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PHOTOINDUCED REACTIONS—LXXI

PHOTOREARRANGEMENT OF 3-HYDROXYFLAVONES TO 3-ARYL-3-HYDROXY-1,2-INDANDIONES[1]

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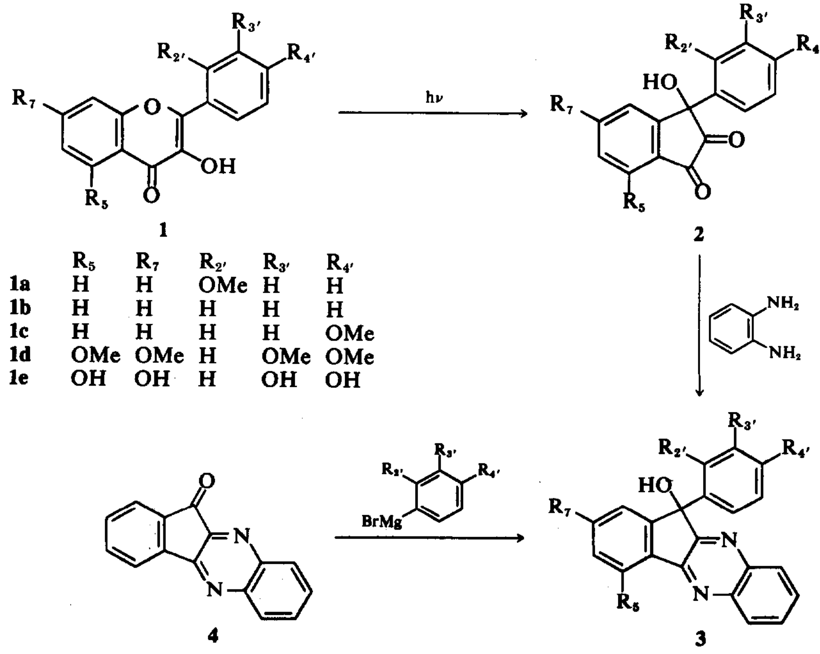
Abstract—3-Hydroxyflavones (1) were found to undergo a novel photorearrangement to 3-aryl-3-hydroxy-1,2-indandiones (2) which were characterized as *o*-phenylenediamine adducts, 1-aryl-1-hydroxy-11H-indeno[1,2-b]quinoxalines (3). To the contrary, 3-methoxyflavone underwent photochemical intramolecular hydrogen transfer. Photochemical reactivities of several other flavonoids were examined. It appears that the 5-hydroxyl H-bonded to the 4-carbonyl causes photoresistance in flavonoids.

Although many flavonoids have absorption bands in the visible region and are widely distributed in plants which are under influence of sunlight, their photochemical activity has received little attention.[2-6] The photoreactions reported are concerned with oxidation of 3-hydroxy- and 3-methoxyflavones, related to the oxidative transformation of flavonoids *in vivo*.[2-4] This paper deals with a novel photorearrangement of 3-hydroxyflavones and the photoreactivity of other flavonoids.

Irradiation of 3-hydroxy-2′-methoxyflavone (**1a**) in 1:1 benzene-isopropyl alcohol with light above 290 nm gave a crystalline isomer **2a** in essentially quantitative yield. The IR bands at 3420 and 1770 and 1730–1740 cm^{-1} suggest the presence of hydroxy and a cisoid α-dicarbonyl groups, respectively. This was confirmed by conversion of **2a** into a monoacetate (86% yield) and an *o*-phenylenediamine adduct **3a** (96% yield). The structure of **2a** was unequivocally established by a synthesis of **3a** from 11H-indeno[1,2-b]quinoxaline (**4**)[7] and *o*-anisylmagnesium bromide.

