Linear Furano Compounds: Synthesis of 7*H*-Furo[3,2-g][1]benzopyran-7-ones

Y. GEETANJALI, B. RAJITHA, and M. Kanakalingeswara RAO*
Department of Chemistry, Regional Engineering College, Warangal-506 004 A. P., India
(Received March 18, 1985)

Synopsis. A novel synthesis of 2-aroyl-7*H*-furo[3,2-g]-[1]benzopyran-7-ones, viz., **IIIa** and **b** was reported by condensing 2-benzoyl- and 2-(*p*-methoxybenzoyl)-3-methyl-5-acetyl-6-hydroxybenzofuran (**Ia** and **b**) with $C_6H_5CH_2$-COONa-Ac_2O. **VI** was synthesised by condensing 7-hydroxy-6-benzoyl-4,8-dimethylcoumarin (**IV**) with **V**. The basic ethers (**IIId—j**) were synthesised by demethylating **IIIb** with pyridinehydrochloride and resultant **IIIc** was condensed with *N,N*-dialkyl-2-haloalkanamine hydrochlorides. UV, IR, ^{1}H NMR, and Mass spectral data are also given.

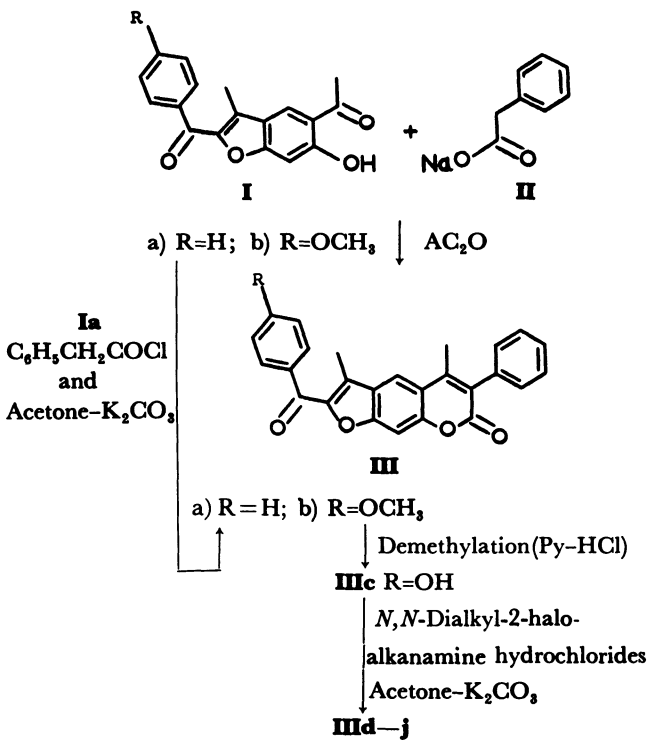
2-(*p*-Hydroxybenzoyl)benzofuran,[1] 2-(*p*-hydroxybenzoyl)-3-ethylbenzofuran,[1] unsubstituted -7*H*-furo-[3,2-g][1]benzopyran-7-one, psoralene[2] and substituted -7*H*-furo[3,2-g][1]benzopyran-7-ones,[3] viz., 3-[*p*-(2-dimethylamino-1-methylethoxy)phenyl]-, 3-[*p*-[2-(diethylamino)ethoxy]phenyl]-, and 3-[*p*-(3-piperidinopropoxy)-phenyl]-substituted 2-phenyl-9-methyl-7*H*-furo-[3,2-g][1]benzopyran-7-ones have shown antifertility activity. The antifertility activity of these compounds is attributed to the presence of *p*-hydroxybenzoyl group and *p*-[2-(dialkylamino)alkoxy]-benzoyl and *p*-[2-(dialkylamino)alkoxy]phenyl groups.

