[Chem. Pharm. Bull. 27(12)3078—3085(1979)]

UDC 547.724.1.04 : 547.834.2.04

Studies on Furan Derivatives. VII.[1] Reactions of α-(2-Furyl)-β-(5-nitro-2-furyl)ethynyl

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(Received June 16, 1979)

Addition of amines to α-(2-furyl)-β-(5-nitro-2-furyl)ethynyl (I) gave N-substituted α-(2-furyl)-β-(5-nitro-2-furyl)vinylamines. Bromination of I gave stereoisomers which were identified as *E*- and *Z*-forms, judging from their ultraviolet absorption spectra. The reaction of I with N-substituted pyridinium ylides was not uniform. Only the common indolizines, namely 3-substituted 1-(5-nitro-2-furyl)-2-(2-furyl)indolizines, were obtained by reaction in dioxane, whereas 3-substituted 1-(4-alkylated 5-nitro-2-furyl)-2-(2-furyl)-indolizines were isolated by reaction in dimethylformamide, together with the common indolizines.

Keywords——nitrofuran derivatives; indolizine derivatives; amination; bromination; 1,3-dipolar cycloaddition; new ethoxycarbonylmethylation; new acetonylation; stereoisomers; N-pyridinium ylides

Many 5-nitrofurans substituted at the 2 position with vinyl, azomethine, and heterocyclic moieties have been prepared for studies on their biological activity.[3] However, only a small number of 5-nitro-2-furylethynyls have been described.[4] In previous papers,[5] we reported a simple preparation procedure for 5-nitro-2-furylethynyls by the deamination of 5-nitro-2-furylvinylamines. We next sought to obtain new types of nitrofuran derivatives *via* various reactions of 5-nitro-2-furylethynyls.

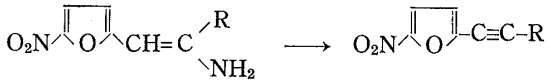


Chart 1

The present paper deals with amination, bromination, and 1,3-dipolar cycloaddition reactions of α-(2-furyl)-β-(5-nitro-2-furyl)ethynyl (I).

Amination

Compound I was allowed to react with secondary alicyclic amines (pyrrolidine, piperidine, and morpholine) in benzene, giving the corresponding tertiary enamines (IIa—c) in good yields. To determine the position of the amino group, hydrolysis of IIa—c was carried out to afford 2-furyl 5-nitro-2-furfuryl ketone (III), which gave a melting point and spectral properties identical with those previously reported in the literature.[6] Thus, the structures of IIa—c were assigned as N-substituted α-(2-furyl)-β-(5-nitro-2-furyl)vinylamines. Their physical and spectral data are listed in Tables I and VI. Similarly, the addition of ammonia to I in methanol gave α-(2-furyl)-β-(5-nitro-2-furyl)vinylamine (IV), which was identical

1) Part VI of this series, K. Yamamoto, and A. Tanaka, *J. Heterocycl. Chem.*, **16**, 1293 (1979).
2) Location: *Keyakidai, Sakado-shi, Saitama.*
3) H. Saikachi and A. Tanaka, *Yakugaku Zasshi*, **83**, 147 (1963); E. Szarvasi, *J. Med. Chem.*, **16**, 281 (1973); H.A. Burch and L.E. Benjamin, *ibid.*, **17**, 451 (1974).
4) *a*) I. Saikawa, S. Takano, and T. Maeda, *Yakugaku Zasshi*, **87**, 1514 (1967); *b*) S. Yoshina, I. Maeda, and K. Asai, *ibid.*, **88**, 984 (1968); *c*) T. Sasaki and T. Yoshioka, *Bull. Chem. Soc.*, **44**, 803 (1971).
5) A. Tanaka, T. Usui, and S. Yoshina, *Heterocycles*, 3, 1087 (1975); *idem*, *J. Heterocycl. Chem.*, **16**, 493 (1979).
6) S. Yoshina, A. Tanaka, and T. Usui, *Yakugaku Zasshi*, **98**, 286 (1978).

with an authentic sample[7] (mixed melting point and infrared (IR) spectrum). Thus, it was found that the addition of amines to I gave α-(2-furyl)-β-(5-nitro-2-furyl)vinylamines and not α-(5-nitro-2-furyl)-β-(2-furyl)vinylamines, because of the electron-withdrawing nature of the nitrofuran group at the β-position in I.

