Tetrahedron Vol. 43, No. 8, pp. 1827 to 1834, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00

FLAVONOIDS, 40.[+] SYNTHESIS OF 3-ALKYL- AND -ARYLTHIOFLAVANONES AND THEIR TRANSFORMATIONS INTO SULFUR-CONTAINING FLAVONOIDS[≠]

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(*Received in UK* 16 *February* 1987)

Abstract - trans-3-Mesyloxyflavanones 1 were converted into cis- and trans--3-(alkylthio)- and -(phenylthio)flavanones 2-4 by nucleophilic substitution reaction with thiols or thiolates. Flavanones 2-4 were useful intermediates in the synthesis of various sulfur-containing derivatives; flavanones, flavones and dihydrochalcones possessing alkyl- or arylthio, -sulfinyl and -sulfonyl group. Oxidation of cis- and trans- isomers of 4 led to completely different products.

In preceding parts of this series we have reported on reactions of 3 -alkyl- and -arylsulfonyloxyflavanones with various nucleophiles demonstrating their usefulness in the synthesis of 3-substituted-flavonoids[1-3]. As a continuation of this work we now present our results on the reaction of 3-mesyloxyflavanones with thiols.

The reaction of trans-3-mesyloxyflavanone (1a) with aliphatic thiols (ethanethiol, propanethiol) in the presence of either phase-transfer catalyst (K_2CO_3/Adogen-464/PhH; a modified Lissel procedure[4]) or excess of triethylamine (Simons method[5]) afforded the mixture of the corresponding cis- and trans-3--(alkylthio)flavanones (2a, 3a)[6], and the minor product flavone (5a) formed in a concurrent elimination reaction[1-3]. The former system provided better yield but it was found to be responsive to the reaction time. After the disappearence of 1a a secondary transformation of 2a, 3a into 1-(2-hydroxyphenyl)-2-(alkylthio)-3-phenyl--1-propanones [2'-hydroxy-α-(alkylthio)dihydrochalcones] (6a, 7a) was observed. Dihydrochalcones 6a and 7a were prepared as sole products from 1a using longer reaction period and a large excess of thiol.

These products are presumed to form by a base-catalyzed ring-opening of 2a,3a into 2'-hydroxy-α-(alkylthio)chalcones (A) and the reduction of the intermediates A with the excess thiol. Similar secondary transformation has also been observed in the syntesis of 3-(acetylthio)flavanones[1].

Treatment of trans-3-mesyloxy-4'-R^1-flavanones (1a-e) with benzenethiol under phase-transfer conditions furnished the expected cis- and trans-3-(phenylthio)-4'--R^1-flavanones (4a-e) but better yield was achieved in benzene solution using thiolate anion as the nucleophile. Application of more polar solvent resulted in lower yield (Table 1).

[+]Part 39. see ref. 1.

[≠]A part of this work was presented at the International Bioflavonoid Symposium (VII. Hungarian Bioflavonoid Symposium), May 16-18, 1985, Szeged, Hungary

By-products were 4'-R^1-flavones (5a-e), 1-(2-hydroxyphenyl)-2-(phenylthio)-3-(4-R^1-phenyl)-1-propanones (8c-e), 2'-hydroxy-4-R^1-chalcones (9a-e), 3-hydroxy-4'-R^1-flavanones (10a-e) and diphenyl disulfide (11)(Table 1).