Similar irradiation of other 3-hydroxyflavones,



1

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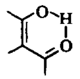
3

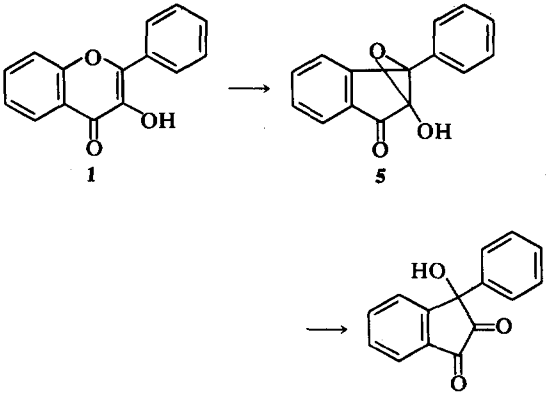
4

	R5	R7	R2′	R3′	R4′
1a	H	H	OMe	H	H
1b	H	H	H	H	H
1c	H	H	H	H	OMe
1d	OMe	OMe	H	OMe	OMe
1e	OH	OH	H	OH	OH

1b, **1c** and **1d**, gave the corresponding hydroxyindandiones, **2b** (84%), **2c** (71%) and **2d** (69%), respectively, although they were obtained as amorphous solids, which however were characterized as their *o*-phenylenediamine adducts, **3b**, **3c** and **3d**, respectively. Among these adducts, **3b** and **3c** were also synthesized by the same method used for **3a**. The rearrangement occurred by irradiation with visible light; thus **1b** gave **2b** in 56% yield.

Quercetin (**1e**) resisted photolysis—three explanations may account for the loss of its excitation energy: (1) Tautomerisation occurred at the 5-OH and 4-CO groups as seen in the photoenolization of *o*-hydroxybenzophenone,[8] (2) De-protonation from the excited state as seen in the resistance of *p*-hydroxybenzophenone to photoreduction in isopropyl alcohol,[9] and (3) Intramolecular quenching through the H-bond between the 5-OH and 4-CO groups as seen in the photo-resistance of certain compounds having intramolecular H-bonding of the type [4, 10–12].

The formation of **2** from **1** provides the first example of the photorearrangement of flavonoids. The rearrangement may occur via a 2,3-epoxy-2-hydroxy-1-indanone intermediate (**5**) which can be formed by a formal $[_\sigma 2 + _\pi 2]$ cycloaddition,[13] analogous to the photochemical transformation of 2-cyclohexenones into bicyclo[3.1.0]hexan-2-ones or of 2,5-cyclohexadienones into bicyclo[3.1.0]hex-3-en-2-ones (so-called lumiketones), as shown below.



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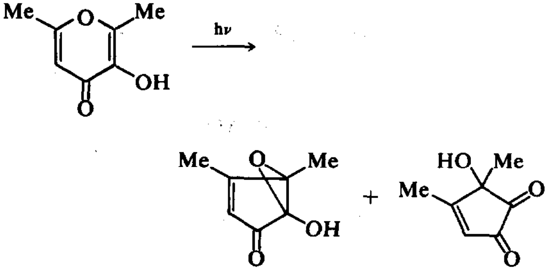
The latter type of photoreaction is known to proceed by a stepwise process involving the n,π* triplet state. However, the available experimental data at present cannot distinguish whether the photorearrangement of 3-hydroxyflavones proceeds in one step or stepwise. After the completion of our work, Shiozaki and Hiraoka reported the same skeletal rearrangement in the photolysis of 2-hydroxy-γ-pyrones;[15] thus irradiation of 3,6-dimethyl-2-hydroxy-γ-pyrone gave rearrangement products **6** and **7** corresponding to **5** and **2**, respectively. This strongly supports the intermediary formation of **5**.