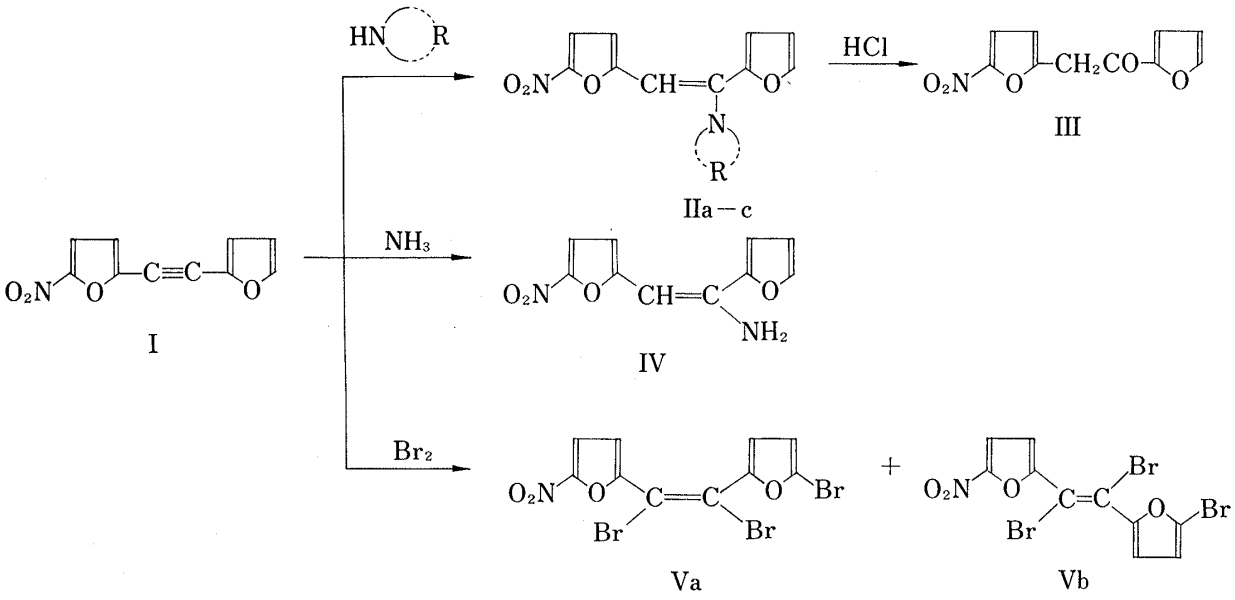
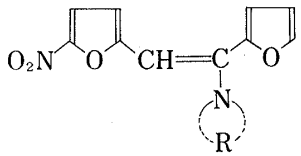


Chart 2

Table I.



Compd. No.	—N R	Yield (%)	mp (°C)	Appearance Solvent	Formula	Analysis Found (Calcd.) C	H	N
IIa	-N	89	119—120	Red prisms Ligroin	$C_{14}H_{14}N_2O_4$	61.49 (61.31	5.23 5.15	10.04 10.21)
IIb	-N	82	108—109	Red prisms Ligroin	$C_{15}H_{16}N_2O_4$	62.33 (62.49	5.45 5.59	9.98 9.72)
IIc	-N O	70	143—144.5	Red prisms Ligroin	$C_{14}H_{14}N_2O_5$	58.13 (57.93	4.86 4.86	9.65 9.65)

Bromination

One molar equivalent of bromine in chloroform was added to a solution of I in chloroform in small portions at room temperature to give a viscid solid (V) with partial recovery of I (50%). Similar addition of 2 molar equivalents of bromine gave the same viscid solid (V). Compound V was chromatographed on silica gel, eluting with petroleum benzin, to give two kinds of crystals, mp 91—92° (Va) and mp 148—150° (Vb). Mass spectra of Va and Vb gave a common molecular ion peak (*m/e* 339, 441, 443, and 445) and showed identical fragmenta-

7) S. Yoshina, A. Tanaka, and T. Usui, *Yakugaku Zasshi*, **97**, 1007 (1977).

tion. In the IR spectra, the absorption band for C≡C had disappeared, and the nuclear magnetic resonance (NMR) spectra showed similar patterns of two 2,5-disubstituted furan rings. Thus, Va and Vb were considered to be the geometrical isomers of α,β-dibromo-α-(5-bromo-2-furyl)-β-(5-nitro-2-furyl)vinyl. The elemental analysis data for Va and Vb were consistent with a molecular formula of $C_{10}H_4Br_3NO_4$ for both. The ultraviolet (UV) spectra of both showed very similar absorption patterns and maxima, but there was a difference in the absorption coefficient (log ε) at the absorption maximum (375 nm) between Va (4.00) and Vb (4.08).

