Methyl Derivatives of Tetrahydrobenzo- and Benzofurocoumarins, a New Class of Potential Photoreagents Toward DNA

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A number of new tetracyclic furocoumarin derivatives with a linear structure or with various angular arrangements, were synthetized. The new compounds are characterized for having an additional cyclohexene or phenyl ring condensed at the 4',5' double bond of the furan ring of the furocoumarin nucleus. The syntheses were performed starting from the appropriate hydroxycoumarins on which the tetrahydrobenzofuran or benzofuran moiety was built. Methyl groups have been introduced into positions which look most promising for enhancement of the photoreactivity of the compounds toward DNA.

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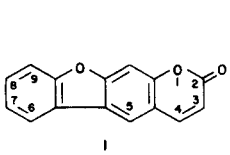
Introduction.

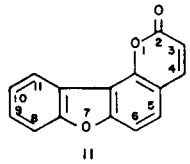
Extensive photochemical and photobiological studies have been performed to date mainly on two series of furocoumarins, that is on psoralens (see for reviews: [2-4]) and, more recently, angelicins [5-8].

Other furocoumarins with a modified annulation geometry [9] as well as coumarins exhibiting a different molecular arrangement, such as naphtocoumarins [10] and pyridopsoralens [11], are under investigation.

Owing to our interest for drug molecules able to photoreact with DNA and their connected biological activity, we planned to prepare a new series of tetracyclic furocoumarin derivatives. These new compounds derive from the condensation of a cyclohexene or phenyl ring at the 4',5' double bond of the furan ring of the furocoumarin nucleus and may have both a linear psoralen-like geometry I, or angular structures II, III and



I



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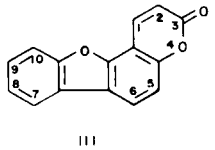
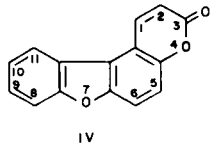


III



IV

IV, related to that of angelicin, of allopsoralen and of isopseudopsoralen, respectively. Methyl groups have been introduced on those positions which among the psoralens and angelicins series, appeared to enhance the photoreactivity fo the molecules [3,5,8].

Results and Discussion.

Generally, the synthetic pathway followed by MacLeod *et al.* [12] to obtain the unsubstituted tetrahydrobenzopsoralen (6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one) **(9)** and benzopsoralen (2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one) **(13)**, has been employed to prepare the methyl derivatives of tetrahydrobenzo- and benzofurocoumarins with various molecular arrangement, as illustrated by the formulae I and IV.

The appropriate methylhydroxycoumarins were condensed with 2-bromocyclohexanone and the corresponding ethers were cyclized in alkaline medium obtaining

