Reaction of β-Arylidennaphthylamines with 4-Hydroxycoumarin. A Correction in Structural Assignment of The Product. III.

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The reaction of 4-hydroxycoumarin with β-arylidennaphthylamines constitutes a convenient synthetic route to the hitherto unknown 2*H*-benzo[*f*][1]benzopyrano[4,3-*b*]quinolin-2-one, **VI**. The X-ray crystallography data conform with the present benzopyrano[4,3-*b*]quinolin-2-one ring system and disprove the benzopyrano[3,4-*c*]quinolin-2-one structure previously assigned for such reaction products.

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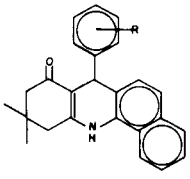
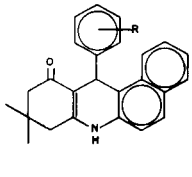
As a part of a program directed towards the synthesis and spectral property determination of heterocyclic derivatives with possible pharmacological activity we have reported recently that the dimedone addition to α- or β-arylidennaphthylamines [3,4] affords the benz[*c*]acridin-8-ones or the benz[*a*]acridin-11-ones, **I** and **II**, (Scheme 1) respectively, instead of the benzophenanthren-4-ones **III** and **IV** (Scheme 2). These findings have been rationalized in terms of the existence of a Hoffman-Martius type rearrangement [5] in these reactions.

Scheme 1

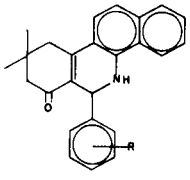


I

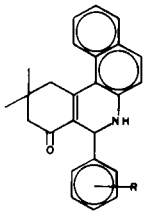


II

Scheme 2



III



IV

Since Lielbriedis [6] has reported also that the addition of 4-hydroxycoumarin to β-arylidennaphthylamines yields the benzopyrano[3,4-*c*]quinolin-2-ones **V** (Scheme 3), it was deemed of interest to study this reaction and examine the results in the light of those obtained when dimedone was added to the same intermediate.

Treatment of β-arylidennaphthylamines with 4-hydroxycoumarin in refluxing ethanol afforded a mixture of two products, **VI** and **VII** (Scheme 3). This mixture was separated by fractional crystallization. The major compound obtained, **VI**, displayed characteristic ir absorptions (nujol) at 1663, 1528 typical of vinylogous urethanes [7], 1490 and 3309 cm^{-1} typical of secondary amines (Table 1).

Scheme 3

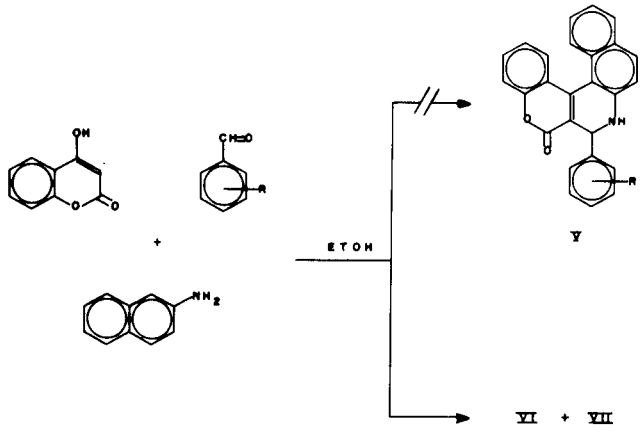


Table 1

Physical and Spectral Data for Compounds VI

Compound No.	R	Mp°C	Yield %	Molecular Formula	IR (nujol) cm-1
a	H	> 300	32	$C_{26}H_{17}NO_2$	3307, 1663,1528
b	*o*-OMe	> 300	49	$C_{27}H_{19}NO_3$	3309, 1664, 1527
c	*o*-Cl	409-410	40	$C_{26}H_{16}NO_2Cl$	3290, 1670, 1527
d	*o*-Me	> 300	27	$C_{27}H_{19}NO_2$	3301, 1668, 1528
e	*o*-Br	> 300	35	$C_{26}H_{16}NO_2Br$	3302, 1673, 1528
f	*o*-NO_2	> 300	27	$C_{26}H_{16}N_2O_4$	3313, 1659, 1528
g	*p*-OMe	373-375	28	$C_{27}H_{19}NO_3$	3320, 1670, 1528
h	*p*-Me	> 300	26	$C_{27}H_{19}NO_2$	3308, 1660, 1528
i	*p*-Br	378-380	28	$C_{26}H_{16}NO_2Br$	3310, 1657, 1528