In stereoisomers of 5-nitro-2-furylvinyls, it has generally been observed that the absorption coefficient at the absorption maximum of the Z-isomer is smaller than that of the *E*-isomer.[8] The melting point of Vb is higher than that of Va. Thus, we assume that the structure of Va is *Z*-form and that of Vb is *E*-form.

Reaction with N-Pyridinium Ylides

There have been many reports on the synthesis of indolizines by the reaction of acetylenes with N-pyridinium ylides.[9] However, there is only one report covering nitrofurans; it deals with 1-benzoyl and 1-(4-methylbenzoyl)-2-(5-nitro-2-furyl)-3-benzoylindolines.[4c] Therefore, the reactions of I with some N-pyridinium ylides were examined. The N-pyridinium bromides (VIa—j) used are listed in Table II. First, compound I was allowed to react with VIa and sodium hydride in dioxane at room temperature; it gave 3-ethoxycarbonyl-2-(2-furyl)-1-(5-nitro-2-furyl)indolizine (VIIa) in 4% yield with a high recovery of I (86%). The structure of VIIa was identified by comparison with an authentic sample[10] (mixed melting point and spectral data).

In order to improve the yield of the desired product (VIIa), the yield of this reaction was examined with various ratios of VIa and sodium hydride to I. These experimental results are summerized in Table III. Although the yield of VIIa increased with increasing amount of the ylide, more than 49% of the starting material (I) was always recovered. When I was allowed to react with VIa (5 molar equivalents) and sodium hydride (5 molar equivalents) in dioxane at 80—90° until I completely disappeared (2 hr), the yield of VIIa increased to 56%. Compounds VIIb—j were prepared from the corresponding N-pyridinium ylides.

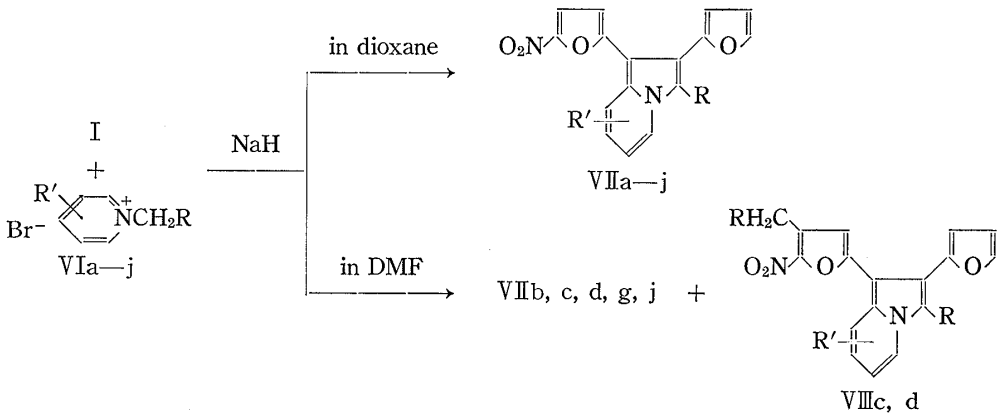
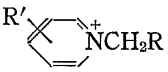


Chart 3

8) S. Yoshina, A. Tanaka, and K. Izumi, *Yakugaku Zasshi*, **88**, 405 (1968); S. Yoshina and A. Tanaka, *ibid.*, **88**, 410 (1968).
9) V. Boekelheide and K. Fahrenholtz, *J. Amer. Chem. Soc.*, **83**, 458 (1961); C.H. Hendrick, E. Ritchie, and W.C. Taylor, *Aust. J. Chem.*, **20**, 2467 (1967); T. Sasaki, K. Kanematsu, and Y. Yukimoto, *J. Chem. Soc. (C)*, **1970**, 481.
10) A. Tanaka and T. Usui, *J. Heterocycl. Chem.*, in Press.

