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BORON TRIFLUORIDE IN THE SYNTHESIS OF PLANT PHENOLICS: SYNTHESIS OF PHENOLIC KETONES AND PHENYL STYRYL KETONES

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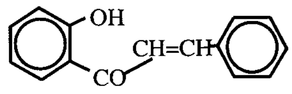
ABSTRACT

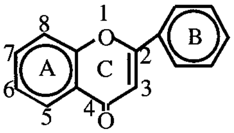
The use of acid-boron trifluoride complexes has been found to be a convenient general method for the preparation of phenolic ketones and phenyl styryl ketones. Resorcinol and pyrogallol react with boron trifluoride-acetic acid complex at room temperature, giving resacetophenone and gallacetophenone in 80-90 percent yield. 2,6-Dimethoxyhydroquinone and antiarol (3,4,5-trimethoxyphenol), when dissolved in boron trifluoride-acetic acid complex and poured into ice after leaving overnight at room temperature, give the corresponding acetophenones in 60-70 percent yield. With 2-napththol, a boron trifluoride complex of the ketone is first obtained and boiling with water for a few minutes gives 1-acetyl-2-naphthol in 93 percent yield. When cinnamic acid dissolved in chloroform is saturated with boron trifluoride, resorcinol added, and the solution left overnight at room temperature, 2,4-dihydroxyphenyl styryl ketone is obtained in 70 percent yield. Pyrogallol under similar conditions gives an 80 percent yield of the corresponding phenyl styryl ketone. Both 2,6-dimethoxyhydroquinone and antiarol condense readily with the boron trifluoride complex of cinnamic acid to give 2,5-dihydroxy-4,6-dimethoxyphenyl, and 2-hydroxy-4,5,6-trimethoxyphenyl styryl ketone respectively.

Boron trifluoride and its derivatives have been used as catalysts in condensations and rearrangements during the past century since the commercial production of boron trifluoride by the Harshaw Chemical Company in 1936 made it readily available. The use of boron trifluoride complexes for the synthesis of phenolic ketones, phenyl styryl ketones and other phenolics is of more recent date and has been the subject of extensive investigation in the present work.

Phenolic ketones and phenyl styryl ketones are necessary intermediates for the synthesis of flavonoid compounds, which are naturally occurring coloring matters found in plants. They belong to the large class of oxygen heterocyclics, the chromones.



2-Hydroxyphenyl styryl ketone



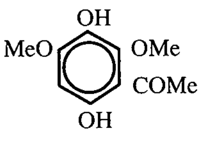
Flavone
(2-phenyl chromone)

The A ring of the vast majority of flavones are derived from phenolic compounds, such as resorcinol and phloroglucinol, from which the phenolic ketones and phenyl styryl ketones can be derived by condensation of the boron triflouride complexes of the appropriate acid.

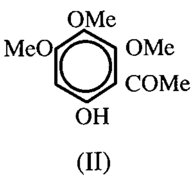
Although boron trifluoride is a milder catalyst than other acid catalysts, like the aluminum chloride used in the Friedel-Crafts reaction (Olah), it has certain advantages over other catalysts, as reactions often proceed more smoothly and cleaner products are obtained. However, this method is limited to reactive nuclei having one or more phenolic hydroxyl groups, or their methyl ethers.

Synthesis of Phenolic Ketones

Phenolic ketones have been prepared in the present work by condensation of boron trifluoride complexes of acids with mono-, di- and trihydroxy phenols and their derivatives and with naphthols. A simple and convenient method is described for the preparation of 2,5,-dihydroxy-4,6-dimethoxyacetophenone (I) and 2-hydroxy-4,5,6-trimethoxyacetophenone (II), which cannot be prepared by the Hoesch reaction. This is a variation of the Gattermann aldehyde synthesis in which hydrogen cyanide is replaced by acetonitrile and other nitriles.



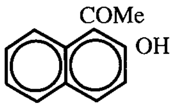
(I)



(II)

(II) is obtained in relatively low yield by the Friedel-Crafts reaction.

I-Acetyl-2-naphthol (III) is obtained in 95% yield by the boron tri-flouride-acid complex method. It cannot be prepared by the Nencki reaction using zinc chloride, and is obtained in poor yield by the Fries migration of 2-naphthyl acetate.