Scheme I

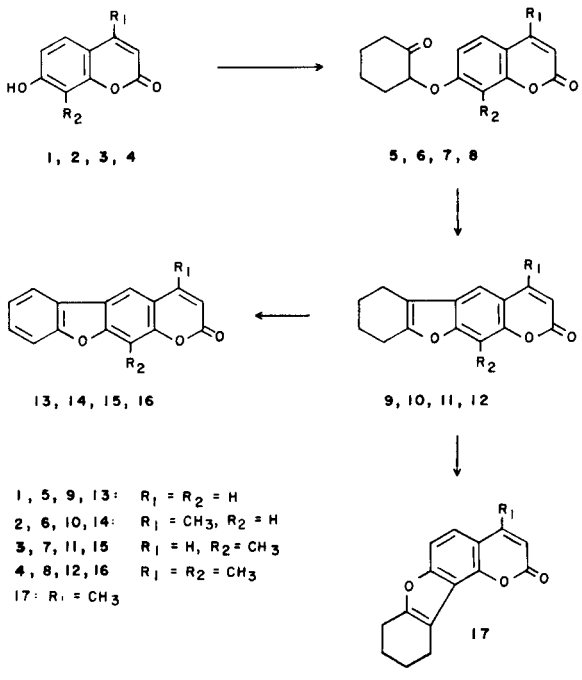


Table I

^{1}H-NMR of Various Tetrahydrobenzofurocoumarins

Psoralen Type

Compound	3	4	5	11	6 and 9	7 and 8	4-Me	11-Me
9	6.26 d J = 9.6	7.70 d J = 9.6	7.21 [a] s	7.32 [a] s	2.80-2.44 m	2.09-1.69 m	—	—
10	6.21 q J = 1.2	—	7.51 [a] s	7.32 [a] s	2.83-2.52 m	2.08-1.77 m	2.48 d J = 1.2	—
11	6.31 d J = 9.5	7.74 d J = 9.5	7.26 s	—	2.87-2.48 m	2.05-1.72 m	—	2.56 s
12	6.13 q J = 1.3	—	7.27 s	—	2.84-2.36 m	2.06-1.72 m	2.41 d J = 1.3	2.47 s

Angelicin Type

Compound	3	4	5	8 and 11	9 and 10	4-Me	6-Me
22	6.32 d J = 9.5	7.73 d J = 9.5	7.04 broad s	3.11-2.63 m	2.00-1.73 m	—	2.51 d J = 0.5
23	6.17 q J = 1.2	—	7.13 broad s	3.07-2.68 m	2.05-1.73 m	2.44 d J = 1.2	2.50 broad s

Isopseudopsoralen Type

Compound	2	5	8 and 11	9 and 10	1-Me	6-Me
28	6.19 q J = 1.2	7.02 broad s	2.99-2.71 m	2.15-1.73 m	2.64 d J = 1.2	2.54 broad s

Allopsoralen Type

Compound	2	5	7 and 10	8 and9	1-Me	6-Me
32	6.15 q J = 1.2	6.90 q J = 0.7	2.90-2.62 m	1.97-1.77 m	2.69 d J = 1.2	2.59 d J = 0.7

[a] May be interchanged

the desired tetrahydrobenzofurocoumarins. Treatment of the tetrahydrobenzofurocoumarins with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene solution yielded the corresponding benzofurocoumarins.

In particular, the synthesis of methyl derivatives of tetrahydrobenzopsoralen and benzopsoralen was performed starting from 7-hydroxycoumarins, with methyl groups in the 4- and/or 8- position (Scheme I). Thus 4-methyltetrahydrobenzopsoralen (**10**), 11-methyltetrahydrobenzopsoralen (**11**) and 4,11-dimethyltetrahydrobenzopsoralen (**12**), were synthesized, which gave the corresponding benzofurocoumarins **14, 15, 16** by dehydrogenation.

As expected [12,14], cyclization of the 2'-oxocyclohexenyl ethers of the 7-hydroxycoumarins, yielded almost exclusively the linearly annulated furocoumarins (psoralen type, I), indicating that the 6-position, *para* to the coumarinate ion, is strongly activated, with respect to the 8 position, *ortho* to the coumarinate ion.

Scheme II

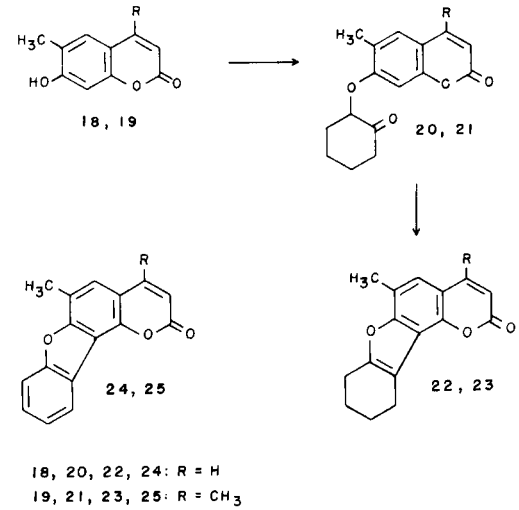


Table II

H-NMR of Various Benzofurocoumarins

Psoralen Type

Compound	3	4	5	11	6, 7 and 8	9	4-Me	11-Me
13	6.38 d J = 9.5	7.81 d J = 9.5	7.45 [a] s	7.95 [a] s	7.99-7.25 m	8.00-7.85 m	—	—
14	6.25 q J = 1.1	—	7.43 [a] s	8.05 [a] s	7.60-7.25 m	8.00-7.85 m	2.53 d J = 1.1	—
15	6.39 d J = 9.5	7.84 d J = 9.5	7.83 s	—	7.96-7.29 m	8.00-7.85 m	—	2.66 s
16	6.24 q J = 1.3	—	7.89 s	—	7.60-7.21 m	8.00-7.85 m	2.51 d J = 1.3	2.61 s

