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Studies on Furan Derivatives. VIII.[1] Preparation of Some New Nitrofuran Derivatives and Determination of Antibacterial Activity

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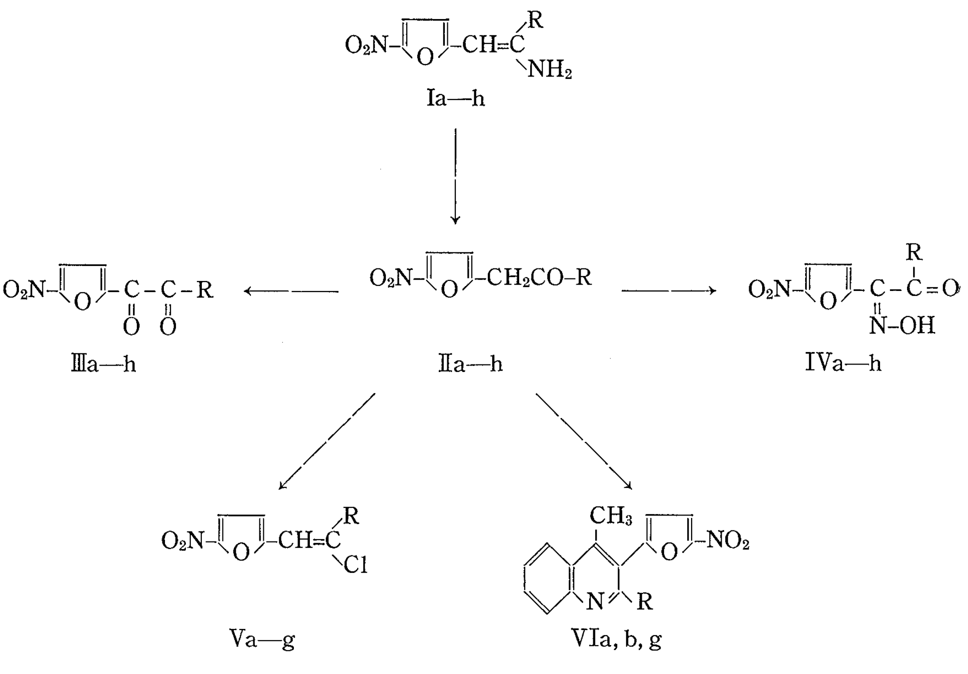
α-Substituted β-(5-nitro-2-furyl)ethanediones, α-substituted β-(5-nitro-2-furyl)-ethanedione β-oximes, α-substituted α-chloro-β-(5-nitro-2-furyl)vinyls, and 2-substituted 3-(5-nitro-2-furyl)-4-methylquinolines were prepared from aryl or 2-furyl 5-nitro-2-furfuryl ketones, which were easily obtained by the hydrolysis of α-aryl- or α-(2-furyl)-β-(5-nitro-2-furyl)vinylamines. α-Substituted β-(5-nitro-2-furyl)ethanedione β-oximes exhibited moderate antibacterial activity *in vitro* against gram-negative and gram-positive organisms.

Keywords——nitrofuran derivatives; primary vinylamines; antibacterial activity; quinoline derivatives; Nifuroxime analogs

In a series of papers,[1,3] we have described the synthesis and antibacterial activity of a number of nitrofuran derivatives which were obtained by various reactions of α-substituted β-(5-nitro-2-furyl)vinylamines or α-(2-furyl)-β-(5-nitro-2-furyl)ethynyl. We next planned the preparation of new nitrofuran derivatives by using aryl or 2-furyl 5-nitro-2-furfuryl ketones



a: R=2-furyl, b: R=phenyl, c: R=4-chlorophenyl, d: R=4-bromophenyl, e: R=4-iodophenyl, f: R=4-methoxyphenyl, g: R=4-nitrophenyl h: R=1-naphthyl.

Chart 1

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[1] Part VII of this series, A. Tanaka, and T. Usui, *Chem. Pharm. Bull.*, **27**, 3078 (1979).