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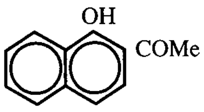

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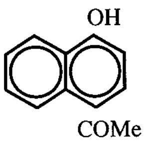


(V)

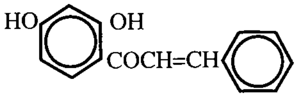
Reacting 1-naphthol and boron trifluoride-acetic acid complex at room temperature and boiling the complex with water gives 2-acetyl-1-naphthol (IV) and 4-acetyl-1-naphthol (V) in 70 and 25 percent yields, respectively. When the reaction was carried out on a steam-bath for 4 to 5 hours, (IV) and (V) were obtained in 85 percent and 10 percent respectively.

Condensations of 1- and 2-napthols with the boron trifluoride complexes of propionic and lauric acid have been studied. Somewhat better yields of the ketones were obtained with propionic acid than with lauric acid, reflecting the effect of chain length and bulk of the two substrates. These ketones have been of interest in the past (Buu-Hoi Ng, 1955), as potential protective agents against lethal radiations. The preparation of phenolic ketones by the boron trifluoride-acid complex method is summarized in Table 1.

A note of the ferric chloride reaction to distinguish between isomers: although phenols generally give a positive ferric chloride reaction, the presence of a hydroxyl group adjacent to a carbonyl group intensifies the coloration due to the chelation effect. Throughout the literature, this method has been used to distinguish between o- and p-isomers of phenolic ketones. Thus p-hydroxyacetephenone gives a light red color with ferric chloride, while o-hydroxyacetophenone gives a reddish violet coloration. This reaction can also be used to distinguish between the 2- and 4-isomers of ketones from 1-napththol. (See Methods and Materials).

Synthesis of Phenyl Styryl Ketones

The general procedure was to saturate a solution of cinnamic acid in chloroform with boron trifluoride at 0°, add the phenol, pass boron trifluoride again, and allow the reaction mixture to stand overnight at room temperature. Thus resorcinol gave 2,4-dihydroxyphenyl styryl ketone (VI) in 70 percent yield. Pyrogallol under similar conditions gave an 80 percent yield of the corresponding chalkone (VII). Following a similar procedure 2-hydroxy-4,6-di-



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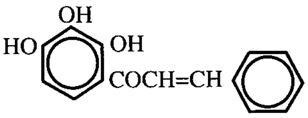
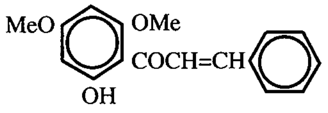


(VII)

Table 1. Phenolic ketones prepared by the boron fluoride-acid complex method.

Phenol	Acid	Temp C	Time hr	Product	M. p.	Lit. m.p.	(References)
1.	2.	3.	4.	5.	6.	7.	
Phenol	Acetic	28-30	24	p-Hydroxyacetophenone	109	109	(Klingel 1885, Pauly et al. 1915)
Hydroquinone	Acetic	100	5	2-Acetylhydroquinone	202	202-3	(Amin and Shah 1955)
Resorcinol	Acetic	28-30	18	Resacetophenone	147	142-4	(Cooper 1955)
Resorcinol	Acetic	100	4	Resacetophenone	147	142-4	(Cooper 1955)
				2,4-Diacetylresorcinol	85	85	(Dean et al. 1953)
Resorcinol	Acetic	125	6	4,6-Diacetylresorcinol	182	182	(Dean et al. 1953)
				Resacetophenone	147	142-4	(Cooper 1955)
Phloroglucinol	Acetic	28-30	18	2,4-Diacetylphloroglucinol	168	168	(Dean et al. 1953)
Phloroglucinol monomethyl ether	Acetic	100	4	2,4-Diacetylphloroglucinol 1-methyl ether	106	106	(Dean et al. 1953)
Phloroglucinol dimethyl ether	Acetic	100	4	2,4-dimethoxy-6-hydroxyacetophenone	82	81	(Dean et al. 1953)
				2,6-Dimethoxy-4-hydroxyacetophenone	185	185.5	(Canter et al. 1931)
C-Methyl-phloroglucinol	Acetic	28-30	24	C-Methylphloroacetophenone	210	211	(Nakezawa et al. 1953)
C-isoAmyl-phloroglucinol	Acetic	28-30	24	2,4,6-Trihydroxy-3-isoamyl acetophenone	190		
C-isoAmyl phloroglucinol	Propionic	28-30	24	2,4,6-trihydroxy-3-iso-amyl propiophenone	175		
Pyrogallol	Acetic	28-30	18	Gallacetophenone	173	171-2	(Badwar et al. 1943)
2,6-Dimethoxy hydro-quinone	Acetic	28-30	18	2,5-Dihydroxy-4,6-dimethoxyacetophenone	162	162-3	(Mauthner 1937, Sastri et al. 1946)
Antiarol	Acetic	28-30	18	2-Hydroxy-4,5,6-trimethoxyaceto phenone fusion	b.p. 140 at 1mm mp 30.5-31.5 pt. 32	b.p.184-6 at 27mm mp 41-42	(Baker 1941) (Oliverio et al 1948) (Rabjohn et al. 1959)
1-Naphthol	Acetic	28-30	18	2-Acetyl-1-naphthol	102	103 98	(Freidlander 1895) (Lederer 1932, Stoughton 1935)
				4-Acetyl-1-naphthol	198	198	(Lederer 1932)
1-Naphthol	Acetic	100	5	2-Acetyl-1-naphthol	102	103 98	(Freidlander 1895) (Lederer 1932, Stoughton 1935)
				4-Acetyl-1-naphthol	198	198	(Lederer 1932)
1-Naphthol	Propionic	28-30	18	2-Propionyl-1-naphthol	82	81 81-82	(Hantzsh 1906, Godzweig et al. 1891) (Brewster et al. 1942)
				4-Propionyl-1-naphthol	187	188-9	(Stoughton 1935)
1-Naphthol	Propionic	100	5	2-Propionyl-1-naphthol	82	81 81-2	(Hantzsh 1906, Godzweig et al. 1891) (Brewster et al. 1942)
1-Naphthol	Lauric	100	5	2-Lauroyl-1-naphthol	75	74-5	(Desai et al. 1940)
2-Naphthol	Acetic	28-30	18	1-Acetyl-2-naphthol	64	64-5	(Fries 1921)
2-Naphthol	Propionic	28-30	18	1-Propionyl-2-naphthol	71	70-71	(Gulati et al. 1933)
2-Naphthol	Propionic	100	5	1-Propionyl-2-naphthol	71	70-71	(Gulati et al. 1933)
2-Naphthol	Lauric	28-30	18	1-Lauroyl-2-naphthol	95	95-6	(Desai et al. 1946)
2-Naphthol	Lauric	100	5	1-Lauroyl-2-naphthol	95	95-6	(Desai et al. 1946)