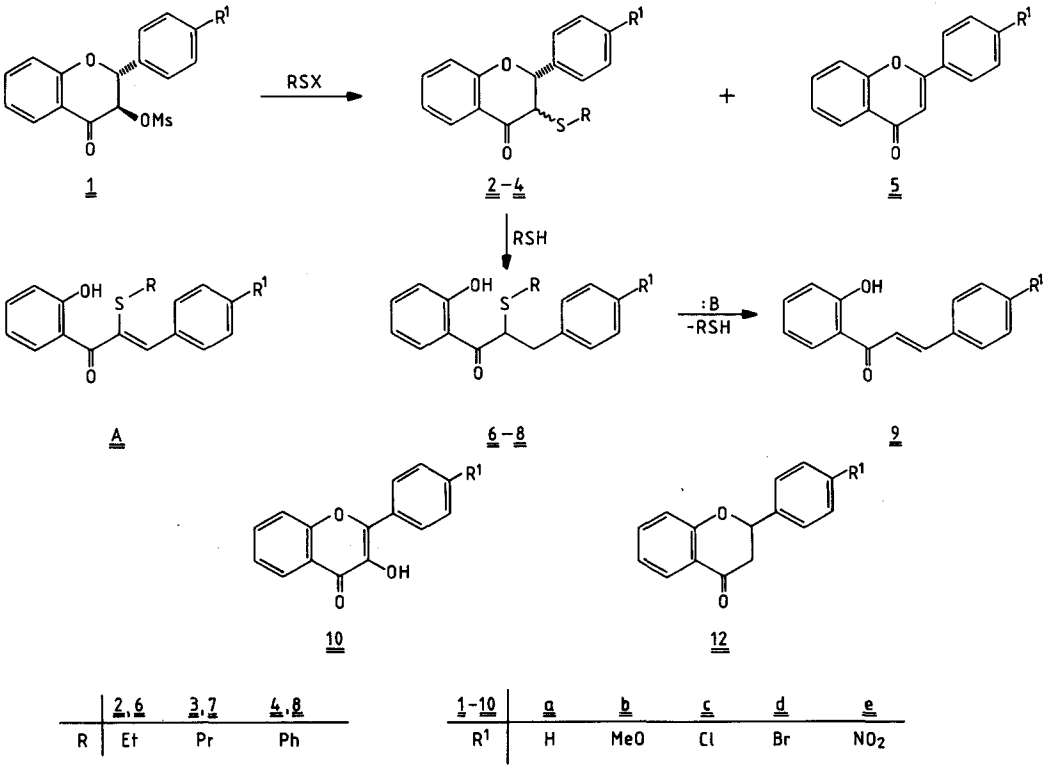


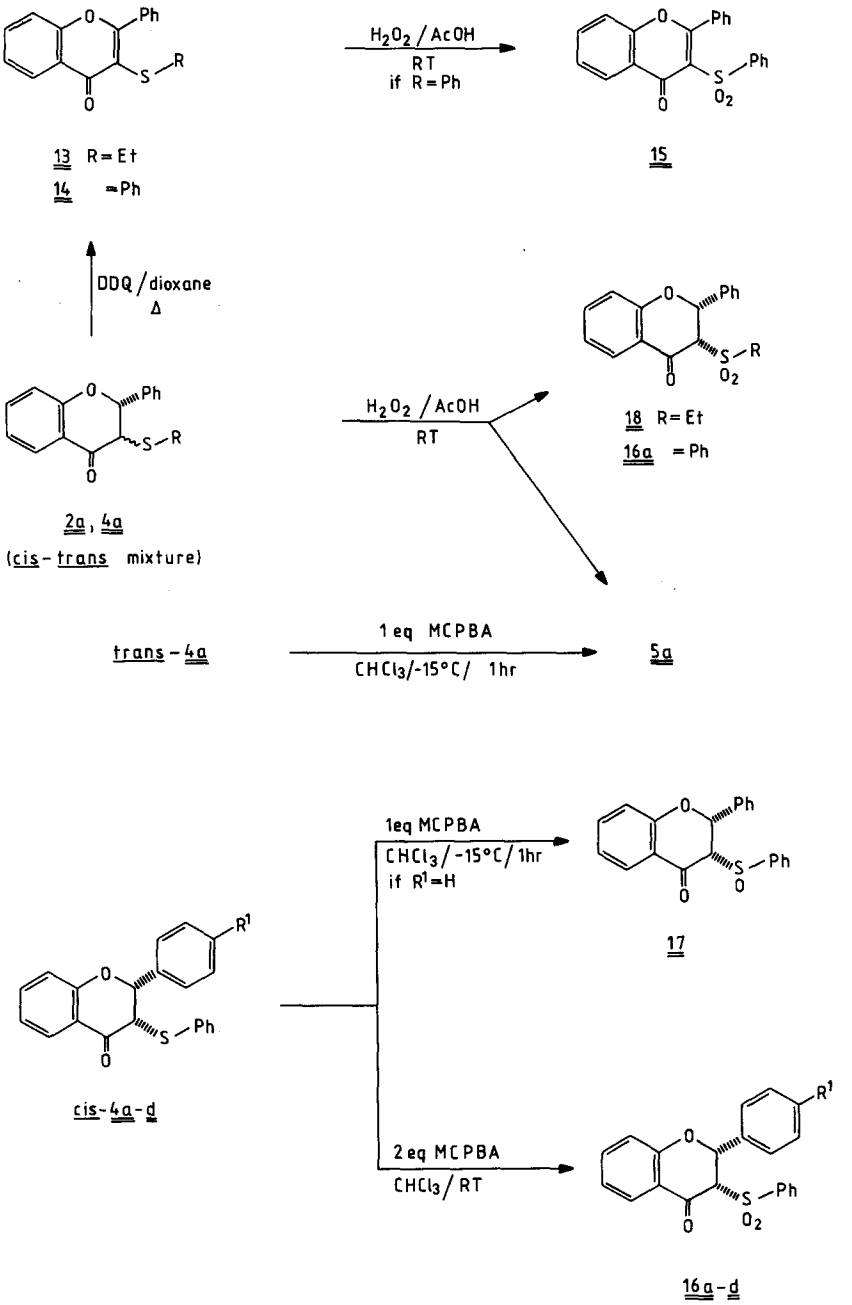
Table 1. Product-ratio data of the reaction of trans-3-mesyloxyflavanones with PhSX