Angelicin Type

Compound	3	4	5	8	9, 10 and 11	4-Me	6-Me
24	6.39 d J = 9.5	7.77 d J = 9.5	7.30 broad s	8.44-8.33 m	7.66-7.39 m	—	2.61 broad s
25	6.12 d J = 1.2	—	7.20 q J = 0.9	8.30-8.17 m	7.56-7.22 m	2.35 d J = 1.2	2.46 d J = 0.9

Isopseudopsoralen Type

Compound	2	5	8	9, 10 and 11	1-Me	6-Me
29	6.33 q J = 1.2	7.27 broad s	8.82-8.28 m	7.69-7.32 m	2.93 d J = 1.2	2.63 d J = 0.6

Allopsoralen Type

Compound	2	5	7, 8 and 9	10	1-Me	6-Me
33	6.14 q J = 1.2	6.87 q J = 0.8	7.64-7.21 m	7.96-7.80 m	2.71 d J = 1.2	2.70 d J = 0.8

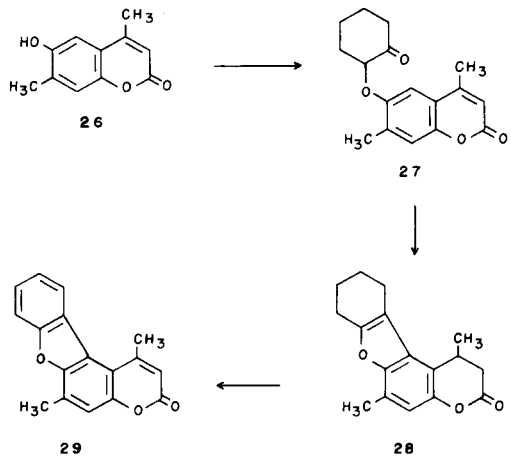
[a] May be interchanged

However, trace amounts of the angular angelicin type isomers II were observed in the crude products (tlc, ^{1}H nmr) and during the preparation of 4-methyltetrahydrobenzopsoralen (**10**) a slight amount of the isomer, 4-methyltetrahydrobenzoangelicin (**17**) was isolated and characterized.

Accordingly, the synthesis of methyl derivatives of tetrahydrobenzoangelicin (8,9,10,11-tetrahydro-2*H*-benzofuro-[2,3-*h*]-1-benzopyran-2-one), **22** and **23** and benzoangelicin (2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one), **24** and **25**, (structure II) started from 7-hydroxycoumarins containing at least one methyl group in the 6 position; in this case, however, yields of the cyclization reaction appeared to be lowered, even using longer reaction times.

The tetrahydrobenzoallopsoralen derivative (7,8,9,10-tetrahydro-3*H*-benzofuro[3,2-*f*][1]benzopyran-3-one), **32**, (structure III) was obtained starting from 4,7-dimethyl-5-hydroxycoumarin (Scheme IV); owing to the fact that also in this case the position *para* to coumarinate ion is involved, the cyclization gave in high yield the desired product.

Scheme III



The dimethyl derivative of tetrahydroisopseudopsoralen (8,9,10,11-tetrahydro-3*H*-benzofuro[2,3-*f*][1]benzopyran-3-one), **28**, (structure IV), was obtained by cyclization of