methoxyphenyl styryl ketone (VIII) from phloroglucinol dimethyl ether, 2,5-dihydroxy-4,6-dimethoxyphenyl styryl ketone (IX) from 2,6-dimethoxyhydroquinone, and 2-hydroxy-4,5,6-trimethoxyphenyl styryl ketone (X) from antiarol, were prepared.



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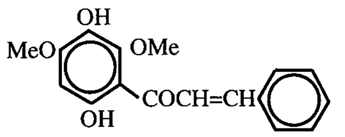

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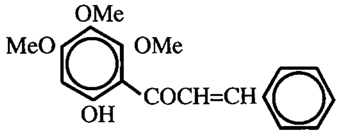
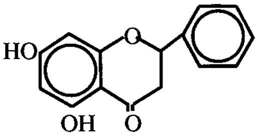


(X)

In the case of phloroglucinol it was necessary to heat the chloroform solution. The product was 5,7-dihydroxyflavanone (XI), accompanied by a small amount of the chalkone (XII).



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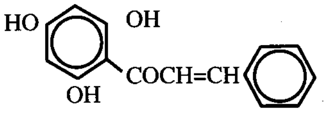
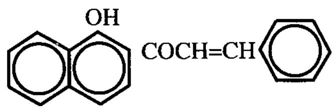


(XII)

Both 1- and 2-napththol condensed smoothly with cinnamic acid-boron trifluoride complex in chloroform solution. While 1-naphthol gave chalkone (XIII), the sole product obtained from 2-naphthol was flavanone (XIV).



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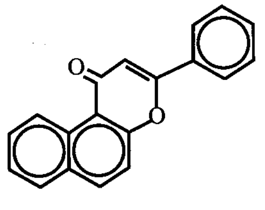

(XIV)

The preparation of chalkones and flavanones by the boron fluoride-acid complex method is summarized in Table 2.

p-Hydroxyacetophenone

Distilled phenol (10 g) was thoroughly mixed with boron fluoride-acetic acid complex (50 g) in a round-bottom flask provided with a calcium chloride guard tube. The reaction mixture was shaken well and allowed to stand at 28-30° for 24 hours. The viscous mass was poured over crushed ice and steam-distilled until one liter of distillate collected. The residue was cooled and the product collected and crystallized from aqueous ethanol. The colorless needles (9.5 g), (95%), had m.p. 109°. The substance gave a light red color with ferric chloride.