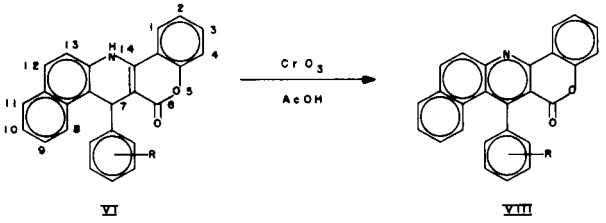
However, the ^{1}H-nmr data of these compounds could not be obtained due to their insolubility in the solvents normally used for these analyses. Therefore, we took recourse by oxidizing the compounds **VI** with chromic anhydride in acetic acid and were thereby able to obtain more structural information. The ir spectra (chloroform) for the oxidized product **VIII** (Scheme 4) exhibited a strong δ-lactone carbonyl band at 1728-1746 cm^{-1} [8]. Its ^{1}H-nmr spectrum showed a doublet of doublets at δ 8.75 (J = 10 Hz, 1

Table 2
Physical and Spectral Data for Compounds VIII

Compound No.	R	Mp°C	Yield %	Molecular Formula	Analyses % C	Analyses % H	Spectral Data
a	H	275-277	73	$C_{26}H_{15}NO_2$	83.63 (83.41)	4.04 (4.00)	ir (chloroform): 1746, 1538 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.8 (dd, J = 10, 1 Hz, 1H) 8.1-6.91 (m, 14 H) ms: M^+ at m/z 373
b	*o*-OMe	> 295	30	$C_{27}H_{17}NO_3$	80.38 (80.10)	4.24 (4.20)	ir (chloroform): 1728, 1526 cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.75 (dd, J = 10, 1 Hz, 1H) 8.2-6.8 (m, 13 H), 3.9 (s, 3H)
c	*o*-Cl	277	70	$C_{26}H_{14}ClNO_2$	76.56 (76.50)	3.45 (3.42)	ir (chloroform): 1747, 1539, cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.8 (dd, J = 10, 1 Hz, 1H) 8.3-6.7 (m, 13 H); ms: M^+ at m/z 407
d	*o*-Me	263	77	$C_{27}H_{17}NO_2$	83.70 (83.60)	4.42 (4.40)	ir (chloroform): 1747, 1537, cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.82 (dd, J = 10, 1 Hz, 1H) 8.1-6.9 (m, 13 H), 2.4 (s, 3H)
e	*o*-Br	270	79	$C_{26}H_{14}BrNO_2$	69.04 (68.96)	3.12 (3.10)	ir (chloroform): 1747, 1539, cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.7 (dd, J = 10, 1 Hz, 1H) 8.2-6.8 (m, 13 H); ms: M^+ at m/z 451
f	*o*-NO_2	> 295	26	$C_{26}H_{14}N_2O_4$	74.63 (74.60)	3.37 (3.31)	ir (chloroform): 1728, 1526 cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.8 (dd, J = 10, 1 Hz, 1H) 8.7-7.1 (m, 13H)
g	*p*-OMe	248	72	$C_{27}H_{17}NO_3$	80.38 (80.15)	4.24 (4.19)	ir (chloroform): 1744, 1537 cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.7 (dd, J = 10, 1 Hz, 1H) 8.1-6.8 (m, 13 H), 4.0 (s, 3H); ms: M^+ at m/z 403
h	*p*-Me	240	70	$C_{27}H_{17}NO_2$	83.70 (83.62)	4.42 (4.38)	ir (chloroform): 1745, 1538 cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.8 (dd, J = 10, 1 Hz, 1H) 8.1-6.9 (m, 13 H), 2.35 (s, 3H)
i	*p*-Br	> 295	30	$C_{26}H_{14}BrNO_2$	69.04 (68.92)	3.12 (3.06)	ir (chloroform): 1745, 1537 cm^{-1}; ^1H nmr (deuteriochloroform)): δ 8.7 (dd, J = 10, 1 Hz, 1H) 8.0-6.7 (m, 13 H)