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[3] *a*) A. Tanaka, T. Usui, and S. Yoshina, *Heterocycles*, 3, 1087 (1975); *b*) *Idem*, *J. Heterocycl. Chem.*, **15**, 555 (1978); *c*) *Idem*, *ibid.*, **16**, 493 (1979); *d*) A. Tanaka and T. Usui, *Chem. Pharm. Bull.*, **26**, 3576 (1978); *e*) *Idem*, *J. Heterocycl. Chem.*, **16**, 1409 (1979).

(IIa—h) as starting materials. α-Substituted β-(5-nitro-2-furyl)ethanediones (III), α-substituted β-(5-nitro-2-furyl)ethanedione β-oximes (IV), α-substituted α-chloro-β-(5-nitro-2-furyl)vinyls (V), and 2-substituted 3-(5-nitro-2-furyl)-4-methylquinolines (VI) were prepared and these compounds were tested for antibacterial activity.

Synthesis

The ketones (IIb—h) were easily obtained by acidic hydrolysis of the corresponding enamines (Ib—h).[3b)] IIb—h showed an infrared (IR) absorption band at 1675—1685 cm^{-1} (C=O), and the absence of primary amine absorption. The nuclear magnetic resonance (NMR) spectra of IIb—h were in accord with the assigned structures, *i.e.*, they indicated the presence of a methylene group.

TABLE I. Physical Data for IIb—h

Compd. No.	Yield (%)	mp (°C)	Appearance	Formula	Analysis (%) Calcd (Found) C	H	N
IIb	95	79—80	Yellow leaves	$C_{12}H_9NO_4$	62.34 (62.18	3.92 3.75	6.06 6.00)
IIc	95	90—91.5	Yellow needles	$C_{12}H_8ClNO_4$	54.26 (54.03	3.04 2.85	5.27 5.33)
IId	93	82.5—84	Yellow needles	$C_{12}H_8BrNO_4$	46.48 (46.53	2.60 2.45	4.52 4.63)
IIe	95	122—124	Yellow needles	$C_{12}H_8INO_4$	40.36 (40.58	2.26 2.27	3.92 4.00)
IIf	98	107—108	Yellow prisms	$C_{13}H_{11}NO_5$	59.77 (59.58	4.24 4.35	5.36 5.33)
IIg	91	98—100	Yellow prisms	$C_{12}H_8N_2O_6$	52.18 (52.00	2.92 3.02	10.14 10.08)
IIh	90	103—104	Yellow leaves	$C_{16}H_{11}NO_4$	68.32 (68.03	3.94 4.21	4.98 4.88)

TABLE II. Physical Data for IIIa—h

Compd. No.	Yield (%)	mp (°C)	Appearance	Recrystallization Solvent	Formula	Analysis (%) Calcd (Found) C	H	N
IIIa	25	178—179[a)]	Yellow prisms	Petroleum benzin	$C_{10}H_5NO_6$	51.07 (51.16	2.14 2.13	5.96 6.15)
IIIb	42	120—122	Yellow prisms	MeOH	$C_{12}H_7NO_5$	58.78 (58.53	2.88 2.92	5.71 5.66)
IIIc	45	118—119	Yellow prisms	Petroleum benzin	$C_{12}H_6ClNO_5$	51.54 (51.54	2.16 2.38	5.01 5.13)
IIId	63	104.5—105.5	Yellow needles	MeOH	$C_{12}H_6BrNO_5$	44.47 (44.18	1.87 2.05	4.32 4.22)
IIIe	60	128—129	Yellow needles	MeOH	$C_{12}H_6INO_5$	38.84 (38.99	1.63 1.68	3.77 3.56)
IIIf	45	138—140	Yellow needles	MeOH	$C_{13}H_9NO_6$	56.73 (56.55	3.30 3.11	5.09 5.23)
IIIg	38	137—138	Yellow needles	Petroleum benzin	$C_{12}H_6N_2O_7$	49.67 (49.56	2.08 2.19	9.65 9.88)
IIIh	66	127—128	Yellow needles	MeOH	$C_{16}H_9NO_5$	65.09 (64.83	3.07 3.18	4.74 4.75)

a) Lit.[4)] mp 171—172°.