Starting mat.	Method[a]	Reaction time	Yield (%)						
			1[b]	4	5	8	9	10	Ph_2S_2 (11)
1a	A	46 h	Ø	84.7	tr	Ø	6.8	tr	38.4
	C	26 h	Ø	90.6	tr	Ø	<1.0	Ø	2.9
	C_1	1 h	10.2	72.0	tr	Ø	4.3	5.0	8.9
	C_2	72 h	30.3	44.6	12.0	Ø	3.9	Ø	16.0
	C_3	35 min	1.0	77.5	4.3	Ø	17.5	Ø	11.8
	C_4	30 min	1.5	73.3	tr	Ø	17.6	Ø	17.7
	C_5	20 min	Ø	30.5	tr	Ø	46.9	Ø	64.2
1b	A	90 h	Ø	62.6	3.3	Ø	5.6	5.7	43.4
	C	30 h	5.0	77.1	2.1	Ø	ni	Ø	4.6
1c	A	90 h	Ø	53.5	Ø	ni	14.2	7.8	39.1
	C	7.5 h	6.9	84.1	3.2	Ø	2.2	2.1	5.7
1d	A	25.5 h	tr	73.6	Ø	8.1	6.5	ni	34.6
	C	2.5 h	6.1	85.4	2.0	Ø	1.9	1.3	6.9
1e	A	21.5 h	Ø	32.2	9.0	18.45	4.1	11.2	50.5
	C	36 h	11.7	65.4	4.5	Ø	2.85	Ø	5.5

[a]Details are given in Experimental Section
[b]Unreacted starting material
tr: traces
ni: not isolated product

Chalcones 9 are supposed to form from dihydrochalcones 8 in a reaction involving elimination of benzenethiol. This pathway is supported by the co-occurence of 8 and 9 when R^1 is an electron-attracting substituent (see Table 1) as well as by the fact that treatment of either 4a or 6 with bases gave 9a (or an equilibrium mixture of 9a and its cyclic isomer flavanone (12)).

3-(Ethylthio) flavone (13) and 3-(phenylthio)flavone (14) were prepared from 2a and 4a (cis-trans mixture), respectively, by means of a 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) dehydrogenation process[1,3,7]. Oxidation of 14 with hydrogen peroxide in acetic acid gave 3-(phenylsulfonyl)flavone (15). These transformations have practical importance providing new route to flavones claimed



to posses biological activity. Earlier 3-(methylthio)flavones have been reported as CNS-depressants[8,9] whereas for 6-methyl-3-(arylsulfonyl)-2-aryl- or -heteroarylchromones, synthesized from 2'-hydroxy-5'-methyl-2-(arylsulfonyl)acetophenones via α-(arylsulfonyl)chalcones, antiallergic effect[10] was described.

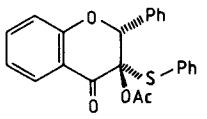
Oxidation of cis-4a-d with m-chloroperbenzoic acid (MCPBA) (2 eq) resulted in cis-3-(phenylsulfonyl)-4'-R[1]-flavanones (16a-d) with excellent yields. From cis-4a with MCPBA (1 eq) cis-3-(phenylsulfinyl)flavanone (17) was synthesized under controlled conditions[11]. At the same time, similar reaction of trans-4a led exclusively to 5a and no traces of any sulfine or sulfone could be detected in the mother liquor.

Treatment of a cis-trans mixture of 2a or 4a with hydrogen peroxide afforded only 18 and 16a, respectively, besides 5a. Spontaneous transformation of the primary product trans-3-(ethyl- or phenylsulfinyl)flavanone into 5a can be rationalized in terms of the cis-elimination of sulfenic acid being activated by the presence of the aryl group[12,13].

Umino et al.[14] patented the formation of a small amount of trans-3-(methylsulfinyl)flavanones besides the cis isomers by condensing 2'-hydroxy-2-(methylsulfinyl)acetophenone with araldehydes, whereas Strandtmann et al.[15] obtained only 5a in a similar reaction.

Thermolysis of 17 in refluxing benzene gave 5a, as the sole product, but in hot acetone both 5a and (presumably via a Pummerer-type reaction) 14 were formed. This reaction sequence was supported by the treatment of 17 with acetic anhydride. This reaction gave rise to the "regular"[12,16] Pummerer product 3-acetoxy-3-(phenylthio)flavanones (19,20), as minor components, as well as to 14 (formed directly from the α-thiocarbonium ion[12,16,17] 21) and 5a (direct elimination product); the 14:5a ratio being dependent on the presence or absence of acid catalyst. Similar acid-catalyzed Pummerer reaction have also been observed with 3-(methylsulfinyl)flavanones[9,18].

In sum, mesylates 1 were found to show high reactivity toward thiols and thiolates. This nucleophilic substitution reaction offers a convenient method for the synthesis of various 3-(alkylthio)- or -(arylthio)flavanones, precursors of other sulfur-containing flavonoids.