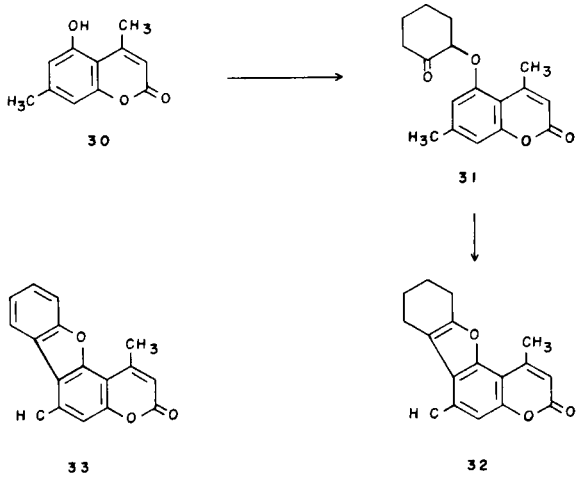
4,7-dimethyl-6-(2'-oxocyclohexyloxy)coumarin (Scheme III) in boiling diethylaniline; any attempt, in fact, to cyclize this compound in alkaline medium lead to complete decomposition.

By the above outlined synthetic pathways the following new tetrahydrobenzo- and benzofurocoumarins were synthesized:

11-methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*][1]-benzopyran-2-one (**11**); 4,11-dimethyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*][1]benzopyran-2-one (**12**); 6-methyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**22**); 4,6-dimethyl-8,9,10,11-tetrahydro-2*H*-benzofuro-[2,3-*h*]-1-benzopyran-2-one (**23**); 1,6-dimethyl-8,9,10,11-tetrahydro-3*H*-benzofuro[3,2-*f*][1]benzopyran-3-one (**28**); 1,6-dimethyl-7,8,9,10-tetrahydro-3*H*-benzofuro[2,3-*f*][1]-benzopyran-3-one (**32**); 4-methyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**14**); 11-methyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**15**); 4,11-dimethyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**16**); 6-methyl-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**24**); 4,6-dimethyl-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**25**); 1,6-dimethyl-3*H*-benzofuro[3,2-*f*]-[1]benzopyran-3-one (**29**); and 1,6-dimethyl-3*H*-benzofuro-[2,3-*f*][1]benzopyran-3-one (**33**).

We finally also report the synthesis of the already described compounds: 6,7,8,9-tetrahydro-2*H*-benzofuro-[3,2-*g*]-1-benzopyran-2-one (**9**), 2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**13**) [12] and 4-methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**10**) [13], for comparison purpose as well as to have their complete characterization.

Scheme IV



EXPERIMENTAL

Melting points (uncorrected) were determined using a Büchi-Tottoli SPM-20 capillary melting point apparatus. Analytical thin layer chromatography (tlc) was performed on pre-coated silica gel plates 60-F-254 (Merck; 0.25 mm), developing with ethyl acetate-cyclohexane mixture (35:65). Preparative column chromatography was performed using silica gel (Merck; 0.063-0.200 mm). The ^{1}H-nmr spectra were recorded on a Varian FT-80A spectrometer with TMS as internal standard and deuteriochloroform as solvent, coupling constants are given in Hz; the relative peak areas and the decoupling experiments were in agreement with all assignments.

Methylcoumarins *O*-(2'-Oxocyclohexyl) Ethers **5**, **6**, **7**, **8**, **20**, **21**, **27**, **31**.

A solution of 4-methyl-7-hydroxycoumarin (**2**) (3.2 g, 18.5 mmoles) in 120 ml of acetone was reacted with 2-bromocyclohexanone (5.4 g, 30.4 mmoles) in the presence of anhydrous potassium carbonate (6.0 g) by refluxing the mixture for 20 hours. After chilling the potassium carbonate was filtered off and washed with fresh acetone. The pooled filtrate and acetone washings were concentrated to dryness and the residue crystallized from methanol giving 3.1 g (61%) of 4-methyl-7-(2'-oxocyclohexyloxy)coumarin (**6**), mp 167°; nmr: δ 1.69-2.64 (m, -$(CH_2)_4$-, 8H), 2.37 (d, Me-4, 3H, $J_{4Me,3}$ = 1.2), 4.61-4.88 (m, =CH-O-, 1H), 6.10 (q, H-3, 1H, $J_{3,4Me}$ = 1.2), 6.69 (d, H-8, 1H, $J_{8,6}$ = 2.5), 6.83 (dd, H-6, 1H, $J_{6,5}$ = 8.7 and $J_{6,8}$ = 2.5), 7.47 (d, H-5, 1H, $J_{5,6}$ = 8.7).