Results and Discussion

Based on the above reports, 2-[*p*-[2-(dialkylamino)-alkoxy]-benzoyl]-7*H*-furo[3,2-g][1]benzopyran-7-ones-(**IIId—j**) were synthesised by developing the 2-pyrone ring on 2-benzoyl-and 2-(*p*-methoxybenzoyl)-3-methyl-5-acetyl-6-hydroxybenzofuran(**Ia** and **b**). 2-Benzoyl- and 2-(*p*-methoxybenzoyl)- 3,5-dimethyl-6-phenyl-7*H*-furo-[3,2-g][1]benzopyran-7-ones(**IIIa** and **b**) were synthesised to study structure and antifertility activity relationships.† **IIIa** and **b** were synthesised by refluxing a mixture of **Ia** and **b**, $C_6H_5CH_2COONa$ and Ac_2O at 180°C for 20—22 h in 70 and 80% yields. This method provides a convenient synthetic route for the synthesis of -7*H*-furo[3,2-g] [1]benzopyran-7-ones **IIIa** and **b** (Scheme 1). **IIIa** was also synthesised in 50% yield by refluxing a mixture of **Ia** with phenylacetyl chloride and freshly baked K_2CO_3 in dry acetone. **IIIb** was demethylated with pyridine hydrochloride to give 2-(*p*-hydroxybenzoyl)-3,5-dimethyl-6-phenyl-7*H*-furo[3,2-g][1]benzopyran-7-one(**IIIc**). **IIIc** was then, condensed with a number of *N,N*-dialkyl-2-haloalkanamine hydrochlorides in 1:1 mol ratio, and freshly baked K_2CO_3 in dry acetone for 20—22 h to give **IIId—j** (Scheme 1) in 60 to 70% yield.

2-Benzoyl-3-phenyl-5,9-dimethyl-7*H*-furo[3,2-g][1]-benzopyran-7-one(**VI**) (Scheme 2) was synthesised by condensing 7-hydroxy-6-benzoyl-4,8-dimethylcoumarin-(**IV**) with ω-bromoacetophenone (**V**) in 1:1 mol ratio freshly baked K_2CO_3 in dry acetone for 12 h (Scheme 2). The spectral data is summarized in Table 1. All the

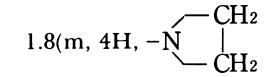
†Antifertility activity is reported elsewhere.



Scheme 1.

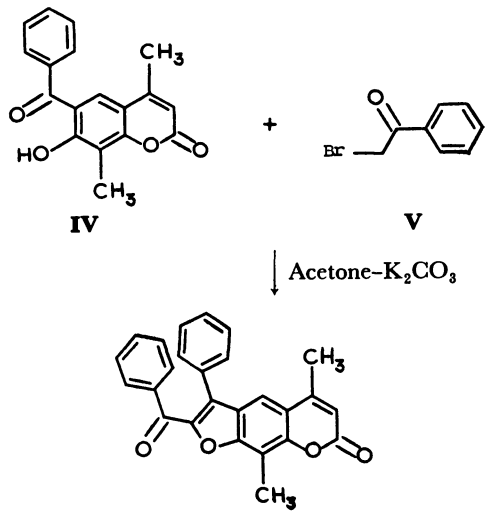
compounds exhibited two distinct UV absorption maxima in the region λ 288—292 nm and 355—358 nm. The IR spectra of these compounds have shown a lactone carbonyl group absorption at 1705—1720 cm^{-1} and an aroyl carbonyl group absorption at 1620—1630 cm^{-1}. The linear nature of the compounds **IIIa, b, d,** and **g** is confirmed by the observation of two singlets for the protons C_4 and C_9 in the ^{1}H NMR spectra of these compounds in the region δ 7.88—7.83 and δ 7.48—6.9 respectively. Further, the ^{1}H NMR spectrum, of compound **IIId** displayed two triplets at δ 4.1 and 2.8 respectively for