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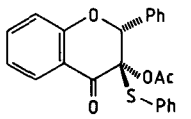

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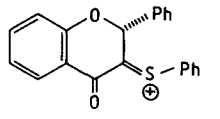

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EXPERIMENTAL SECTION

Mp's were determined with a Kofler apparatus and are uncorrected. IR spectra were record with a Perkin-Elmer 283 instrument in KBr discs unless otherwise stated. ^{1}H-NMR spectra were measured on a Bruker WP 200 SY (200 MHz) spectrometer in $CDCl_3$ solutions (internal standard TMS, δ = 0 ppm). Mass spectra were recorded with a VG-7035 GC-MS system (EI). Kieselgel 40 (Merck, 0.063-0.2 mm) was used for column chromatography, eluent was PhH unless otherwise specified. TLC was performed on Kieselgel 60 F_{254} using 4:1 PhMe-EtOAc or PhH as developing system.

All the isolated flavones (5a-e), 3-hydroxyflavones (10a-e), and 2'-hydroxychalcones (9a, c-e) were identified by means of mp, mixed mp, TLC comparison and/or IR spectra.

3-(Ethylthio)flavanone(2a). Method A. A mixture of 1a[2] (3.14 mmol), EtSH (16.3 mmol), anh. K_2CO_3 (4.34 mmol), Adogen-464 (0.1 mmol) and abs. PhH (16 ml) was stirred at room temp. When the reaction was complete (TLC monitoring) the insoluble material was filtered off, washed with PhH. The combined PhH fractions were washed with H_2O, dried ($MgSO_4$), the concentrated residue was fractionated by

column chromatography and 132 mg (14.7 %) of 6a, 622 mg (68.7 %) of 2a and 110 mg (15.8 %) of 5a was obtained. The eluted 2a was found to be a 3:1 mixture of cis and trans isomers by ^{1}H-NMR, attempts to separate the isomers remained unsuccesful. 2a, oil; IR (film) 2963 (CH_3), 2921 (CH_2), 2864 (CH_3 + CH_2S), 1680br (C=O), 1302, 1224, 972sh, 952 (flavanone skeleton) MS 284 (M^+, 13 %), 224 (89), 223 (59), 221 (9), 164 (100), 151 (29), 147 (34), 135 (76.5), 134 (30), 121 (63), 120 (32), 105 (20.5), 103 (25.5), 102 (20), 92 (46), 91 (76), 77 (64.5), cis-2a, ^{1}H-NMR 7.99 (dd, H-5), 5.70(d, H-2), 3.61 (d, H-3) (J_{23} = 2.1 Hz), 2.43 (q, CH_2), 1.08 (t, CH_3). trans-2a, H-NMR 7.84 (dd, H-5), 5.66 (d, H-2), 3.96 (d, H-3) (J_{23} = 4.5 Hz), 2.56 (q, CH_2), 1.25 (t, CH_3).

Method B. A soln of 1a (3.14 mmol), EtSH (32.6 mmol), Et_3N (32.5 mmol) in abs. Me_2CO (40 ml) was allowed to stand at room temp for 72 hrs, then poured into ice-cold diluted HCl and extracted with CH_2Cl_2. The dried and evaporated extract was fractionated by column chromatography (4:1 petroleum ether-EtOAc) to give 18 mg (2.0 %) of 6a, 511 mg (57.2 %) of 2a (cis/trans = 7:3; ^{1}H-NMR), 35 mg (3.5 %) of unreacted 1a and 130 mg (18.6 %) of 5a.

3-(Propylthio)flavanone (3a). According to Method A, using 6.6 mmol of PrSH. Column chromatographic separation afforded 827 mg (88.3 %) of 3a (cis/trans = 3:1), and 34 mg (4.9 %) of 5a. 3a oil; IR (film) 2956 (CH_3), 2923 (CH_2), 2865 (CH_3 + CH_2S), 1682 (C=O), 1320sh, 1300, 1224, 951 (flavanone skeleton). MS 298 (M^+, 9), 224 (100), 223 (66), 221 (8), 207 (7), 178 (56), 165 (22,), 147 (41), 135 (33), 121 (45), 120 (26), 104 (9.5), 103 (16), 102 (8), 93 (8), 92 (13), 91 (27.5), 77 (23.5). cis-3a, ^{1}H-NMR 8.03 (dd, H-5), 5.69 (d, H-2), 3.58 (d, H-3) (J_{23} = 2.2 Hz), ≈ 2.4 (m, SCH_2), 1.4 (m, CH_2CH_3), 0.79 (t, CH_3), trans-3a, ^{1}H-NMR 7.88 (dd, H-5), 5.66 (d, H-2), 3.93 (d, H-3) (J_{23} = 4.5 Hz), ≈ 2.45 (m, SCH_2), 1.6 (m, CH_2), 0.95 (t, CH_3).

3-(Phenylthio)-4'-R^1-flavanones (4a-e) and 1-(2-hydroxyphenyl)-2-(phenylthio)--3-(4-R^1-phenyl)-1-propanones (8d,e). 3 mmol of 1a-e^2 and 4.25 mmol of PhSH were reacted and worked up according to Method A. Results are given in the Table.