Hz) assigned to the proton at C-8 [9]. The signal for the aromatic protons appeared between δ 7.1-8 (Table 2).

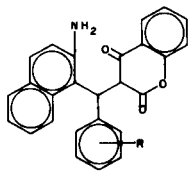
Scheme 4



Definitive evidence for the structure of the compounds **VI** and **VIII** was obtained by single-crystal X-ray diffraction analysis of compound **VIIIg**. Figure 1 shows a perspective view and atom labelling of **VIIIg**. The bond lengths and bond angles are shown in Tables 3 and 4. The pyranone ring can be described as a "flattened sofa" with the bond C(11)-O(1) protruding out of the plane. All other individual rings are essentially planar within the experimental error, nevertheless, the entire benzopyranobenzo-[*f*]quinolin-2-one ring system deviates significantly from planarity. The two "best" mean planes are defined through the naphthalene and the benzopyranopyridine rings. These exhibit a dihedral angle of 21.0 (6)°. The *p*-methoxyphenyl group at C-7 is situated nearly perpendicular, 68.6(6)° and 61.5(6)0 angles to the above-mentioned planes, to the remainder of the structure. The most interesting feature of the crystallographic data is, however, that they correspond to the structure of the benzopyrano[4,3-*b*]quinolin-2-one, **VIII**, and not to the benzopyrano[3,4-*c*]quinolin-2-one, **V** (Scheme 3). As shown by investigations of the mechanism of the reaction of an β-arylidennaphthylamine with dimedone [3,4], this reaction may take place through a Hoffman-Martius type rearrangement. Therefore, the formation of compounds **VI** instead of the compounds **V** is consistent with the presence of an intermediate **IX** proposed in the reaction of β-arylidennaphthylamines with 4-hydroxycoumarin.

Table 3
Bond lengths (Å)

C(1)-C(2)	1.399(3)	C(1)-C(10b)	1.423(3)
C(1)-C(17)	1.494(3)	C(2)-C(3)	1.400(3)
C(2)-C(11)	1.480(4)	C(3)-N(4)	1.338(3)
C(3)-C(16a)	1.452(4)	N(4)-C(4a)	1.347(3)
C(4a)-C(5)	1.437(4)	C(4a)-C(10b)	1.427(3)
C(5)-C(6)	1.338(4)	C(6)-C(6a)	1.424(3)
C(6a)-C(7)	1.408(4)	C(6a)-C(10a)	1.423(4)
C(7)-C(8)	1.366(4)	C(8)-C(9)	1.394(5)
C(9)-C(10)	1.370(4)	C(10)-C(10a)	1.412(3)
C(10a)-C(10b)	1.471(3)	C(11)-O(12)	1.380(3)
C(11)-O(1)	1.199(2)	O(12)-C(12a)	1.383(3)
C(12a)-C(13)	1.384(4)	C(12a)-C(16a)	1.383(4)
C(13)-C(14)	1.376(4)	C(14)-C(15)	1.382(5)
C(15)-C(16)	1.371(4)	C(16)-C(16a)	1.392(3)
C(17)-C(18)	1.391(4)	C(17)-C(22)	1.374(3)
C(18)-C(19)	1.370(3)	C(19)-C(20)	1.387(3)
C(20)-C(21)	1.378(4)	C(20)-O(2)	1.367(3)
C(21)-C(22)	1.388(3)	O(2)-C(23)	1.416(3)



IX

Table 4
Bond angles (degrees)