Table 1. Characterization Data of **IIIa—j** and **VI**

Compd[a-c]	Mp θ_m/°C	Formula	UV[d] λ_{max}/nm (log ε)	IR (KBr) -C=O/cm^{-1} Lactone	IR (KBr) -C=O/cm^{-1} Aroyl	^{1}H NMR ($CDCl_3$) δ (J in Hz)
IIIa	208	$C_{26}H_{18}O_4$,	290(4.23), 355(4.23)	1705	1625	7.98(m, 2H, 2′,6′-H), 7.83(s, 1H, 4-H), 7.35(m, 8H, 6-C_6H_5-H, 3′,4′,5′-H), 7.48(s, 1H, 9-H), 2.62(s, 3H, 5-CH_3), 2.38(s, 3H, 3-CH_3)
IIIb	270	$C_{27}H_{20}O_5$	290(4.48), 355(4.50)	1705	1625	8.25(d, 2H, J=9, 2′,6′-H), 7.88(s, 1H, 4-H), 7.32(m, 5H, 6-C_6H_5-H), 6.95(d, 2H, J=9, 3′,4′-H), 7.18(s, 1H, 9-H), 2.65(s, 3H, 5-CH_3), 2.38(s, 3H, 3-CH_3), 3.95(s, 3H, 4′-OCH_3-H)
IIIc	286	$C_{26}H_{18}O_5$	290(4.87), 358(4.92)	1680	1625	
IIId	110	$C_{30}H_{27}NO_5$	292(4.28), 358(4.36)	1715	1622	7.83(d, 2H, J=9, 2′,6′-H), 7.63(s, 1H, 4-H), 7.13(m, 5H, 6-C_6H_5-H), 6.75(d, 2H, J=9, 3′,5′-H), 7.0(s, 1H, 9-H), 4.1(t, 2H, J=6, -O-CH_2-), 2.8(t, 2H, J=6, -CH_2-N≺), 2.61(s, 3H, 5-CH_3), 2.35(s, 6H, -N-$(CH_3)_2$), 2.30(s, 3H, 3-CH_3)
IIIe	103	$C_{31}H_{29}NO_5$	292(4.74), 355(4.77)	1710	1620	—
IIIf	95—97	$C_{32}H_{31}NO_5$	290(4.30), 355(4.36)	1710	1620	—
IIIg	101	$C_{32}H_{29}NO_5$	290(4.30), 358(4.36)	1715	1625	7.9(d, 2H, J=9, 2′,6′-H), 7.64(s, 1H, 4-H), 7.1(m, 5H, 6-C_6H_5-H), 6.71(d, 2H, J=9, 3′,5′-H), 6.9(s, 1H, 9-H), 4.1(t, 2H, J=6, -O-CH_2-), 2.8—2.74(m, 5H, -CH_2-N≺, 5-CH_3), 2.7—2.2(m, 7H, -N-$(CH_2)_2$), 1.8(m, 4H, 
IIIh	108	$C_{33}H_{31}NO_5$	290(4.42), 355(4.47)	1720	1625	—
IIIi	98	$C_{34}H_{33}NO_5$	292(4.44), 258(4.53)	1720	1625	—
IIIj	105	$C_{32}H_{29}NO_6$	288(4.33), 355(4.91)	1720	1625	—
VI	190—192	$C_{26}H_{18}O_4$	290(4.45), 358(4.50)	1715	1625	—

a) Satisfactory elemental analysis obtained for all the compounds. b) Compounds **IIIa—c** were obtained in 80, 70, and 90% yield, respectively. Compounds **IIId—j** and VI were obtained in 60—65 and 50% yield respectively. c) All the compounds were crystallized from dioxane. d) The UV spectra of compounds **IIIa—f, h, j,** and **IIIg, i** were recorded in chloroform and methanol respectively.

the protons of -O-CH_2- and -CH_2-N≺ of (alkylamino)-alkoxyl group, whereas in the case of compound **IIIg**, the protons of -O-CH_2- have displayed a triplet and the protons of -CH_2-N≺ and C_5-CH_3 groups have been observed as a multiplet in the region δ 2.80—2.74. The mass spectra of compounds **IIIa, b,** and **VI** showed molecular ions M$^+$394(8.1%), M$^+$424(100%), and M$^+$394(1.5%) respectively.