The steam distillate was saturated with NaCl and ether extracted. This yielded a minute amount of an oil which failed to give a reddish violet color with ferric chloride (characteristic of O-hydroxy-acetophenone), and was identified as phenol.

2-Acetylhydroquinone

A mixture of hydroquinone (2 g), boron fluoride-acetic acid complex (10 g) was heated at 100° for 5 hours. The product obtained after pouring over crushed ice crystallized from aqueous ethanol in yellowish silky needles (1.5 g), (70%), m.p. 202°. It gave a green ferric chloride reaction.

Resacetophenone

(a) A mixture of resorcinol (2 g), boron fluoride-acetic acid complex (10 g) was kept at room temp (28-30°) for 18 hr and poured over crushed ice (200 g). The product crystallized from hot water in colorless needles (1.7 g)(85%), m.p. 147°. It gives a light red ferric chloride reaction.

(b) A mixture of resorcinol (2 g), boron fluoride-acetic acid complex (10 g) was heated at 100° for 4 hr. The mixture was poured into water (250 ml) and boiled for 10 min. The product obtained on cooling crystallized from hot water in colorless needles (1.4 g), (70%), m.p. 147°. It gave a light red ferric chloride reaction.

2,4- and 4,6-Diacetyl resorcinol

A mixture of resorcinol (2.0 g), boron fluoride-acetic acid complex (10 g) was heated at 125° for 6 hr. The mixture was cooled and poured into water (250 ml) and boiled for 10 min. The yellow crystalline product obtained on cooling was filtered and extracted thoroughly with hot petroleum ether (60-80°).

The petroleum ether extract on concentration and cooling gave a crystalline product which was filtered and recrystallized from aqueous ethanol. Colorless needles (0.4 g), (20%), m.p. 182° (lit. m.p. of 4,6-diacetyl-resorcinol 182°). It gave a red-brown ferric chloride reaction.

The petroleum ether filtrate on evaporation to dryness yielded a residue which crystallized from aqueous ethanol in colorless needles (0.4 g), (20%), m.p. 85° (lit. m.p. for 2,4-diacetylresorcinol 85°).

The residue after petroleum ether extraction yielded

Table 2. Chalkones and Flavanones prepared by the boron fluoride-cinnamic acid complex method

Phenol	Acid	Temp	Time	Product	M.p.	Lit. m.p.	(References)
1.	2.	3.	4.	5.	6.	7.	
Resorcinol	cinnamic	20-30	18	2,4-dihydroxyphenystryl	150	150	(Shinoda et al. 1928)
Phloroglucinol	"	b.p. of chloroform	2	5.7-dihydroxyflavanone	150	202	(Rosenmund et al. 1928)
					200	203	(Rosenmund et al. 1928)
				2,4,6-trihydroxyphenylstyryl ketone	210	210	(Rosenmund et al. 1928)
						189-90	
Phloroglucinol dimethyl ether	"	28-30	18	2-hydroxyl-4,6-dimethoxy phenylstyryl ketone	92	91-92	(Kostanecki et al. 1899)
Pyrogallol	"	28-30	18	2,3,4-trihydroxyphenylstyryl ketone	166	165-66	(Ellison 1927)
2,6-Dimethoxyhydroquinone	"	28-30	18	2,5-dihydroxy-4,5-dimethoxyphenylstyryl ketone	160	156-8	(Rajagopalan et al. 1948)
Antiarol	"	28-30	18	2-hydroxy-4,5,6-trimethoxyphenylstyryl ketone	100	103-4	
						132-3	(Oliverio et al. 1948, Narasimhachari et al. 1949)
1-Naphthol	"	28-30	18	2-cinnamoyl-1-naphthol	125	125	(Kostanecki 1898)
2-Naphthol	"	28-30	18	2-naphthaflavanone	118	117	(Tambor et al. 1926)

resacetophenone which crystallized from hot water in colorless needles (0.6 g), (30%), m.p. 147°.

2,4-Diacetylphloroglucinol

Dry phloroglucinol (2 g) was mixed with boron fluoride-acetic acid complex (10 g) and the reaction mixture, after 18 hr standing at 28-30°, was poured over crushed ice (200 g). The boron fluoride complex was boiled with water (50 ml) for 10 min. When the yellow color disappeared and a brown solid resulted, it was filtered. It crystallized from aqueous ethanol in prisms (1.7 g), (85%), m.p. 168°. It gave a red ferric chloride coloration.