Oxidation of the methylene group of IIa—h was examined first, since α-diketone nitrofuran derivatives are very rare.[4] It is well known that selenium dioxide is a selective oxidation reagent for methyl or methylene adjacent to carbonyl. When a mixture of IIa—h, selenium dioxide, and acetic anhydride was heated for 5—6 hr at 90—100°, the corresponding α-substituted β-(5-nitro-2-furyl)ethanedione (IIIa—h) was obtained in moderate yield. The reaction with sodium dichromate or potassium permanganate yielded an intractable product, and the yield of α-diketones was very low. Ultraviolet (UV) spectra of IIIa—h showed an absorption band (306—310 nm) corresponding to that of 5-nitro-2-furfural (310 nm).[5]

Next, nitrososation of IIb—h was carried out to obtain 5-nitro-2-furfuraldoxime[6] (Nifuroxime) analogs. Nifuroxime has been used as a veterinary medicine. Compounds IIb—h reacted smoothly with nitrous acid in 50% methanol to give the desired α-substituted β-(5-nitro-2-furyl)ethanedione β-oximes (IVb—h). In the NMR spectra, the H-3 and H-4 protons on the nitrofuran ring showed a two-proton singlet. A similar phenomenon has also been observed in the case of 3-(5-nitro-2-furyl)isoxazoles.[7]

α-Substituted α-chloro-β-(5-nitro-2-furyl)vinyls (Vb—g) were easily prepared in good yields by the chlorination of IIb—g with phosphorus pentachloride.

On the other hand, there are many reports on the synthesis of 5-nitro-2-furyl-heterocyclic compounds. These derivatives, however, do not include 5-nitro-2-furylquinolines. Since some 5-nitro-2-furylvinylquinolines[8] exhibit potent antibacterial activity, quinoline derivatives possesing a 5-nitro-2-furyl group are of particular interest. Fehnel[9] reported that 4-alkyl- and 4-aryl-quinolines are obtained by the acid-catalyzed condensation reaction of *o*-aminoaryl ketones with some carbonyl compounds having the –CH_2CO– grouping, including desoxybenzoin, *etc.*, which had previously been considered incapable of undergoing Friedlander-type reaction with *o*-aminoaryl ketones. Therefore, we tried to apply Fehnel's method to IIa—h, since the nitrofuran ring is generally very unstable to bases. The reactions of

Table III. Physical Data for IVb—h

Compd. No.	Yield (%)	mp (°C)	Appearance	Formula	Analysis (%) Calcd (Found) C	H	N
IVb	91	161—162	Yellow leaves	$C_{12}H_8N_2O_5$	55.39 (55.13	3.10 2.91	10.77 10.58)
IVc	91	131—133	Yellow needles	$C_{12}H_7ClN_2O_5$	48.92 (48.92	2.39 2.39	9.51 9.55)
IVd	96	136—138	Yellow needles	$C_{12}H_7BrN_2O_5$	42.50 (42.63	2.08 2.35	8.26 8.21)
IVe	96	165—166	Yellow needles	$C_{12}H_7IN_2O_5$	37.33 (37.05	1.83 2.02	7.26 7.00)
IVf	98	167—169 (dec.)	Yellow prisms	$C_{13}H_{10}N_2O_6$	53.80 (53.63	3.47 3.18	9.65 9.56)
IVg	97	162—163 (dec.)	Yellow prisms	$C_{12}H_7N_3O_7$	47.22 (47.05	2.31 2.08	13.77 14.00)
IVh	94	156—158 (dec.)	Yellow leaves	$C_{16}H_{10}N_2O_5$	61.94 (61.83	3.25 3.08	9.03 9.28)

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[7] A. Krutosikova, J. Kovac, M. Dandarova, and M. Valentiny, *Collect. Czech. Chem. Commun.*, **43**, 288 (1978).