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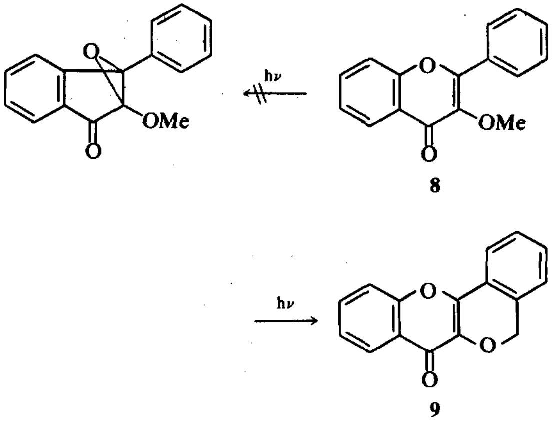
In this connection, the photochemical reactivity of several other flavonoids was examined. In order to see whether the presence of the 3-OH group is prerequisite for the photorearrangement of **1**, 3-methoxyflavone (**8**) was submitted to photolysis under nitrogen. No rearrangement product corresponding to **5** could be detected in the photolysate but a tetracyclic product **9** resulted from intramolecular hydrogen transfer. A product similar to **9** is known to be formed from 3-methoxyflavones by irradiation either under nitrogen[2] or oxygen.[4]



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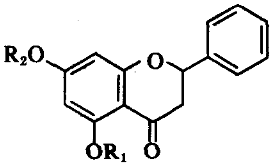
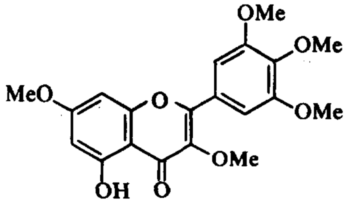
The photolysis of several flavonoids were also carried out in isopropyl alcohol and/or benzene. Alpinetin (7-hydroxy-5-methoxyflavanone; **10**) underwent photochemical change, which was qualitatively detected, whereas pinocembrin (5,7-dihydroxy-flavanone; **11**), pinostrobin (5-hydroxy-7-methoxyflavanone; **12**) and pentamethylmyricetin (5-hydroxy-3,7,3′,4′,5′-pentamethoxyflavone; **13**) did not change. This again suggests that the presence of an H-bond between the 5-OH and 4-CO groups suppresses photochemical reactivity in flavonoids. 5,7,2′-Trimethoxyisoflavone (**14**) was found to resist photolysis.



	R_1	R_2
10	Me	H
11	H	H
12	H	Me



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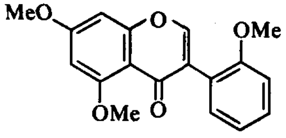

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EXPERIMENTAL

Photolysis of **1a**

A soln of **1a**[16] (700 mg) in a mixture of 150 ml benzene and 300 ml isopropyl alcohol was irradiated internally with a 450 W high-pressure mercury lamp surrounded by a Pyrex water-cooling jacket under bubbling N_2 for 8 hr. During irradiation the pale yellow soln turned to bright orange. Evaporation of the solvent *in vacuo* left **2a** as orange crystals (700 mg) which showed a single spot on TLC (silica gel, 10:1 benzene–acetone). Recrystallization from benzene gave orange plates, m.p. 188–189°; IR(KBr) 3420, 1770 and 1730–1740 cm^{-1}; λ_{max}^{EtOH} 273 nm (ϵ 9600); NMR($CDCl_3$) τ: 1·9–3·2 (m, 8H, aromatic H), 2·95 (s, 1H, OH) and 6·63 (s, 3H, OMe); *m/e* 268 (M^+). (Found: C, 71·70; H, 4·70. Calc for $C_{16}H_{12}O_4$: C, 71·63; H, 4·51%).

o-*Phenylenediamine adduct* **3a**

(a) *From* **2a**. A soln of **2a** (180 mg) and 90 mg *o*-phenylenediamine in 40 ml AcOH was heated at 100° for 30 min. Dilution of the mixture with water deposited **3a** (221 mg), which was recrystallized from benzene to give colorless plates, m.p. 222–223°; IR(KBr) 3300, 1615, 1575 and 1510 cm^{-1}; λ_{max}^{EtOH} 262 (sh) (ϵ 20700), 269 (23300), 347 (15400) and 365 nm (16300); *m/e* 340 (M^+). (Found: C, 77·86; H, 4·75; N, 8·03. Calc for $C_{22}H_{16}O_2N$: C, 77·63; H, 4·74; N, 8·23%).