TABLE II. Br^-  NCH_2R

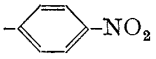
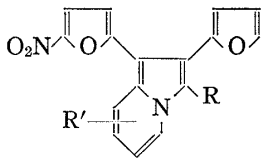
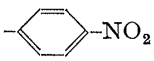
Compd. No.	R	R′
VIa	–COOEt	H
VIb	–COOEt	2-CH_3
VIc	–COOEt	4-CH_3
VId	–$COCH_3$	H
VIe	–$COCH_3$	2-CH_3
VIf	–$COCH_3$	4-CH_3
VIg	–COPh	H
VIh	–COPh	2-CH_3
VIi	–COPh	4-CH_3
VIj		H

TABLE III. Reaction of I with VIa and NaH in Dioxane

Molar ratio I/VIa/NaH	Yield (%) of VIIa	Recovery (%) of I
1/1/1	4	86
1/2/2	20	78
1/3/3	20	78
1/4/4	33	62
1/5/5	36	56
1/10/10	42	50

TABLE IV. 

Compd. No.	R	R′	Yield (%)	mp (°C)	Appearance Solvent	Formula	Analysis Found (Calcd.) C	H	N
VIIb	–COOEt	5-CH_3	17	132.5—134	Orange prisms Benzene	$C_{20}H_{16}N_2O_6$	63.05 (63.15	4.38 4.24	7.13 7.37)
VIIc	–COOEt	7-CH_3	5	193.5—195	Red needles Benzene	$C_{20}H_{16}N_2O_6$	62.95 (63.15	4.35 4.24	7.43 7.37)
VIId	–$COCH_3$	H	40	250 —251	Red prisms $CHCl_3$	$C_{18}H_{12}N_2O_5$	64.00 (64.28	3.38 3.60	8.21 8.33)
VIIe	–$COCH_3$	5-CH_3	48	175 —177	Red prisms Benzene	$C_{19}H_{14}N_2O_5$	64.88 (65.14	4.21 4.03	7.90 8.00)
VIIf	–$COCH_3$	7-CH_3	47	201 —203	Red needles Benzene	$C_{19}H_{14}N_2O_5$	65.22 (65.14	4.23 4.03	7.87 8.00)
VIIg	–COPh	H	10	221 —223	Red prisms Benzene	$C_{23}H_{14}N_2O_5$	69.31 (69.34	3.54 3.54	7.00 7.03)
VIIh	–COPh	5-CH_3	11	168 —170	Red prisms Benzene	$C_{24}H_{16}N_2O_5$	69.66 (69.90	3.85 3.91	6.65 6.79)
VIIi	–COPh	7-CH_3	45	199.5—200.5	Red prisms Benzene	$C_{24}H_{16}N_2O_5$	69.95 (69.90	3.98 3.91	7.03 6.79)
VIIj		H	10	243 —245	Red prisms Benzene	$C_{22}H_{13}N_3O_6$	63.55 (63.61	3.38 3.15	10.25 10.12)

Recently, we reported[10] that the reaction of I with N-ethoxycarbonylmethylpyridinium ylide in dimethylformamide gave an unexpected product, 3-ethoxycarbonyl-1-(4-ethoxycarbonylmethyl-5-nitro-2-furyl)-2-(2-furyl)indolizine, together with 3-ethoxycarbonyl-2-(2-furyl)-1-(5-nitro-2-furyl)indolizine, in contrast to the results obtained by the same reaction in dioxane. We next carried out studies to extend the scope of this alkylation. Each of VIb, c, d, g, j was allowed to react with I and sodium hydride in dimethylformamide. Thus VIb, g, and j gave only VIIb, g, and j, whereas VIc and d gave VIIIc and d together with the common indolizines (VIIc and d).

We consider that the failure of VIb, g, and j to yield alkylated products arises from the difficulty of approach of the ylide carbanions to the 4-position of the nitrofuran ring, because of the steric effect of the substituents on the pyridine ring. Further extention of this alkylation reaction to other nitro-aromatics is now under investigation.

A possible mechanism for this alkylation reaction is outlined in Chart 4. Even though ionic intermediates are present, a radical ionic pathway cannot yet be excluded.

The structures of VIIb—j and VIIIc and d were confirmed by their spectral and elemental analysis data.