[8] K. Miura, T. Oohashi, S. Matsuda, and Y. Igarashi, *Yakugaku Zasshi*, **83**, 771 (1963); K. Miura, M. Ikeda, T. Oohashi, I. Okada, and Y. Igarashi, *ibid.*, **84**, 341 (1964); *idem*, *ibid.*, **84**, 537 (1964); K. Miura, M. Ikeda, T. Oohashi, Y. Igarashi, I. Okada, T. Shikimi, and S. Ishii, *ibid.*, **85**, 289 (1965).

Table IV. Physical Data for Vb—g

Compd. No.	Yield (%)	mp (°C)	Appearance	Formula	Analysis (%) Calcd (Found) C	H	N
Vb	68	122—123.5	Green needles	$C_{12}H_8ClNO_3$	57.73 (57.70	3.23 3.05	5.61 5.58)
Vc	43	160—161.5	Green needles	$C_{12}H_7Cl_2NO_3$	50.73 (50.88	2.48 2.53	4.93 5.18)
Vd	53	152—153	Green needles	$C_{12}H_7BrClNO_3$	43.87 (44.11	2.15 2.00	4.26 3.98)
Ve	62	135—137	Green needles	$C_{12}H_7ClINO_3$	38.38 (38.09	1.88 2.03	3.73 3.89)
Vf	94	105—106	Orange needles	$C_{13}H_{10}ClNO_4$	55.83 (55.58	3.60 3.45	5.01 5.28)
Vg	13	193—195	Yellow needles	$C_{12}H_7ClN_2O_5$	48.92 (48.99	2.39 2.48	9.51 9.43)

Table V. Physical Data for VIa,b,g

Compd. No.	Yield (%)	mp (°C)	Appearance	Recrystallization Solvent	Formula	Analysis (%) Calcd (Found) C	H	N
VIa	11	169—170.5	Pale yellow prisms	MeOH	$C_{18}H_{12}N_2O_4$	67.50 (67.35	3.78 3.52	8.75 8.99)
VIb	29	180—182	Orange prisms	MeOH	$C_{20}H_{14}N_2O_3$	72.72 (72.56	4.27 4.43	8.48 8.46)
VIg	13	194—196	Orange prisms	Benzene	$C_{20}H_{13}N_3O_5$	64.00 (64.25	3.49 3.32	11.20 11.38)

IIa, IIb, and IIg with *o*-aminoacetophenone gave 2-(2-furyl)-, 2-phenyl-, and2-(4-nitrophenyl)-3-(5-nitro-2-furyl)-4-methylquinolines (VIa, b, g), respectively. In the case of this reaction with IIc—f, h only intractable products were formed and the corresponding quinolines (VIc—f, h) could not be obtained.

The structures of the compounds prepared above were fully characterized on the basis of their elemental analyses and spectral data. The preparations of IIa, IVa, and Va have been reported elsewhere.[10]

Biological Results

All the compounds prepared above, together with IIa, IVa, and Va were tested *in vitro* for activity against gram-negative and gram-positive bacteria. The minimum inhibitory concentration (MIC) was determined by the twofold agar-dilution method.[11] One loopful of an overnight culture in Trypto-Soy Broth (Eiken) was inoculated onto 10 ml drug-containing agar layers in Petri dishes. Bacterial growth was observed after inoculation for 20 hr at 37°. The MIC was defined as the lowest drug concentration which prevented visible bacterial growth. The activities of IIa—h and IIIa—h were low (>50 μg/ml) towards all the bactera tested. The data for IVa—h, Va—g, and VIa, b, g are presented in Table VI; Nifuroxime

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[9] E.A. Fehnel, *J. Org. Chem.*, **31**, 2899 (1966).
[10] S. Yoshina, A. Tanaka, and T. Usui, *Yakugaku Zasshi*, **97**, 1007 (1977); *idem*, *ibid.*, **98**, 286 (1978).
[11] This method was developed by the Japan Society of Chemotherapy; *Chemotherapy*, **23**, 1 (1975).