Scheme 2.

Experimental

Melting points of all the compounds **IIIa—j** and **VI** were taken in open capillaries and are uncorrected. UV absorption spectra were taken on Shimadzu UV 240 Ultraviolet Visible spectrophotometer, IR spectra were recorded on Perkin-Elemer spectrophotometer, and ^{1}H NMR spectra on a Varian EM 390-90 MHz NMR spectrophotometer with TMS as an internal standard.

The procedures given below are typical of the general procedure employed.

2-(*p*-Methoxybenzoyl)-3,5-dimethyl-6-phenyl-7*H*-furo[3,2-*g*]-[1]benzopyran-7-one (IIIb). Five ml of Ac_2O was added to an intimate mixture of **Ib** (16.20 g; 0.05 mol) and sodium phenylacetate (15.8 g; 0.1 mol), and the mixture was refluxed in an oil bath at 180° for 24 h. The reaction mixture was cooled and poured onto a crushed ice (5g). The solid obtained was recrystallized from dioxane. Yield: 14 g (70%), Found: C, 76.37; H, 4.65%. Calcd for $C_{27}H_{20}O_5$: C, 76.41; H, 4.71%

2-(*p*-Hydroxybenzoyl)-3,5-dimethyl-6-phenyl-7*H*-furo[3,2-*g*]-[1]benzopyran-7-one (IIIc). IIIb (12.72 g; 0.03 mol) was added to the freshly distilled pyridine hydrochloride (34.5 g;

0.3 mol), and the mixture was refluxed for 30 min. The cooled reaction mixture was poured into water, and the solid filtered off, washed with water, dried, and crystallized from dioxane. Yield: 10.8 g(90%). Found: C, 76.02; H, 4.31%. Calcd for $C_{26}H_{18}O_5$: C, 76.09; H, 4.39%.

2-[*p*-(2-Pyrrolidinylethoxy)benzoyl]-3,5-dimethyl-6-phenyl-7*H*-furo[3,2-*g*][1]benzopyran-7-one (IIIg). **IIIc** (1.23 g; 0.003 mol) was dissolved in acetone (400 ml) and to this 1-(2-chloroethyl)pyrrolidine hydrochloride (0.510 g; 0.003 mol) and freshly baked K_2CO_3 (3g) were added, and the mixture was refluxed for 22 h. The inorganic impurities were filtered off and the residue was poured into ice cold water, filtered, washed with water, and crystallized from aqueous dioxane as colorless flakes. Yield: 0.950 g(65%). Found: C, 75.69; H, 5.65; N, 2.69%. Calcd for $C_{32}H_{29}NO_5$: C, 75.73; H, 5.71; N, 2.76%

2-Benzoyl-3-phenyl-5,9-dimethyl-7*H*-furo[3,2-*g*][1]benzopyran-7-one(VI). A mixture of **IV** (0.294 g; 0.001 mol) and ω-bromoacetophenone (0.199 g; 0.001 mol) in acetone (300 ml) was refluxed for 12 h cooled, and the inorganic impurities were filtered off. Acetone was recovered by distillation and the residue was poured into ice cold water. The solid obtained was recrystallized from dioxane as shining needles. Yield: 0.908 g(50%). Found: C, 79.10, H, 4.49%. Calcd for $C_{26}H_{18}O_4$: C, 79.18; H, 4.56%.

We are grateful to Prof. K. Koteswara Rao, Principal, REC, Warangal for providing facilities and to the CSIR, New Delhi, for the award of a Senior research fellowship to YG.

References

1) M. Bisagni, NG. PH. Buu-Hoi, and R. Royer, *J. Chem. Soc.*, **1955**, 3693.
2) Pomashehenko, *Farmakol. Alkaloidov Glykozidov.*, **70**, 2231V(1967).
3) B. Rajitha, Y. Geetanjali, M. K. L. Rao, V. V. Somayajulu, and C. K. Atal, *Proc. Indian Acad. Sci.*, **90**, 291 (1981).