2,4-Diacetylphloroglucinol-1-methyl ether

A mixture of phloroglucinol monomethyl ether (2 g) and boron fluoride acetic acid complex was heated at 100° for 4 hr. The mixture was cooled and poured into water (250 ml) and boiled for 10 min. The colorless crystalline product together with a small amount of sticky material, obtained on cooling, was filtered. It crystallized from aqueous ethanol in colorless needles (1.6 g), (80%), m.p. 106°. It gave a red ferric chloride coloration.

2,4-Dimethoxy-6-hydroxyacetophnone and 2,6-dimethoxy-4-hydroxyacetophenone

A mixture of phloroguicinol dimethyl ether (2.0 g) and boron fluoride-acetic acid complex was heated at 100° for 4 hr. The mixture ws cooled and poured into water (250 ml) and boiled for 10 min. The yellowish brown crystalline product obtained on cooling was subjected to steam distillation. The distillate on cooling gave a colorless product which crystallized from ethanol in colorless needles (0.48 g), (24%), m.p. 82° (lit. m.p. for 2,4-dimethoxy-6-hydroxyacetophenone 82°). It gave a red ferric chloride reaction.

The residual mother liquor after steam distillation was filtered hot to separate a small amount of resinous matter. The filtrate on cooling gave a product which crystallized from ethanol in colorless needles (0.8 g), (40%), m.p. 185° (lit. m.p. for 2,6-dimethoxy-4-hydroxyacetophenone 185.5°). It did not give a ferric chloride reaction.

C-Methylphloracetophenone

A mixture of C-methylphloroglucinol (2 g), boron fluoride-acetic acid complex (10 g) was kept at 28-30° for 24 hr and poured over crushed ice (250 g). The complex obtained was collected and boiled with water (50 ml) for 10 min, and the product obtained on cooling crystallized from aqueous ethanol in pale yellow needles (1.0 g), (50%), m.p. 210°. It gave a brownish red ferric chloride reaction.

2,4,6-Trihydroxy-3-isoamylacetophenone

A mixture of C-isoamylphloroglucinol (2 g), boron fluoride-acetic acid complex (10 g) was kept at 28-30° for 24 hr. The reaction mixture was then poured into water (250 ml) and boiled for 10 min. On cooling, a yellow brown crystalline product was obtained which was recrystallized from hexane (Norit) in yellow needles (1.4 g), (70%), m.p. 190°. (Found: C,65.8; H, 8.4. $C_{13}H_{18}O_4$ requires: C, 65.5; H, 8.6%). It gave a red ferric chloride coloration.

2,4,6-Trihydroxy-3-isoamylpropiophenone

A mixture of C-isoamylphloroglucinol (1 g), propionic acid-boron fluoride complex (5 g) was kept mechanically agitated for 1 hr and then left at 28-30° for 24 hr. The reaction mixture was then treated with water (250 ml) and the mixture boiled for 10 min. After cooling, the semi-solid mass was ether extracted and the ether extract washed with 1% $NaHCO_3$ solution, dried and distilled. The product obtained after distillation of the ether and chromatographic purification over alumina, crystallized from hexane in pale brown needles (0.6 g), (63%), m.p. 180°. (Found: C, 66.9; H, 7.9. $C_{14} H_{20} O_4$ requires: C, 66.6; H. 7.9%). It gave a brownish red ferric chloride coloration.

Gallacetophenone

This was prepared from pyrogallol (2 g) and boron fluoride-acetic acid complex (10 g) at 28-30° for 18 hr. The product crystallized from hot water containing sulphurous acid in colorless needles (1.8 g), (90%), m.p. 173°. (lit m.p. 171-2 (Badwar 1943)). It gave a dark red ferric chloride reaction.

2,5-Dihydroxy-4,6-dimethoxyacetophenone

A mixture of 2,6-dimethoxyhydroquinone (2 g), boron fluoride-acetic acid complex (10 g) after 18 hr standing at 28-30° and pouring over crushed ice yielded a complex which after decomposition with hot water crystallized from aqueous acetone in yellow needles (1.2 g), (60%), m.p. 162°. (Found: C, 56.3; H, 5.8. $C_{10}H_{12}O_5$ requires: C, 56.6; H, 5.7%). It gave a green ferric chloride reaction which changed to blood-red on standing.