TABLE VI. Antibacterial Activity (incubation time 20 hr ,MIC values in μg/ml)

Compd. No.	*Str. hem.* Group A089	*Sta. aur.* 209P-JC	*Sta. aur.* 72r	*Sal. ent.* 1891	*E. coli* NIHJ-JC	*E. coli* K-60	*Kle. pneu.* ST-101	*Pro. vulg.* *HX* 19	*Ps. aerg.* 347
IVa	25	3.13	6.25	12.5	12.5	25	6.25	6.25	50
IVb	25	3.13	12.5	12.5	50	>50	12.5	25	25
IVc	12.5	3.13	6.25	50	25	>50	12.5	6.25	25
IVd	12.5	3.13	6.25	50	25	>50	12.5	6.25	25
IVe	12.5	3.13	3.13	50	25	>50	12.5	6.25	25
IVf	25	3.13	12.5	50	50	>50	25	12.5	50
IVg	25	3.13	6.25	50	50	>50	25	12.5	50
IVh	12.5	3.13	6.25	50	50	>50	25	25	25
Va	>25	6.25	—	1.56	—	—	—	>25	>25
Vb	>3.13	>3.13	>3.13	>3.13	3.13	>3.13	3.13	>3.13	>3.13
Vc	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13
Vd	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25
Ve	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5
Vf	>6.25	>6.25	>6.25	>6.25	3.13	>6.25	3.13	>6.25	>6.25
Vg	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25
VIa	6.25	6.25	6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25
VIb	>12.5	6.25	6.25	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5
VIg	>25	>25	>25	>25	>25	>25	>25	>25	>25
Nifuroxime	25	25	25	12.5	25	25	12.5	50	50
AF-2	<0.39	0.78	1.56	0.78	1.56	3.13	0.78	6.25	12.5

Compd. No.	*Ps. aerg.* K-99	*Sta. aur.* Smith	*Sta. epi.* 12228	*Ser. mar.* IID 620	*E. coli* K74	*Pro. molg.* IFO 3168	*Pro. ret.* IFO 13501	*Sal. pull.* Thuyu
IVa	>50	6.25	6.25	>50	25	>50	>50	6.25
IVb	>50	6.25	3.13	>50	>50	>50	>50	25
IVc	>50	6.25	1.56	>50	>50	>50	>50	50
IVd	>50	3.13	1.56	>50	>50	>50	>50	50
IVe	>50	3.13	1.56	>50	>50	>50	>50	50
IVf	>50	6.25	3.13	>50	>50	>50	>50	50
IVg	>50	3.13	1.56	>50	>50	>50	>50	50
IVh	>50	6.25	1.56	>50	>50	>50	>50	>50
Va	—	—	—	—	—	—	—	12.5
Vb	>3.13	1.56	1.56	>3.13	>3.13	>3.13	>3.13	>3.13
Vc	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13	>3.13
Vd	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25
Ve	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5
Vf	>6.25	3.13	3.13	>6.25	>6.25	>6.25	>6.25	>6.25
Vg	>6.25	>6.25	1.56	>6.25	>6.25	>6.25	>6.25	>6.25
VIa	>6.25	6.25	>6.25	>6.25	>6.25	>6.25	>6.25	>6.25
VIb	>12.5	3.13	>12.5	>12.5	>12.5	>12.5	>12.5	>12.5
VIg	>25	>25	>25	>25	>25	>25	>25	>25
Nifuroxime	>100	>100	>100	100	25	50	25	12.5
AF-2	50	<0.39	<0.39	25	6.25	12.5	12.5	1.56

and AF-2[12] are included for comparison. The oximes (IVa—h) were found to possess moderate activity, IVa (R=2-furyl) being the most active. When the substituent R was phenyl or naphthyl, the activity was lower. The replacement of the *p*-proton on the phenyl ring with a halogen, methoxyl, or nitro group did not lead to a significant change of the activity. Although Va—g could not be tested at high concentration due to their low solubilities, some

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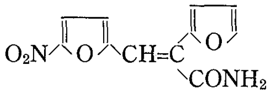
[12] 

of them showed activity at 1.56—3.13 μg/ml (MIC). The quinolines (VIa, b, g) showed activity only against gram-negative bacteria.