(b) *From* **4**. To a soln of **4**[7] (0·3 g) in 50 ml of a 1:1 mixture of dry ether and THF was added dropwise a soln of *o*-anisylmagnesium bromide prepared from 1·2 g *o*-bromoanisole, 0·16 g Mg ribbon and a few ml of a 1:1 mixture of dry ether and THF. The addition was continued until TLC (silica gel, 3:1 benzene–acetone) of an aliquot did not show a spot of the starting material. The ppt (almost quantitative) of **3a** formed on adding dil HCl to the mixture was collected, dried and recrystallized from benzene to give colorless plates, m.p. 223–224°, identical with the sample obtained in (a) (IR and mixed m.p.).

Acetate of **2a**. A soln of **2a** (77 mg) and a drop of pyridine in 3 ml Ac_2O was heated at 100° for several min and let stand at room temp overnight. Dilution with 100 ml water deposited 77 mg of yellow crystals which were collected by filtration and recrystallized from EtOH to give bright yellow plates, m.p. 187–188°; IR(KBr) 1770, 1730–1740 and 1230 cm^{-1}; λ_{max}^{EtOH} 273 nm (ϵ 9500); NMR($CDCl_3$) τ: 1·9–3·3 (m, 8H, aromatic H), 6·57 (s, 3H, OMe) and 7·89 (s, 3H, OCOMe). (Found: C, 69·55; H, 4·59. Calc for $C_{18}H_{14}O_5$: C, 69·67; H, 4·55%).

Photolysis of **1b**

A soln of **1b**[17] (834 mg) in a mixture of 150 ml benzene and 300 ml isopropyl alcohol was irradiated as described. The resulting reddish soln was evaporated *in vacuo* to a solid, which was chromatographed on 30 g of silica gel. Elution with 300 ml benzene gave 119 mg of recovered **1b**. Successive elution with 500 ml benzene, 500 ml 3:1 benzene–chloroform and 400 ml chloroform yielded 681 mg of **2b** as a reddish amorphous solid, m.p. 133–135°, which did not crystallize, IR(KBr) 3480 and 1740 cm^{-1} (broad). An amorphous solid was deposited from its EtOH soln. (Found: C, 73·22; H, 5·16. Calc for $C_{15}H_{10}O_3\frac{1}{2}C_2H_5OH$: C, 73·55; H, 5·02%).

A similar result was obtained by irradiating with visible light from a 550 W iodine-tungsten lamp through window glass. The yield of **2b** was 56%.

o-*Phenylenediamine adduct* **3b**

(a) *From* **3b**. A soln of **2a** (460 mg) and *o*-phenylenediamine (270 mg) in 100 ml AcOH was treated as described. Recrystallization of crude **3b** (504 mg) from benzene gave colorless crystals, m.p. 244–245°; IR(KBr) 3300, 1625, 1580 and 1515 cm^{-1}; λ_{max}^{EtOH} 259 (sh) (ϵ 24600), 268 (29700), 352 (16000) and 369 nm (17200); *m/e* 310 (M^+). (Found: C, 81·46; H, 4·73; N, 8·82. Calc for $C_{21}H_{14}ON_2$: C, 81·27; H, 4·55; N, 9·03%).

(b) *From* **4**. Reaction of 0·3 g of **4** and PhMgBr prepared from 2·03 g bromobenzene and 0·21 g Mg ribbon was carried out as described. Recrystallization of crude **3b** (0·382 g) from benzene gave colorless crystals, m.p. 245–246°, identical with the sample obtained in (a) (IR and Mass).

Photolysis of **1c**

A soln of **1c**[18] (300 mg) in a mixture of 150 ml benzene and 300 ml isopropyl alcohol was irradiated for 3⅓ hr. A reddish residue obtained by evaporation was chromatographed on 30 g silica gel. Elution with 150 ml 2:1 benzene–chloroform, then with 300 ml chloroform yielded 65 mg of recovered **1c**. Elution with 900 ml chloroform yielded 221 mg of **2c** as amorphous solid which failed to crystallize.

o-Phenylenediamine adduct **3c**

(a) *From* **2c**. A soln of **2c** (150 mg) and *o*-phenylenediamine (72 mg) in 40 ml AcOH was treated as usual. Recrystallization of crude **2c** (135 mg) from EtOH gave straw-colored crystals, m.p. 247–249°; IR(KBr) 3200, 1615, 1580 and 1515 cm^{-1}; λ_{max}^{EtOH} 262 (sh) (ϵ 28000), 269 (28600), 353 (14600) and 370 nm (14900). (Found: C, 77·53; H, 4·72; N, 8·25. Calc for $C_{22}H_{16}O_2N_2$: C, 77·63; H, 4·74; N, 8·23%).