Method C. A mixture of 1a-e (3 mmol), PhSNa (3.1 mmol) and abs. PhH (20 ml) was stirred at room temp. When the reaction completed the insoluble salts were filtered off and washed with PhH. The combined PhH fractions were washed with H_2O, dried and concentrated, the oily residue was separated by column chromatography. The filter-cake was dissolved in H_2O, extracted with CH_2Cl_2, dried and evaporated to give pure 10.

Starting from 1a some modified experiments were performed as follows:
Method C_1: 25 mol % Adogen-464 was added as catalyst.
Method C_2: 25 mol % 18-Crown-6 was added as catalyst.
Method C_3: MeCN was used instead of PhH.
Method C_4: Me_2CO was used instead of PhH.
Method C_5: Me_2CO was used instead of PhH, quantity of PhSNa was 4.9 mmol.

Product-ratio data are summarized in the Table. Diphenyl disulfide (11) was identified on the basis of mp., IR spectra[19] and microanalysis. 4a-e were obtained as isomer mixture (cis/trans = 4:1 - 7:3; ^{1}H-NMR). This mixtures were subjected to fractional crystallization from 4:1 petroleum ether - EtOAc to give pure cis-4a-e and trans-4a, respectively. Attempts to isolate pure trans-4b-d failed and these derivatives were characterized by ^{1}H-NMR data.

Cis-4a, mp. 79-81.5 °C; IR 1681 (C=O), 1300, 1227, 952 (flavanone skeleton) ^{1}H-NMR 7.98 (dd, H-5), 5.75 (d, H-2), 3.97 (d, H-3) (J_{23} = 2.1 Hz). Found: C, 57.29; H, 4.98; S, 9.63. $C_{21}H_{16}O_2S$ requires: C, 75.88; H, 4.85; S, 9.65. trans-4a, mp. 95-98 °C; IR 1702 (C=O), 1293, 1226, 959 (flavanone skeleton). ^{1}H-NMR 7.88 (dd, H-5), 5.69 (d, H-2), 4.32 (d, H-3) (J_{23} = 5.9 Hz). Found: C, 76.26; H, 5.01; S, 9.38. $C_{21}H_{16}O_2S$ requires: C, 75.88, H, 4.85; S, 9.65.

Cis-4b , mp. 121-123 C; IR 2834 (MeO), 1692 (C=O), 1308sh, 1300, 1223, 959, 943 (flavanone skeleton), 1251, 1028 (Ar-O-Me). ^{1}H-NMR 7.95 (dd, H-5), 5.72 (d, H-2), 3.96 (d, H-3) (J_{23} = 2.1 Hz), 3.84 (s, MeO). Found: C,72.99; H, 5.28; S, 9.06. $C_{22}H_{18}O_3S$ requires: C, 72.91, H, 5.01; S, 8.85. trans-4b, H-NMR 7.91 (dd, H-5), 5.64 (d, H-2), 4.33 (d, H-3) (J_{23} = 6.3 Hz), 3.78 (s, MeO).

Cis-4c,mp. 116-118 °C; IR 1682 (C=O), 1305, 1221, 964, 958, 953 (flavanone skeleton), 1087 (Ar-Cl). ^{1}H-NMR 7.95 (dd, H-5), 5.73 (d, H-2), 3.93 (d, H-3) (J_{23}= = 2.3 Hz). Found: Cl, 9.63; S, 8.66. $C_{21}H_{15}ClO_2S$ requires: Cl, 9.66; S, 8.74. trans-4c, ^{1}H-NMR 7.88 (dd, H-5), 5.64 (d, H-2), 4.30 (d, H-3) (J_{23} = 6.8 Hz).

Cis-4d, mp. 136-138 °C; IR 1678 (C=O), 1304, 1221, 964, 950 (flavanone skeleton), 1063 (Ar-Br). ^{1}H-NMR 7.91 (dd, H-5), 5.69 (d, H-2), 3.92 (d, H-3) (J_{23}= 2.2 Hz). Found: Br, 19.40; S, 7.55. $C_{21}H_{15}BrO_2S$ requires: Br, 19.43; S, 7.79. trans-4d, ^{1}H-NMR 7.85 (dd, H-5), 5.59 (d, H-2), 4.28 (d, H-3) (J_{23} = 6.9 Hz).

Cis-4e, mp. 157-160 °C (PhH-EtOAc); IR 1689 (C=O), 1518, 1347, 861, 852 (NO_2), 1316, 1307, 1219, 953 (flavanone skeleton), 1114 (C-NO_2). ^{1}H-NMR 8.35 (dd, H-3',5'), 7.99 (dd, H-5), 5.85 (d, H-2), 3.97 (d, H-3) (J_{23} = 2.2 Hz). Found: N, 3.62; S, 8.66. $C_{21}H_{15}NO_4S$ requires: N, 3.71; S, 8.50. trans-4e, ^{1}H-NMR 8.15 (dd, H-3',5'), 7.91 (dd, H-5), 5.71 (d, H-2), 4.32 (d, H-3) (J_{23} = 7.3 Hz).