Experimental

All melting points were determined with a Yanaco MP-1 apparatus and are uncorrected. Infrared spectra were recorded using a Jasco IRA-1 infrared spectrophotometer. Nuclear magnetic resonance spectra

Table VII. Spectral Data for IIb—h

Compd. No.	MS (M+)	IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: for C=O	NMR[a] δ (CDCl$_3$)
IIb	231	1680	4.48 (2H, s, CH$_2$), 6.60 (1H, d, J=4 Hz, NF H-3), 7.34 (1H, d, J=4 Hz, NF H-4), 7.20—8.20 (5H, m. phenyl H).
IIc	265	1675	4.45 (2H, s, CH$_2$), 6.62 (1H, d, J=4 Hz, NF H-3), 7.34 (1H, d, J=4 Hz, NF H-4), 7.51 (2H, d, J=9 Hz, phenyl H), 7.95 (2H, d, J=9 Hz, phenyl H).
IId	309	1685	4.44 (2H, s, CH$_2$), 6.72 (1H, d, J=4 Hz, NF H-3), 7.31 (1H, d, J=4 Hz, NF H-4), 7.67 (2H, d, J=9 Hz, phenyl H), 7.85 (2H, d, J=9 Hz, phenyl H).
IIe	357	1680	4.42 (2H, s, CH$_2$), 6.60 (1H, d, J=4 Hz, NF H-3), 7.32 (1H, d, J=4 Hz, NF H-4), 7.72 (2H, d, J=9 Hz, phenyl H), 7.90 (2H, d, J=9 Hz, phenyl H).
IIf	261	1675	3.74 (3H, s, CH$_3$), 4.45 (2H, s, CH$_2$), 6.67 (1H, d, J=4 Hz, NF H-3), 7.39 (1H, d, J=4 Hz, NF H-4), 7.07 (2H, d, J=9 Hz, phenyl H), 8.07 (2H, d, J=9 Hz, phenyl H).
IIg	276	1695	4.45 (2H, s, CH$_2$), 6.67 (1H, d, J=4 Hz, NF H-3), 7.35 (1H, d, J=4 Hz, NF H-4), 8.20 (2H, d, J=9 Hz, phenyl H), 8.47 (2H, d, J=9 Hz, phenyl H).
IIh	281	1675	4.58 (2H, s, CH$_2$), 6.67 (1H, d, J=4 Hz, NF H-3), 7.37—9.00 (8H, m, NF H-4 and naphthyl H).

a) s, singlet; d, doublet; m, multiplet; NF, nitrofuran ring.

Table VIII. Spectral Data for IIIa—h

Compd. No.	IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: for C=O	UV $\lambda_{\max}^{\text{EtOH}}$ nm	NMR[a] δ (CDCl$_3$)
IIIa	1640, 1680	233, 310	6.37 (1H, q, J=1.8 Hz, J=3.8 Hz, F H-4), 7.43 (1H, d, J=4 Hz, NF H-3), 7.66 (1H, d, J=3.8 Hz, F H-3), 7.77 (1H, d, J=4 Hz, NF H-4), 7.85 (1H, d, J=1.8 Hz, F H-5).
IIIb	1660	240, 306	7.30—8.30 (7H, m, NF H-3 and 4, and phenyl H).
IIIc	1665	265, 308	7.45 (1H, d, J=4 Hz, NF H-3), 7.55 (1H, d, J=4 Hz, NF H-4), 7.53 (2H, d, J=9 Hz, phenyl H), 8.03 (2H, d, J=9 Hz, phenyl H).
IIId	1660	270, 308	7.39 (1H, d, J=4 Hz, NF H-3), 7.53 (1H, d, J=4 Hz, NF H-4), 7.70 (2H, d, J=9 Hz, phenyl H), 7.90 (2H, d, J=9 Hz, phenyl H).
IIIe	1660	308	7.42 (1H, d, J=4 Hz, NF H-3), 7.57 (1H, d, J=4 Hz, NF H-4), 7.80 (2H, d, J=9 Hz, phenyl H), 7.90 (2H, d, J=9 Hz, phenyl H).
IIIf	1680	228, 310	7.43 (1H, d, J=4 Hz, NF H-3), 7.50 (1H, d, J=4 Hz, NF H-4), 7.05 (2H, d, J=9 Hz, phenyl H), 8.07 (2H, d, J=9 Hz, phenyl H).
IIIg	1680	267, 308	7.45 (1H, d, J=4 Hz, NF H-3), 7.66 (1H, d, J=4 Hz, NF H-4), 8.37 (4H, s, phenyl H).
IIIh	1675	245, 309	7.35—8.30 (9H, m, NF H-3 and 4, and naphthyl H).