C(2)-C(1)-C(10b)	117.9(2)	C(2)-C(1)-C(17)	119.0(2)
C(10b)-C(1)-C(17)	123.1(2)	C(1)-C(2)-C(3)	120.3(2)
C(1)-C(2)-C(11)	121.7(2)	C(3)-C(2)-C(11)	117.9(2)
C(2)-C(3)-N(4)	122.2(2)	C(2)-C(3)-C(16a)	119.8(2)
N(4)-C(3)-C(16a)	118.0(2)	C(3)-N(4)-C(4a)	117.8(2)
N(4)-C(4a)-C(5)	115.6(2)	N(4)-C(4a)-C(10b)	124.1(2)
C(5)-C(4a)-C(10b)	120.3(2)	C(4a)-C(5)-C(6)	120.7(2)
C(5)-C(6)-C(6a)	121.4(3)	C(6)-C(6a)-C(7)	119.5(2)
C(6)-C(6a)-C(10a)	120.4(2)	C(7)-C(6a)-C(10a)	119.9(2)
C(6a)-C(7)-C(8)	121.4(3)	C(7)-C(8)-C(9)	119.1(3)
C(8)-C(9)-C(10)	121.0(2)	C(9)-C(10)-C(10a)	121.7(3)
C(6a)-C(10a)-C(10)	116.9(2)	C(6a)-C(10a)-C(10b)	118.3(2)
C(10)-C(10a)-C(10b)	124.7(2)	C(1)-C(10b)-C(10a)	116.3(2)
C(1)-C(10b)-C(10a)	126.1(2)	C(4a)-C(10b)-C(10a)	117.6(2)
C(2)-C(11)-O-(12)	116.9(2)	C(2)-C(11)-O(1)	127.2(3)
O(12)-C(11)-O(1)	115.9(2)	C(11)-O(12)-C(12a)	122.2(2)
O(12)-C(12a)-C(13)	116.4(3)	O(12)-C(12a)-C(16a)	121.1(2)
C(13)-C(12a)-C(16a)	122.4(2)	C(12a)-C(13)-C(14)	118.1(3)
C(13)-C(14)-C(15)	121.2(3)	C(14)-C(15)-C(16)	119.3(2)
C(15)-C(16)-C(16a)	121.4(3)	C(3)-C(16a)-C(12a)	118.6(2)
C(3)-C(16a)-C(16)	123.7(3)	C(12a)-C(16a)-C(16)	117.5(3)
C(1)-C(17)-C(18)	119.7(2)	C(1)-C(17)-C(22)	122.1(2)
C(18)-C(17)-C(22)	118.1(2)	C(17)-C(18)-C(19)	121.1(2)
C(18)-C(19)-C(20)	120.1(3)	C(19)-C(20)-C(21)	119.7(2)
C(19)-C(20)-O(2)	115.4(2)	C(21)-C(20)-O(2)	124.9(2)
C(20)-C(21)-C(22)	119.3(2)	C(17)-C(22)-C(21)	121.7(2)
C(20)-O(2)-C(23)	118.0(2)		

In conclusion, our present findings are contrary to the results reported by Lielbriedis and coworkers who identified the reaction products from the reaction of β-arylidennaphthylamines with 4-hydroxycoumarin, as benzopyrano[3,4-*c*]quinolin-2-ones **V** and not as benzopyrano[4,3-*b*]quinolin-2-ones **VI**. In the present work, compounds **VII** were also obtained, albeit in low yields. Structural elucidation of compounds **VII** are presently being carried out.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nicolet FT-55X spectrophotometer. The ^{1}H nmr spectra were recorded on a Varian FT-80 spectrometer operating at 80 MHz, in deuteriochloroform solution containing tetramethylsilane as the internal standard with chemical shifts (δ) expressed downfield from TMS. Mass spectra were obtained with a Hewlett-Packard 59854-A quadrupole mass spectrometer.

Crystallography.