8d, mp. 89-91 °C (petroleum ether); IR 1637 (chelated C=O), 1279 (Ar-CO), 1212 (Ar-OH), 1067 (Ar-Br). MS 414 (M+2) + 412 (M^+, <1), 304 (34) + 302 (36), 303 (37) + 301 (31), 287 (6) + 285 (6), 223 (8), 211 (5) + 209 (5), 184 (14) +

† 182 (15), 147 (65), 121 (58), 120 (62), 110 (100), 109 (26), 102 (34), 93 (13). ^{1}H-NMR 11.9 (s, 2'-OH), 7.68 (dd, H-6'), 4.86 (ABX → "A_2X", H-2), 3.61 (ABX → "A_2X", H-3).

8e, mp. 94-95.5 °C (petroleum ether-EtOAc); IR 1642 (chelated C=O), 1518, 1349, 1106, 862, 854 (NO_2), 1290 (Ar-CO), 1203 (Ar-OH). MS 379 ($M^{+\cdot}$, 5), 269 (69), 268 (40), 252 (10), 222 (10.5), 176 (7), 165 (7), 147 (96), 130 (6.5) 121 (100), 120 (35), 110 (100), 109 (26) 102 (12.5), 93 (17), 92 (11). ^{1}H-NMR 11.9 (s, 2'-OH), 8.12 (dd, H-3",5"), 7.73 (dd, H-6'), 4.95 (ABX → "A_2X", H-2), 3.70 (ABX → "A_2X", H-3).

1-(2-Hydroxyphenyl)-2-(ethylthio)-3-phenyl-1-propanone (6a). A mixture of 1a (9.4 mmol), EtSH (40.8 mmol) anh. K_2CO_3 (13 mmol), Adogen-464 (0.3 mmol) and abs. PhH (45 ml) was kept at room temp for 15 days and then worked up according to Method A. The concentrated residue was crystallized from abs. EtOH-petroleum ether to yield 1.83 g (68.4 %) of 6a, mp. 76-78 °C. IR 2954 (CH_3), 2923 (CH_2), 2872 (CH_3 + CH_2S), 1641 (chelated C=O), 1306 (Ar-CO), 1210 (Ar-OH). MS 286 ($M^{+\cdot}$, 21), 268 (3), 226 (38), 224 (17), 223 (22), 207 (7), 151 (36), 147 (20.5), 121 (100), 120 (17), 104 (19), 93 (20), 91 (6), 77 (14), 65 (33.5). ^{1}H-NMR 12.1 (s, 2'-OH), 7.76 (dd, H-6'), 4.59 (ABX → "A_2X", H-2), 3.57 (ABX → "A_2X", H-3), 2.37 (dq, CH_2CH_3), 1.18 (t, CH_3). Found: C, 70.88; H, 6.04; S, 10.98. $C_{17}H_{18}O_2S$ requires: C, 71.30; H, 6.33; S, 11.20.

1-(2-Hydroxyphenyl)-2-(propylthio)-3-phenyl-1-propanone (7a). In a same manner as described for 6a, reaction time 117 hrs. Yield: 84.6 %, mp. 42.5-43.5 °C (EtOH). IR (CCl_4) 2958 (CH_3), 1641 (chelated C=O), 1308, 1286 (Ar-CO), 1204 (Ar-OH). ^{1}H-NMR 12.1 (s, 2'-OH), 7.77 (dd, H-6'), 4.53 (ABX → "A_2X", H-2), 3.56 (ABX → "A_2X", H-3), 2.33 (m, $CH_2CH_2CH_3$), 1.54 (m, $CH_2CH_2CH_3$), 0.91 (t, CH_3). Found: C, 71.55; H, 6.84; S, 10.93. $C_{18}H_{20}O_2S$ requires: C, 71.97; H, 6.71; S, 10.67.

2'-Hydroxychalcone (9a) from 4a. A soln of 4a (0.87 mmol); cis/trans = 7:3) and PhSNa (0.91 mmol) in abs. MeCN (10 ml) was stirred for 3 hrs at room temp, then poured into H_2O, extracted with CH_2CL_2. The dried extract was concentrated in vacuo and separated by column chromatography to afford 51 mg (26.1 %) of 9a besides 128 mg (44.1 %) of unreacted 4a, 121 mg (62.1 %) of 1a and 5 mg (2.6 %) of 5a.

From 6a. A mixture of 6a (0.7 mmol), anh. K_2CO_3 (1.45 mmol) and PhH (10 ml) was refluxed for 18 hrs, then worked up according to Method A. The residue was crystallized from petroleum ether to give 87 mg (55.6 %) of 9a. Presence of flavanone (12) was detected in the mother liquor by TLC.