2-Hydroxy-4,5,6-trimethoxyacetophenone

A mixture of antiarol (2 g), boron fluoride-acetic acid complex (10 g), on standing for 18 hr at 28-30° and pouring over crushed ice, yielded a yellow solid; the complex was broken by boiling with water and the oily product taken up in ether. The ether extract, after washing with cold 1% aqueous Na_2CO_3 solution, led to an oil which was distilled under reduced pressure and the fraction (1.0 g), (50%), distilling at 140°/1 mm collected. The product which solidified on standing had a fusion point of 32°. (Found C, 58.2; H, 5.9 $C_{11}H_{14}O_5$ requires: C, 58.4; H, 6.1%). It gave a red ferric chloride coloration.

2-Acetyl and 4-acetyl-1-naphthol

(a) A mixture of 1-naphthol (2 g) and boron fluoride-acetic acid complex (10 g), after 18 hr at 28-30°, was treated with boiling water. The semi-solid product (2 g) was taken up in ether and the ether layer washed with 5% Na_2CO_3 solution. The alkaline extract on acidification yielded a pale yellow flocculent mass which crystallized from ethanol in pale yellow needles (0.4 g), (20%), m.p. 198° (Lederer, 1932). It gave no ferric chloride reaction.

Evaporation of the ether extract remaining after base extraction yielded a solid which crystallized from petroleum ether in greenish yellow needles (1.4 g), (70%), m.p. 102° (lit. m.p. for 2-acetyl-1-naphthol 103° (Friedlander, 1895); 98° (Lederer, 1932; Stoughton, 1935)). The mixed m.p. with an authentic sample of 2-acetyl-1-naphthol prepared by the Fries migration of 1-naphthyl acetate was undepressed. It gave a green ferric chloride reaction.

The mixture was also separable by chromatography. A solution of the crude reaction product (0.1 g) in benzene (10 ml) was chromatographed on an alumina column. On development with benzene, a yellow band separated, but elution was not possible. Elution with methanol led to a brownish semi-solid substance which crystallized from ethanol in greenish yellow needles (0.04 g), m.p. 102° (2-isomer). The greenish band held strongly on alumina was extracted with hot methanol and the product obtained on evaporation crystallized from ethanol in pale yellow needles (0.01 g), (20%), m.p. 198° (4-isomer).

(b) A mixture of 1-naphthol (2 g) and boron fluoride-acetic acid complex (10 g) at 100° for 5 hr gave a complex which on decomposition with boiling water and treatment with 5% aqueous Na_2CO_3 as above yielded 4-acetyl-1-naphthol, crystallizing from ethanol in pale yellow needles (0.2 g), (10%), m.p. 198°, and 2-acetyl-1-naphthol, crystallizing from hexane in greenish yellow needles (1.7 g), (85%), m.p. 102°.

2-Propionyl- and 4-Propionyl-1-Naphthol

(a) 1-Napththol (2 g) and boron fluoride-propionic acid complex (10 g), kept at 28-30° for 18 hr, gave a complex which on decomposition with boiling water and treatment with 5% aqueous Na_2CO_3 gave 4-propionyl-1-naphthol as the Na_2CO_3 soluble fraction, crystallizing from ethanol in needles (0.4 g) (20%) m.p. 187° (lit. m.p. 188-189° (Stoughton 1935)) and 2-propionyl-1-naphthol as the Na_2CO_3 insoluble fraction, crystallizing from hexane in greenish yellow needles (1.3 g), (65%), m.p. 82° (lit. m.p. 81-82°). The latter gave a green coloration with alcoholic ferric chloride.

The mixture was also separable by chromatography over an alumina column. A solution of the crude reaction product (0.1 g) in benzene yielded a methanol elutable fraction crystallizing from hexane in greenish yellow needles (0.03 g), m.p. 82°. The strongly held band was eluted with hot methanol. Evaporation of methanol yielded a product which crystallized from aqueous ethanol in needles (0.01 g), m.p. 187°. It did not give a ferric chloride reaction.

(b) A mixture of 1-naphthol (2 g) and boron fluoride-propionic acid complex (10 g) at 100° for 5 hr gave a complex which on decomposition with boiling water, yielded a product which crystallized from hexane in yellowish green needles (1.6 g), (80%) m.p. 82° (lit. m.p. for 2-propionyl-1-naphthol 81°, 81-82°). It gave a green coloration with alcoholic ferric chloride.

Chromatography of a solution of the crude reaction product (0.1 g) in benzene over an alumina column yielded a band which could be completely eluted with cold methanol. The methanol eluate on evaporation yielded 2-propionyl-1-naphthol which crystallized from hexane in yellowish green needles, m.p. 82°, identical with the product obtained in (a).