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.54; H, 5.86.

The following 2'-oxocyclohexyl ethers were obtained in an analogous manner.

7-(2'-Oxocyclohexyloxy)coumarin (**5**).

This compound was prepared from 7-hydroxycoumarin (**1**) mp 171° (methanol, 64%) (reported [12] 169-170°); nmr: δ 1.65-2.64 (m, -$(CH_2)_4$-, 8H), 4.60-4.84 (m, =CH-O-, 1H), 6.23 (d, H-3, 1H, $J_{3,4}$ = 9.6), 6.68 (d, H-8, 1H, $J_{8,6}$ = 2.4), 6.81 (dd, H-6, 1H, $J_{6,5}$ = 8.4 and $J_{6,8}$ = 2.4), 7.35 (d, H-5, 1H, $J_{5,6}$ = 8.4), 7.62 (d, H-4, 1H, $J_{4,3}$ = 9.6).

7-(2'-Oxocyclohexyloxy)-8-methylcoumarin (**7**).

This compound was prepared from 7-hydroxy-8-methylcoumarin (**3**) mp 171° (methanol, 69%); nmr: δ 2.36 (s, Me-8, 3H), 1.58-2.68 (m, -$(CH_2)_4$-, 8H), 4.54-4.80 (m, =CH-O-, 1H), 6.23 (d, H-3, 1H, $J_{3,4}$ = 9.4), 6.59 (d, H-6, 1H, $J_{6,5}$ = 8.6), 7.20 (d, H-5, 1H, $J_{5,6}$ = 8.6), 7.59 (d, H-4, 1H, $J_{4,3}$ = 9.4).

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.48; H, 5.89.

4,8-Dimethyl-7-(2'-oxocyclohexyloxy)coumarin (**8**).

This compound was prepared from 4,8-dimethyl-7-hydroxycoumarin (**4**) mp 178° (methanol, 62%); nmr: δ 2.36 (d, Me-4, 3H, $J_{4Me,3}$ = 1.1), 1.56-2.60 (m, -$(CH_2)_4$-, 8H), 2.37 (s, Me-8, 3H), 4.57-4.84 (m, =CH-O-, 1H), 6.12 (q, H-3, 1H, $J_{3,4Me}$ = 1.1), 6.62 (d, H-6, 1H, $J_{6,5}$ = 8.8) 7.32 (d, H-5, 1H, $J_{5,6}$ = 8.8).

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.19; H, 6.36.

6-Methyl-7-(2'-oxocyclohexyloxy)coumarin (**20**).

This compound was prepared from 6-methyl-7-hydroxycoumarin (**18**) mp 207° (methanol, 57%); nmr: δ 2.29 (broad s, Me-6, 3H), 1.58-2.64 (m, -$(CH_2)_4$-, 8H), 4.61-4.85 (m, =CH-O-, 1H), 6.21 (d, H-3, 1H, $J_{3,4}$ = 9.5), 6.51 (s, H-8, 1H), 7.21 (broad s, H-5, 1H), 7.58 (d, H-4, 1H, $J_{4,3}$ = 9.5).

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.52; H, 5.87.

4,6-Dimethyl-7-(2'-oxocyclohexyloxy)coumarin (**21**).

This compound was prepared from 4,6-dimethyl-7-hydroxycoumarin (**19**) mp 189° (methanol, 56%); nmr: δ 2.30 (broad s, Me-6, 3H), 2.36 (d, Me-4, 3H, $J_{4Me,3}$ = 1.2), 1.69-2.68 (m, -$(CH_2)_4$-, 8H), 4.57-4.84 (m, =CH-O-, 1H), 6.08 (q, H-3, 1H, $J_{3,4Me}$ = 1.2), 6.51 (s, H-8, 1H), 7.31 (q, H-5, 1H, $J_{5,6Me}$ = 0.7).

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.26; H, 6.29.

4,7-Dimethyl-6-(2'-oxocyclohexyloxy)coumarin (**27**).