When the reaction was repeated in the presence of Adogen-464 (0.2 mmol) (24 hrs, room temp), column chromatography afforded 57 mg (36.4 %) of 9a and 24 mg (15.3 %) of 12.

cis-3-(Ethylsulfonyl)flavanone (18). A soln of 2a (0.9 mmol; cis/trans = 7:3) and of 30 % aq H_2O_2 (0.5 ml) in AcOH (5 ml) was allowed to stand for 44 hrs at room temp, then poured into H_2O and extracted with Et_2O. The ethereal extract was washed with sat $NaHCO_3$ soln, dried and concentrated, the residue was crystallized from petroleum ether-EtOAc to give 174 mg (62.1 %) of 18, mp. 93-95 °C. IR 1667 (C=O), 1317, 1141 (SO_2) 1210, 946 (flavanone skeleton). ^{1}H-NMR 7.86 (dd, H-5), 6.53 (d, H-2), 4.30 (d, H-3) (J_{23} = 1.1 Hz), 3.29 (q, CH_2), 1.48 (t, CH_3). Found: C, 65.00; H, 4.89; S, 10.18. $C_{17}H_{16}O_4S$ requires: C, 64.54; H, 5.10; S, 10.13. Only 5a but no trans-isomer of 18 was detected in the mother liguor by TLC.

cis-3-(Phenylsulfonyl)-4'-R^1-flavanones (16a-d). MCPBA oxidation. To a stirred soln of cis-4a-d (0.45 mmol) in $CHCl_3$ (10 ml) was added dropwise a soln of MCPBA (1.16 mmol) in $CHCl_3$ (10 ml). After stirring for 18-21 hrs (TLC) the mixture was washed with sat $NaHCO_3$ soln, dried, the solvent was removed in vacuo and the residue was recrystallized.

16a, yield: 85.1 %, mp. 153-154 °C (petroleum ether-EtOH). IR 1678 (C=O), ≈1311, 1149, 1140 (SO_2), ≈1305, 1214, 935 (flavanone skeleton). ^{1}H-NMR 7.89 (dd, H-2",6"), 7.76 (dd, H-5), 6.49 (d, H-2), 5.34 (d, H-3) (J_{23} = 1.45 Hz). Found: C, 69.53; H, 4.53; S, 8.79. $C_{21}H_{16}O_4S$ requires: C, 69.21; H, 4.43; S, 8.80.

16b, yield: 78.9 %, mp. 121-123 °C (EtOH). IR 2830 (MeO), 1682 (C=O), 1307br (SO_2 + flavanone skeleton), 1249, 1035 (Ar-O-Me), 1205, 925 (flavanone skeleton). ^{1}H-NMR (DMSO) 7.87 (dd, H-2",6"), 7.74 (dd, H-5), 6.88 (d, H-3',5'), 6.41 (d, H-2), 5.30 (d, H-3) (J_{23} = 1.3 Hz), 3.69 (s, MeO). Found: C, 67.20; H, 4.60; S, 8.05 $C_{22}H_{18}O_5S$ requires: C, 66.99; H, 4.60; S, 8.13.

16c, yield: 86.9 %, mp. 170-172 °C (EtOH). IR 1683 (C=O), 1313, 1149 (SO_2), 1306, 1202, 930 (flavanone skeleton). ^{1}H-NMR 7.84 (dd, H-2",6"), 7.72 (dd, H-5), 6.55 (d, H-2), 4.37 (d, H-3) (J_{23} = 1.35 Hz). Found: Cl, 8.98; S, 7.80. $C_{21}H_{15}ClO_4S$ requires: Cl, 8.89; S, 8.04.

16d yield: 80.7 %, mp. 170-172 °C (EtOH). IR 1682 (C=O), 1314, 1149 (SO_2), 1306, 1201, 927 (flavanone skeleton). ^{1}H-NMR 7.83 (dd, H-2",6"), 7.72 (dd, H-5),

6.53 (d, H-2), 4.37 (d, H-3) (J_{23} = 1.5 Hz). Found: Br, 18.20; S, 7.20. $C_{21}H_{15}BrO_4S$ requires: Br, 18.02; S, 7.23.

H_2O_2 oxidation. 4a (1.32 mmol; cis/trans = 7:3) was treated with H_2O_2 as described for the prepn of 18 to afford 118 mg (24.7 %) of 16a. Presence of 5a and 10a was detected in the mother liquor by TLC.

cis-3-(Phenylsulfinyl)flavanone (17). A soln of MCPBA (0.94 mmol) in $CHCl_3$ (10 ml) was added dropwise to a stirred and cooled (-18 °C) soln of cis-4a (0.9 mmol) during a 20 min period. After 70 min the mixture was washed with sat $NaHCO_3$ soln (2x45 ml), dried and concentrated in vacuo. The sticky residue was kept in the refrigerator with a mixture of petroleum ether (8 ml) and CCl_4 (1 ml) to give 255 mg (81.1 %) of 17, mp. 100-105 °C (dec.). IR 1681 (C=O), 1304, 1223, 950 (flavanone skeleton), 1037 (SO). ^{1}H-NMR 8.26 (dd, H-5), 5.98 (d, H-2), 3.80 (d, H-3) (J_{23} = 2.65 Hz). Found: C, 72.27; H, 4.73; S, 9.03. $C_{21}H_{16}O_3S$ requires: C, 72.39; H, 4.63; S, 9.03.