X-Ray Analysis Data for 7-(*p*-Methoxyphenyl)-2*H*-benzo[*f*][1]benzopyrano[4,3-*b*]quinolin-2-one (**VIIIg**).

The molecular formula is $C_{27}H_{17}NO_3$, M_w = 403, triclinic, space group, $P\bar{1}$, Z = 2, a = 10.397(1), b = 11.907(2), c = 9.039(1)Å, α = 98.82(1)°, β = 109.92(1)°, γ = 68.92(1)°, V = 981.0(2) Å^3, D_x = 1.36 g cm^{-1}, μ(CuKα) = 6.78 cm^{-1}, crystal size *ca.* 0.04 × 0.14 × 0.48 mm (pale yellow). The cell dimensions and intensities were measured on a Nicolet P 3/F automatic diffractometer using Ni-filtered CuKα radiation (λ = 1.54178 Å) with 2469 unique reflections collected and corrected by Lorentz and polarization effects, 2059 were flagged as observed (F ≥ 3σ(F)] and used for structure solution and refinement.

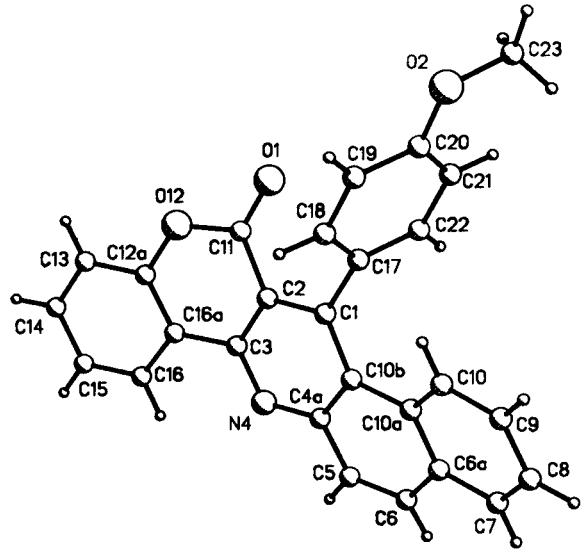


Figure 1

The structure was solved by direct methods and refined by the blocked-cascade least-squares procedure using anisotropic temperature factors for non-H atoms and H-atoms at idealized positions with a fixed isotropic temperature factor (U = 0.06 Å^2). The final discrepancy factors were R = 0.043 and wR = 0.052. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography [10]. All calculations were performed on a NOVA 4S computer using the SHELXTL program package [11].

Reaction of *ortho* and *para*-Substituted-benzaldehydes, β-naphthylamine and 4-hydroxycoumarin. Synthesis of 7-*o* and *p*-Substituted-phenyl-7,14-dihydro-2*H*-benzo[*f*][1]benzopyrano[4,3-*b*]quinolin-2-ones **VIa-i**.

General Procedure.

A mixture of 1.8 × 10^{-3} mole (0.193 g) of benzaldehyde and 1.8 × 10^{-3} mole (0.26 g) of β-naphthylamine in ethanol (10 ml) was stirred under reflux for 24 hours. Then 1.8 × 10^{-3} mole (0.265 g) of 4-hydroxycoumarin in 10 ml of ethanol was added and the mixture heated for 2 hours. The reaction mixture was then allowed to cool. The precipitated product was filtered off and recrystallized from methylene chloride-methanol (7:3) to yield 0.225 g (32%) of **VIa**. The physical and spectral data for the synthesized compounds, **VIa-i**, are recorded in Table 1.

From the mother liquor, after standing for 24 hours, was obtained a colorless solid. Crystallization of this material from

methylene chloride-hexanes gave 0.089 g (13%) of **VIIa**.

The **VIIIa-i** compounds have been prepared from the appropriate dihydroquinolin-2-ones **VIa-i** by chromic anhydride oxidation [3]. The structures of compounds **VIIIa-i** were supported by ir, ^{1}H-nmr, ms and X-ray spectral data. The physical, analytical and spectral data for the synthesized compounds **VIIIa-i** are recorded in Table 2.

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