This compound was prepared from 4,7-dimethyl-6-hydroxycoumarin (**26**) mp 176° (methanol, 36%); nmr: δ 2.35 (d, Me-4, 3H, $J_{4\text{-}Me,3}$ = 1.1), 2.36 (d, Me-7, 3H, $J_{7Me,8}$ = 0.7), 1.50-2.64 (m, -$(CH_2)_4$-, 8H), 4.45-4.68 (m, =CH-O-, 1H), 6.20 (q, H-3, 1H, $J_{3,4Me}$ = 1.1), 6.81 (s, H-5, 1H), 7.12 (q,

H-8, 1H, $J_{8,7Me}$ = 0.7).

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.19; H, 6.27.

4,7-Dimethyl-5-(2'-oxocyclohexyloxy)coumarin (**31**).

This compound was prepared from 4,7-dimethyl-5-hydroxycoumarin (**30**) mp 174° (methanol, 56%); nmr: δ 2.33 (broad s, Me-7, 3H), 2.61 (d, Me-4, 3H, $J_{4Me,3}$ = 1.2), 1.65-2.68 (m, -$(CH_2)_4$-, 8H), 4.69-4.92 (m, =CH-O-, 1H), 6.05 (q, H-3, 1H, $J_{3,4Me}$ = 1.2), 6.27 (dq, H-6, 1H, $J_{6,8}$ = 1.4 and $J_{6,7Me}$ = 0.5), 6.73 (dq, H-8, 1H, $J_{8,6}$ = 1.4 and $J_{8,7Me}$ = 0.7).

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.18; H, 6.24.

Tetrahydrobenzofurocoumarins **9, 10, 11, 12, 17, 22, 23, 28, 32.**

4-Methyl-7-(2'-oxocyclohexyloxy)coumarin (**6**) (2.0 g, 7.3 mmoles) was dissolved in 700 ml of a 1*N* sodium hydroxide solution and was refluxed under nitrogen in the dark. The reaction was stopped when the reaction mixture appeared to be devoid of the starting product (tlc). After cooling, the reaction mixture was acidified with dilute hydrochloric acid and the precipitate obtained was filtered, washing it several times with water and dryed under vacuum. The crude product was crystallized from methanol obtaining 1.35 g (72%) of pure 4-methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**10**), mp 189° (reported [13] 160°); ^{1}H-nmr (see Table I).

From the residue of the mother liquors chromatographed on a silica gel column, eluting by chloroform, the angular isomer 4-methyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**17**) was isolated uncrystallized; nmr: δ 1.77-2.05 (m, H-9 and H-10, 4H), 2.47 (d, Me-4, 3H, $J_{4Me,3}$ = 1.2), 2.56-3.19 (m, H-8 and H-11, 4H), 6.22 (q, H-3, 1H, $J_{3,4Me}$ = 1.2), 7.32 (d, H-6, 1H, $J_{6,5}$ = 8.5), 7.38 (d, H-5, 1H, $J_{5,6}$ = 8.5).

In the same way the following tetrahydrobenzofurocoumarins were obtained:

6,7,8,9-Tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**9**).

This compound was prepared from 7-(2'-oxocyclohexyloxy)coumarin (**5**) mp 160° (reported [12] 148-150°) (methanol, 68%); ^{1}H-nmr (see Table I).

11-Methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**11**).

This compound was prepared from 7-(2'-oxocyclohexyloxy)-8-methylcoumarin (**7**) mp 182° (methanol, 59%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.51; H, 5.53.

4,11-Dimethyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**12**).

This compound was prepared from 4,8-dimethyl-7-(2'-oxocyclohexyloxy)coumarin (**8**) mp 198° (methanol, 56%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 75.98; H, 6.00.

6-Methyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**22**).

This compound was prepared from 6-methyl-7-(2'-oxocyclohexyloxy)-coumarin (**20**) mp 179° (methanol, 38%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.02; H, 5.98.

4,6-Dimethyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*][1]benzopyran-2-one (**23**).