Flavone (5a). Treatment of trans-4a (0.45 mmol) with MCPBA in a same manner as described for 17 afforded 71 mg (71.0 %) of 5a as the only product.

3-(Ethylthio)flavone (13). A soln of 2a (1.25 mmol; cis/trans = 7:3) and DDQ (3.08 mmol) in dioxane (12 ml) was refluxed for 15 hrs, concentrated in vacuo and the dark residue was purified by column chromatography (4:1 petroleum ether--EtOAc) to afford 185 mg (52.3 %) of 13, mp. 90-91 °C (petroleum ether). IR 2980 (CH_3), 2922 (CH_2), 1642 (C=O), 1353, 1227 (flavone skeleton). ^{1}H-NMR 8.28 (dd, H-5), 2.88 (q, CH_2), 1.12 (t, CH_3). Found: C, 72.90; H, 5.04; S, 11.06. $C_{17}H_{14}O_2S$ requires: C, 72.56; H, 5.00; S, 11.36.

3-(Phenylthio)flavone (14). In the same manner as described for the prepn of 13, 1.83 mmol of 4a (cis/trans = 7:3) gave 177 mg (29.2 %) of 14, mp. 131-133 °C (petroleum ether-EtOH). IR 1650 (C=O), 1355, 1210 (flavone skeleton), 1077 (S-Ph). Found: C, 77.05; H, 4.36; S, 9.78. $C_{21}H_{14}O_2S$ requires: C, 76.34; H, 4.27; S, 9.70.

3-(Phenylsulfonyl)flavone (15). A soln of 14 (0.26 mmol) and 30 % aq H_2O_2 (0.3 ml) in AcOH (3 ml) was allowed to react at room temp for 72 hrs and then poured into H_2O. The precipitate was filtered of to give 86 mg (90.1 %) of 15, mp. 224.5-227 °C (petroleum ether-EtOAc). IR 1656, 1651 (C=O), 1350, 1211 (flavanone skeleton), 1330, 1319, 1164, 1145 (SO_2). Found: C, 69.13; 3.98; S, 8.94. $C_{21}H_{14}O_4S$ requires: C, 69.60; H, 3.89; S, 8.85.

Thermolysis of 17 in PhH. A soln of 17 (0.40 mmol) in abs. PhH (15 ml) was refluxed for 16 hrs, concentrated in vacuo and the residue was crystallized from petroleum ether to yield 59 mg (66.1 %) of 5a as the sole product.

Thermolysis of 17 in Me_2CO. A soln of 17 (0.38 mmol) in abs. Me_2CO (10 ml) was refluxed for 64 hrs, the solvent was evaporated and the residue was fractionated by column chromatography to give 33 mg (26.4 %) of 14 and 44 mg (51.8 %) of 5a.

Pummerer reaction of 17 in the presence of acid. Five drops (cca 0.06 ml) cc. H_2SO_4 was added to a soln of 17 (1.28 mmol) in Ac_2O (18 ml) at room temp. After 24 hrs the mixture was poured into H_2O, extracted with CH_2Cl_2. The dried and concentrated extract was fractionated by column chromatography to afford 41 mg (8.2 %) of 19, mp. 180-181.5 (petroleum ether). IR 1756 (OAc), 1694 (C=O), 1293, 1226, 1023 (flavanone skeleton), 1206, 1041 (C-O-Ac). MS 390 (M^+, 4), 348 (12.5), 330 (5), 281 (19), 239 (100), 223 (7), 211 (74), 199 (28), 181 (20), 165 (11), 152 (13), 133 (43), 121 (31), 118 (16.5), 110 (37), 105 (60.5), 77 (23.5). ^{1}H-NMR 7.90 (dd, H-5), 6.50 (s, H-2), 2.12 (s, OAc); a NOE of + 41 % between the H-2 and OAc was registered irradiating δ = 6.50 ppm signal. Further elution yielded 260 mg (61.5 %) of 14, 8 mg (2.6 %) of 10a and 20 mg (7.0 %) of 5a.

Pummerer reaction of 17 without acid catalyst. A soln of 17 (0.29 mmol) in Ac_2O (5 ml) was allowed to stand at room temp for 95 hrs, the solvent was distilled off under reduced pressure. Column chromatography of the residue afforded 17 mg (54.3 %) of 11. Next fraction was a yellow oil (18 mg, 16.1 %) having IR and MS spectra identical with those of 19. ^{1}H-NMR indicated the presence of 19 as the majorcomponent, spectral data of the minor product 20 : 7.80 (dd, H-5), 6.53 (s, H-2), 1.92 (s, OAc); estimated 19/20 ratio = 2:1. Further elution using a PhH--EtOAc mixture with increasing amount of EtOAc yielded 10 mg (10.6 %) of 14 and 47 mg (73.7 %) of 5a.

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