (X=CH$_3$)
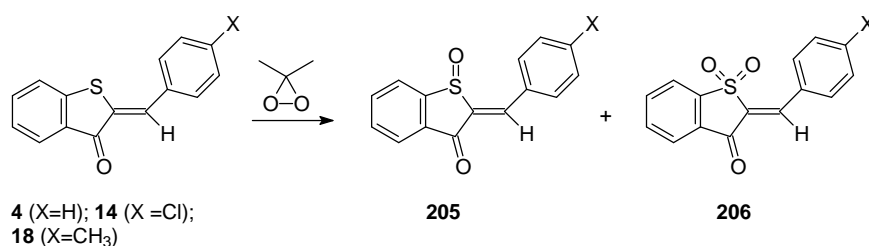
The reaction was shortly discussed by Lévai in a review on dioxirane oxidation of sulfur-containing organic compounds.[36]

Kucharczyk and Horak studied reduction of thioaurones with sodium borohydride and found that depending on the substituents, the reaction lead to reduction of the carbonyl group, or both the carbonyl and the double bond (Scheme 14).[40]

Scheme 14

for X = H; N(CH$_3$)$_2$; OCH$_3$, OH

for X = Cl; 3',4'-diCl
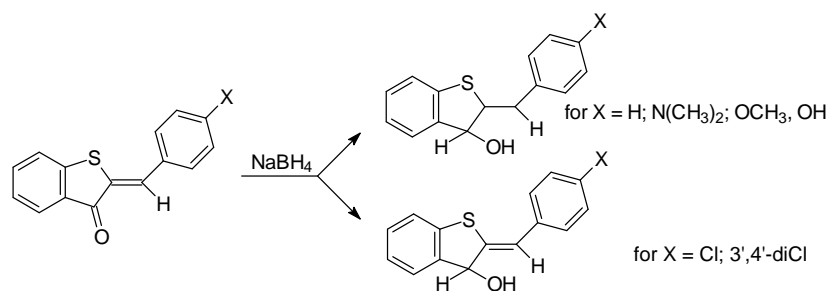
Lévai and Patonay described comparative studies on reactions of aurones and thioaurones with diazomethane. For thioaurones the reaction lead to α-methyl (208) and spirocyclopropane (209) derivatives. The result was different than for related aurones, which gave spiropyrazolines (analogs of 207) (Scheme 15).[37]

Scheme 15

X = H; OCH$_3$; F; Cl; Br; 3',4'-diCl

207

208   +   209
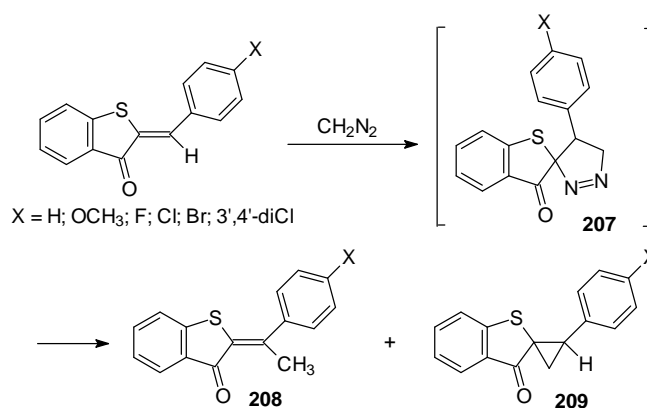
Many thioaurones bear halogen substituents in the aromatic rings (Table 1), and their substitution offer an attractive way to prepare new derivatives. The approach was utilized by Eggers *et al*. to prepare compound (**129**) *via* the Heck reaction, even the yield was relatively low (27 %) (Scheme 16).[31]

Scheme 16
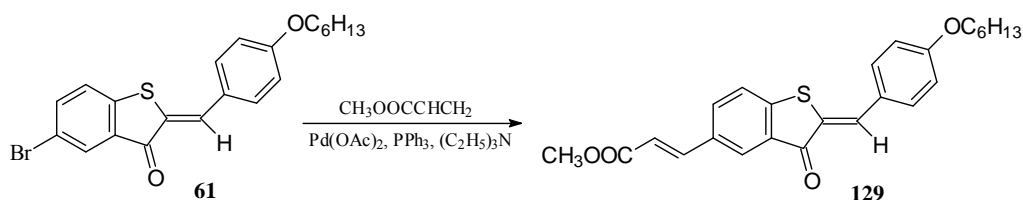
Recently, thioaurones were used as starting material for synthesis of benzothiazepines (**210**) (Scheme 17).[48]

Scheme 17
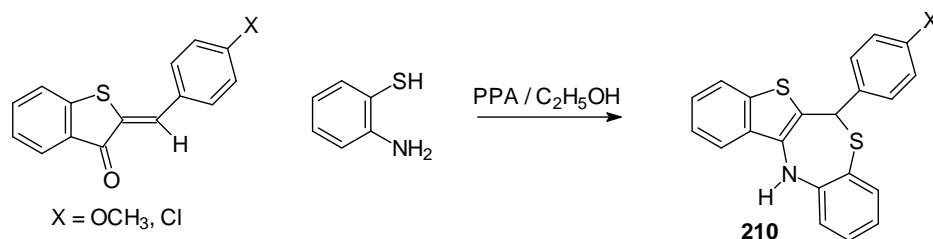
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