2-Lauroyl-1-naphthol

A solution of lauric acid in anhydrous ether was saturated with boron fluoride. The boron fluoride-etherate was removed by distillation under reduced pressure. The residue, m.p. 42-45° was analyzed for boron. (Found: B, 3.86; $C_{12}H_{26}O_2$,-BF_3 requires 4.0%).

A mixture of 1-naphthol (2 g) and boron fluoride-lauric acid complex (10 g) was heated at 100° for 5 hr. After decomposition with hot water, the product crystallized from hexane in needles (1.40 g), (70%), m.p. 75° lit m.p. 74-5 (Desai et al., 1940). It gave a green coloration with alcoholic ferric chloride.

Chromatography of a solution of the crude reaction product (0.1 g) in benzene over an alumina column yielded a single yellow band which could be completely eluted with cold methanol eluate without leaving any residual band, showing the absence of any 4-isomer. The methanol eluate on evaporation yielded 2-lauroly-1-naphthol which crystallized from hexane in yellow green needles, m.p. 75°.

1-Acetyl-2-naphthol

A mixture of 2-naphthol (2 g) and boron fluoride-acetic acid complex (10 g), kept at room temp (28-30°) for 18 hr, was treated with ice-water. A complex, m.p. 184°, separated which was then decomposed with boiling water. The brownish semi-solid product crystallized from petroleum ether, b.p. 60-80°, in pale yellow needles (1.9 g), (95%), m.p. 64° lit m.p. 64-65 (Fires, 1921). It gave a red violet ferric chloride reaction.

1-Propionyl-2-naphthol

(a) A mixture of 2-naphthol (2 g) and boron fluoride-propionic acid complex (10 g), after standing at room temp (28-30°) for 18 hr, was treated with boiling water. The product crystallized from hexane in pale yellow needles (1.5 g), (75%), m.p. 71°. It gave a reddish violet coloration with alcoholic ferric chloride.

(b) A mixture of 2-naphthol (2 g), after heating at 100° for 5 hr and treatment with boiling water gave a product which crystallized from hexane in pale yellow needles (1.7 g), (85%), m.p. 71°, identical with the product obtained in (a).

1-Lauroyl-2-naphthol

(a) A mixture of 2-naphthol (2 g) and boron fluoride-lauric acid complex (10 g) in chloroform (50 cc) was mechanically agitated at 28-30° for 18 hr and the complex obtained after distillation of chloroform *in vacuo,* decomposed by boiling water. The product crystallized from hexane in colorless needles (1.4 g), (70%), m.p. 95°. It gave a pale brown coloration with alcoholic ferric chloride.

(b) A mixture of 2-naphthol (2 g) and boron fluoride-lauric acid complex (10 g) was heated at 100° for 5 hr and the complex decomposed by boiling water. The product crystallized from hexane in colorless needles (1.6 g), (80%), m.p. 95°, identical with the product obtained in (a).

2,4-Dihydroxyphenyl styryl ketone

A solution of cinnamic acid (2.96 g, 0.02 mol) in dry chloroform (50 ml) was saturated with boron trifluoride gas at 0° under agitation. Dry resorcinol (1.1 g, 0.01 mol) was added to the clear solution of the complex and boron trifluoride gas again passed through the mixture at 0° under agitation for a few minutes. The mixture was then left to stand at room temp (28-30°) for 18 hr. The yellowish orange mass was then poured over crushed ice, and after attaining room temp the deep orange chloroform layer was washed with 5% aqueous $NaHCO_3$ and water, dried and distilled. The yellowish orange residue crystallized from aqueous ethanol in yellow plates (0.8 g), (72%), m.p. 150°. (Found: C, 74.7; H, 5.0. $C_{15}H_{12}O_3$ requires: C, 75.0; H, 5.0%). It gave a reddish brown ferric chloride reaction, dissolved in conc. H_2SO_4 with a red color and gave a reddish solution in cold NaOH.

5,7-Dihydroxyflavanone and 2,4,6-trihydroxyphenyl styryl ketone

Cinnamic acid (2.96 g, 0.02 mol) was dissolved in chloroform (50 ml) and boron trifluoride gas passed at 0° under mechanical agitation until saturated. Dry phloroglucinol (1.26 g, 0.01 mol) was added and boron trifluoride gas again passed under mechanical agitation at 0° for a few minutes. Stirring was continued for 3 hr more, and the reaction mixture allowed to stand at room temp for 18 hr. It was then refluxed for 2 hr, during which the color changed from yellow to reddish orange. Worked up as usual, the dark brown oily residue from the chloroform layer solidified on treatment with cold methanol. Three crystallizations from aqueous methanol gave yellowish needles (0.9 g) which melted between 175-190°. Chromatography on a column of Florex, using chloroform as solvent and chloroform-benzene (1:1) as eluent, yielded bright yellow needles (0.6 g), (48%), which on recrystallization from methanol had m.p. 200° (lit. m.p. for 5,7-dihydroxyflavanone 202°; 203-204° (Shinoda et al., 1928). It gave a pink color with magnesium and HCl and a brown color with alcoholic ferric chloride.