a) s, singlet; d, doublet; q, quartet; m, multiplet; F, furan ring; NF, nitrofuran ring.

were recorded on JEOL JNM-60HL and PS-100 spectrophotometers with tetramethylsilane as an internal standard. Mass spectra were obtained (direct solid inlet) on a Shimadzu LKB-9000 instrument. Ultraviolet spectra were taken on a Jasco UVIDEC-1 ultraviolet spectrophotometer.

Preparation of Aryl 5-Nitro-2-furfuryl Ketones (IIb—h)——Conc. HCl (5 ml) was added to 50 ml of 80% MeOH solution of Ib—h (1 g), and the mixture was stirred for 5—6 hr at room temperature, then poured into ice-water. The precipitate was filtered and recrystallized from 50% MeOH to give the corresponding IIb—h almost quantitatively.

Preparation of α-Aryl- or α-(2-Furyl)-β-(5-nitro-2-furyl)ethanediones (IIIa—h)——A mixture of IIa—h (0.002 mol), SeO_2 (0.003 mol), and Ac_2O (15 ml) was heated at 100° for 2—3 hr, and filtered. The filtrate was poured into ice-water, and extracted with benzene. The benzene extract was dried over anhydrous Na_2SO_4 and evaporated down. The residue was chromatographed on silica gel, eluting with benzene, to give the corresponding IIIa—h.

Preparation of α-Aryl-β-(5-nitro-2-furyl)ethanedione β-Oximes (IVb—h)——Conc. HCl (2 ml) and $NaNO_2$ (0.2 g) were added to 70 ml of 50% MeOH solution of IIb—h (0.5 g), and the mixture was warmed for 2—4 hr at 50—60°, then poured into ice-water. The precipitate was filtered and recrystallized from petroleum benzin to yield the corresponding IVb—h in nearly quantitative yield.

TABLE IX. Spectral Data for IVb—h

Compd. No.	MS(M^+)	IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: for C=O, C=N	NMR[a] δ (acetone-d_6)
IVb	260	1630, 1590	7.71 (2H, s, NF H-3 and 4), 7.50—8.20 (5H, m, phenyl H), 12.35 (1H, s, OH).
IVc	294	1640, 1585	7.70 (2H, s, NF H-3 and 4), 7.65 (2H, d, J=9 Hz, phenyl H), 8.08 (2H, d, J=9 Hz, phenyl H), 12.60 (1H, s, OH).
IVd	338	1640, 1580	7.69 (2H, s, NF H-3 and 4), 7.80 (2H, d, J=9 Hz, phenyl H), 7.97 (2H, d, J=9 Hz, phenyl H), 12.60 (1H, s, OH).
IVe	386	1640, 1575	7.71 (2H, s, NF H-3 and 4), 7.83 (2H, d, J=9 Hz, phenyl H), 8.03 (2H, d, J=9 Hz, phenyl H), 12.60 (1H, s, OH).
IVf	290	1630, 1590	3.93 (3H, s, OCH_3), 7.70 (2H, s, NF H-3 and 4), 7.12 (2H, d, J=9 Hz, phenyl H), 8.03 (2H, d, J=9 Hz, phenyl H), 12.30 (1H, s, OH).
IVg	305	1680, 1660	7.72 (2H, s, NF H-3 and 4), 8.38 (2H, d, J=9 Hz, phenyl H), 8.40 (2H, d, J=9 Hz, phenyl H), 12.85 (1H, s, OH).
IVh	310	1655, 1570	7.72 (2H, s, NF H-3 and 4), 7.50—8.80 (7H, m, naphthyl H), 12.43 (1H, s, OH).