(b) *From* **4**. Reaction of **4** (0·3 g) and *p*-anisylmagnesium bromide prepared from 1·20 g *p*-bromoanisole and 0·16 g Mg ribbon was carried out as described. Recrystallization of crude **3c** (almost quantitative) from EtOH gave straw-colored crystals, m.p. 248–250°, identical with the sample obtained in (a) (IR).

Photolysis of **1d**

A soln of **1d**[19] (300 mg) in a mixture of 150 ml benzene and 300 ml isopropyl alcohol was irradiated for 6 hr as described. A reddish brown residue obtained on evaporation was treated with 108 mg *o*-phenylenediamine in 50 ml AcOH as usual. Recrystallization of crude **3d** (248 mg) from 1:1 EtOH–acetone gave colorless crystals, m.p. 288–290°; IR(KBr) 3250–3400, 1620, 1575 and 1515 cm^{-1}; λ_{max}^{EtOH} 282 (ϵ 23300), 328 (10900), 371 (20100) and 382 nm (20700).

Photolysis of **1e**

A soln of quercetin (commercial sample 300 mg) in a mixture of 150 ml benzene and 300 ml isopropyl alcohol was irradiated for 12·5 hr. Crystals obtained by evaporation were identified as pure **1e** (IR and TLC).

Photolysis of 3-methoxyflavone (**8**)

A soln of **8**[20] (330 mg) in a mixture of 150 ml benzene and 300 ml i-PrOH was irradiated for $1\frac{1}{3}$ hr. A residue obtained by evaporation was chromatographed on 30 g silica gel. Elution with 400 ml benzene yielded 100 mg of **9** which was recrystallized from EtOH to give needles, needles, m.p. 178–180°; NMR($CDCl_3$) τ: 1·7 ~ 2·9 (m, 8H, aromatic H) and 4·74 (s, 2H, CH_2).

Elution with 200 ml 1:1 benzene–chloroform, then with 300 ml chloroform yielded 163 mg of a brown polymeric material.

*Photolysis of other flavonoids**

Alpinetin (**10**).† A soln of 49 mg of **10** in 70 ml i-PrOH or benzene was internally irradiated with a 100 W high-pressure mercury lamp under N_2 for 5 hr. After evaporation, the residue was analysed by IR. The IR spectrum was different from that of the starting material. No further investigation was carried out.

Pinocembrin (**11**).† A soln of 61 mg of **11** in 80 ml i-PrOH was internally irradiated under N_2 with a 100 W high-pressure mercury lamp for 11 hr or a 10 W low-pressure mercury lamp (Vycor housing) for 4·5 hr. The starting material was completely recovered unchanged (IR and TLC).

Pinostrobin (**12**).† A soln of 5–6 mg of **12** in 5–6 ml i-PrOH or benzene placed in a quartz tube was externally irradiated with a 100 W high-pressure mercury lamp for 9 hr or 5 hr, respectively. TLC and IR analyses of the photolysate revealed that most of the starting material was recovered unchanged.

Pentamethylmyricetin (**13**). A soln of 152 mg of **13**[21] in 100 ml i-PrOH was irradiated with a 10 W low-pressure mercury lamp under N_2 for 23 hr. The starting material was completely recovered unchanged (IR and TLC).

5,7,2'-Trimethoxyisoflavone (**14**). A soln of 200 mg of **14**[22] in 80 ml benzene was irradiated with a 100 W high-pressure mercury lamp under N_2 for 14 hr. TLC and IR analyses of the photolysate revealed that most of the starting material was recovered unchanged.

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