The reddish zone held on the Florex column was eluted with ethanol and led to a bright red oily residue, which on contact with a few drops of methanol solidified. Three crystallizations from aqueous ethanol gave orange-red needles (0.025 g), (2%), m.p. 210° (lit. m.p. 210°(op. cit.), with 1.2 mol H_2O 189-190°). It gave a reddish brown color with alcoholic ferric chloride.

2-Hydroxy-4,6-dimethoxyphenyl styryl ketone

The chalkone obtained from cinnamic acid (2.96 g, 0.02 mol) and phloroglucinol dimethyl ether (1.54 g; 0.01 mol) crystallized from dilute methanol in yellowish orange needles (1.20 g), (77%), m.p. 92° (lit. m.p. 91-92° (Kostanecki et al., 1899). It gave a dark red ferric chloride reaction.

2,3,4-Trihydroxyphenyl styryl ketone

Following a similar procedure as in the case of the resorcinol derivative 2,3,4-trihydroyphenyl styryl ketone was obtained from pyrogallol (1.26 g, 0.01 mol) and cinnamic acid (2.96 g, 0.02 mol). The product crystallized from aqueous methanol in reddish orange needles (0.96 g), (80%), m.p. 166°. It gave a reddish brown ferric chloride coloration. (Found: C, 70.2; H, 4.9. $C_{15}H_{12}O_4$ requires: C, 70.3; H, 4.7%).

2,5-Dihydroxy-4,6-dimethoxyphenyl styryl ketone

The chalkone was prepared from 2,6-dimethoxyhydroquinone (0.89 g, 0.005 mol) and cinnamic acid (1.48 g, 0.01 mol). The reaction mixture turned greenish and finally red. The product crystallized from aqueous ethanol in yellow needles (0.60 g), (67%), m.p. 160°. (Found: C, 68.3; H, 5.5. $C_{17}H_{16}O_5$ requires: C, 68.0; H, 5.3%). It gave a brown coloration with alcoholic ferric chloride.

2-Hydroxy-4,5,6-trimethoxyphenyl styryl ketone

The chalkone was prepared from antiarol (1.9 g, 0.01 mol) and cinnamic acid (2.96 g, 0.02 mol). The product crystallized from aqueous ethanol in yellow needles (1.4 g), (73%), m.p. 100°. (Found: C, 68.3; H, 5.5. $C_{17}H_{16}O_5$ requires: C, 68.0; H, 5.3%). It gave a brown coloration with alcoholic ferric chloride.

2-Hydroxy-4,5,6-trimethoxyphenyl styryl ketone

The chalkone was prepared from 2,6-dimethoxyhydroquinone (0.89 g, 0.005 mol) and cinnamic acid (1.48 g, 0.01 mol). The reaction mixture turned greenish and finally red. The product crystallized from aqueous ethanol in yellow needles (0.60 g), (67%), m.p. 160°. (Found: C, 68.3; H, 5.5. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.3%). It gave a brown coloration with alcoholic ferric chloride.

2-Cinnamoyl-1-naphthol

Following the standard procedure, 2-cinnamoyl-1-naphthol was obtained from cinnamic acid (2.96 g, 0.02 mol) and 1-naphthol (1.43 g, 0.01 mol). The product crystallized from dilute methanol in orange yellow needles (1.1 g), (76%), m.p. 125°. It dissolved in conc. H_2SO_4 with a yellowish red color and gave a dark grown ferric chloride reaction.

2-Napthaflavanone

The condensation of cinnamic acid (2.96 g, 0.02 mol) and 2-naphthol (1.4 g, 0.01 mol) was carried out at 0° and then at room temp as usual. The chloroform layer yielded a dark oily residue which dissolved in hot methanol. The methanolic solution on chilling deposited pale brown needles, m.p. 110°, which did not give a ferric reaction and did not dissolve in cold 2% NaOH solution. The substance was purified by recrystallization from petroleum ether when colorless needles (0.98 g), (70%), m.p. 118° were obtained. The substance dissolved in conc. H_2SO_4 with a yellow color.

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