[a] s, singlet; d, doublet; m, multiplet; NF, nitrofuran ring.

TABLE X. Spectral Data for Vb—g

Compd. No.	MS(M^+)	UV $\lambda_{\max}^{\text{EtOH}}$ nm	NMR[a] δ ($CDCl_3$)
Vb	249	280, 374	7.15 (1H, s, -CH=), 7.30—7.85 (7H, m, NF H-3 and 4, and phenyl H).
Vc	283	281, 369	7.13 (1H, s, -CH=), 7.30—7.80 (6H, m, NF H-3 and 4, and phenyl H).
Vd	327	285, 373	7.12 (1H, s, -CH=), 7.25 (1H, d, J=4 Hz, NF H-4), 7.41 (1H, d, J=4 Hz, NF H-4), 7.58 (4H, s, phenyl H).
Ve	375	291, 375	7.33 (1H, s, -CH=), 7.35 (1H, d, J=4 Hz, NF H-3), 7.43 (1H, d, J=4 Hz, NF H-4), 7.47 (2H, d, J=9 Hz, phenyl H), 7.80 (2H, d, J=9 Hz, phenyl H).
Vf	279	295, 385	6.95 (1H, s, -CH=), 7.00 (1H, d, J=4 Hz, NF H-3), 7.40 (1H, d, J=4 Hz, NF H-4), 7.24 (2H, d, J=9 Hz, phenyl H), 7.64 (2H, d, J=9 Hz, phenyl H).
Vg	294	267, 368	7.25 (1H, s, -CH=), 7.35 (1H, d, J=4 Hz, NF H-3), 7.42 (1H, d, J=4 Hz, NF H-4), 7.90 (2H, d, J=9 Hz, phenyl H), 8.33 (2H, d, J=9 Hz, phenyl H).

[a] s, singlet; d, doublet; m, multiplet; NF, nitrofuran ring.

Table XI. Spectral Data for VIa,b,g

Compd. No.	MS(M^+)	UV λ_{max}^{EtOH} nm	NMR[a] δ ($CDCl_3$)
VIa	320	234, 257 310	6.47 (1H, q, $J=1.8$ Hz, $J=3.8$ Hz, F H-4), 6.62 (2H, m, F H-3 and NF H-3), 7.40—8.40 (6H, m, F H-5, NF H-4, and quinoline H), 2.62 (3H, s, CH_3).
VIb	330	232, 255 329	6.31 (1H, d, $J=4$ Hz, NF H-3), 7.20—8.40 (10H, m, NF H-4, phenyl H, and quinoline H), 2,60 (3H, s, CH_3).
VIg	375	219, 295	6.87 (1H, d, $J=4$ Hz, NF H-3), 7.50—8.50 (9H, m, NF H-4, phenyl H, and quinoline H), 2.73 (3H, s, CH_3).[b]

a) s, singlet; d, doublet; q, quartet; m, multiplet; F, furan ring; NF, nitrofuran ring. *b*) in DMSO-d_6.

Preparation of α-Aryl-α-chloro-β-(5-nitro-2-furyl)vinyls (Vb—g)——A mixture of IIb—g (0.002 mol), PCl_5 (0.003 mol), and benzene was refluxed for 5—6 hr. The reaction mixture was washed three times with water and the benzene layer was dried over anhydrous Na_2SO_4, then evaporated down. The residue was chromatographed on silica gel, eluting with benzene, to give the corresponding Vb—g.

2-Substituted 3-(5-Nitro-2-furyl)-4-methylquinolines (VIa, b, g)——A mixture of IIa—h (0.002 mol), *o*-aminoacetophenone (0.002 mol), and AcOH (10 ml) containing a catalytic amount of conc. H_2SO_4 was refluxed for 5—6 hr. After cooling, the reaction mixture was poured into ice-water, and extracted with benzene. The benzene extract was washed three times with water, dried over anhydrous Na_2SO_4, and evaporated down. The residue was chromatographed on silica gel, eluting with benzene, to give the corresponding VIa, b, g.

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