This compound was prepared from 4,6-dimethyl-7-(2'-oxocyclohexyloxy)coumarin (**21**). In this case, however, by acidification no precipitate was obtained. The reaction mixture was then extracted several times with ethyl acetate, the solvent was evaporated from the dryed (sodium sulphate) organic phase and the residue chromatographed on a silica gel column, eluting with chloroform, giving the pure **23**, mp 161° (methanol, 26%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 75.92; H, 6.04.

1,6-Dimethyl-7,8,9,10-tetrahydro-3*H*-benzofuro[2,3-*f*][1]benzopyran-3-one (**32**).

This compound was prepared from 4,7-dimethyl-5-(2'-oxocyclohexyloxy)coumarin (**31**) mp 210° (methanol, 64%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.14; H, 6.00.

For the cyclization of 4,7-dimethyl-6-(2'-oxocyclohexyloxy)coumarin (**27**), the cyclohexyl ether was dissolved in *N,N*-diethylaniline and the solution refluxed for 48 hours. After cooling, ethyl acetate was added and the mixture was washed several times with dilute hydrochloric acid and then with water. The solvent was evaporated from the dryed (sodium sulphate) organic phase and the residue chromatographed on a silica gel column eluting with chloroform. From the pooled fractions containing a single spot (tlc) the solvent was evaporated and the residue was crystallized from methanol giving 1,6-dimethyl-8,9,10,11-tetrahydro-3*H*-benzofuro[3,2-*f*][1]benzopyran-3-one (**28**), mp 255° (8%); ^{1}H-nmr (see Table I).

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 75.99; H, 5.97.

Benzofurocoumarins (**13, 14, 15, 16, 24, 25, 29, 33**).

A solution of 4-methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**10**) (0.95 g, 3.7 mmoles) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.7 g, 7.5 mmoles) in 300 ml of benzene was refluxed for 20 hours. After cooling, the solid was filtered off and the solution was concentrated to dryness. The residue was chromatographed on silica gel column eluting with chloroform. From the pooled fractions containing a pure product (tlc), the solvent was evaporated and the residue crystallized from methanol giving 4-methyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**14**) (0.42 g, 49%), mp 224°; ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.82; H, 4.01.

Analogously the following benzofurocoumarins were obtained:

2*H*-Benzofuro[3,2-*g*]-1-benzopyran-2-one (**13**).

This compound was prepared from 6,7,8,9-tetrahydro-2*H*-benzofuro-[3,2-*g*]-1-benzopyran-2-one (**9**) mp 207° (reported [12] 202-203°) (methanol, 74%); ^{1}H-nmr (see Table II).

11-Methyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**15**).

This compound was prepared from 11-methyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**11**) mp 224° (methanol, 50%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.68; H, 3.99.

4,11-Dimethyl-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**16**).

This compound was prepared from 4,11-dimethyl-6,7,8,9-tetrahydro-2*H*-benzofuro[3,2-*g*]-1-benzopyran-2-one (**12**) mp 221° (methanol, 36%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.31; H, 4.60.

6-Methyl-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**24**).

This compound was prepared from 6-methyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**22**) mp 194° (methanol, 54%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.61; H, 3.98.

4,6-Dimethyl-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**25**).

This compound was prepared from 4,6-dimethyl-8,9,10,11-tetrahydro-2*H*-benzofuro[2,3-*h*]-1-benzopyran-2-one (**23**) mp 227° (methanol, 66%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.21; H, 4.57.

1,6-Dimethyl-3*H*-benzofuro[3,2-*f*][1]benzopyran-3-one (**29**).

This compound was prepared from 1,6-dimethyl-8,9,10,11-tetrahydro-3*H*-benzofuro[3,2-*f*][1]benzopyran-3-one (**28**) mp 231° (methanol, 43%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.19; H, 4.51.

1,6-Dimethyl-3*H*-benzofuro[2,3-*f*][1]benzopyran-3-one (**33**).

This compound was prepared from 1,6-dimethyl-7,8,9,10-tetrahydro-3*H*-benzofuro[2,3-*f*][1]benzopyran-3-one (**32**) mp 238° (methanol, 43%); ^{1}H-nmr (see Table II).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.07; H, 4.43.

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