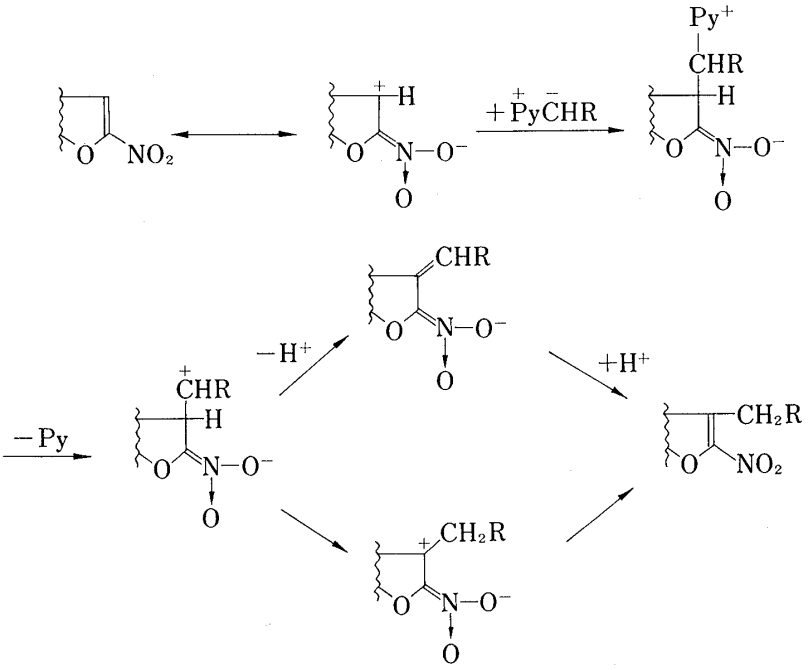
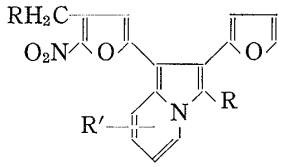


Chart 4

TABLE V.



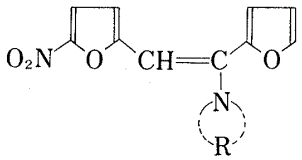
Compd. No.	R	R′	Yield (%)	mp (°C)	Appearance Solvent	Formula	Analysis Found (Calcd.) C	H	N
VIIIc	–COOEt	7-CH_3	13	128—130	Yellow needles Pet. benzin	$C_{24}H_{22}N_2O_8$	61.65 (61.08	4.68 4.75	5.93 6.01)
VIIId	–$COCH_3$	H	6	168—169	Yellow needles Pet. benzin	$C_{21}H_{16}N_2O_6$	64.35 (64.28	3.98 4.11	7.03 7.14)

Experimental

All melting points are uncorrected. The following instruments were used to obtain the physical data. NMR spectra (with TMS as an internal standard): JEOL 60HL and PS-100 spectrometers; IR spectra: Jasco IRA-1; UV spectra: Jasco UVIDEC-1; mass spectra (direct solid inlet): Shimadzu LKB-9000 machine. Column chromatography was carried out on silica gel (Wako gel C-200). Fifty percent NaH was used, purchased from Wako Chemical Industries, Ltd.

Addition of Alicyclic Secondary Amines——A mixture of 0.5 g (0.00246 mol) of I, 0.005 mol of amine (pyrrolidine, piperidine, or morpholine), and 50 ml of benzene was stirred for 3—5 hr at room temperature. 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 recrystallized from ligroin to give the corresponding N-substituted α-(2-furyl)-β-(5-nitro-2-furyl)vinylamines (IIa—c).

TABLE VI.



Compd. No.	MS (M^+)	UV λ_{max}^{EtOH} nm (log ε)	NMR[a] δ (in CDCl)
IIa	274	490(3.90)	5.70 (1H, d, J=4 Hz, NF H-3), 7.30 (1H, d, J=4 Hz, NF H-4), 6.60—6.80 (2H, m, F H-3 and 4), 7.67 (1H, d, J=1.8 Hz, F H-5), 5.42 (1H, s, –CH=), 1.87—2.23, 3.17—3.50 (8H, each m, –N⟨ ⟩).
IIb	298	466(4.24)	5.13 (1H, d, J=4 Hz, NF H-3), 7.30 (1H, d, J=4 Hz, NF H-4), 6.53—6.60 (2H, m, F H-3 and 4), 7.65 (1H, d, J=1.8 Hz, F H-5), 1.50—2.00, 3.00—3.45 (10H, each m, –N⟨ ⟩), 5.62 (1H, s, –CH=).
IIc	290	445(4.29)	5.35 (1H, d, J=4 Hz, NF H-3), 7.28 (1H, d, J=4 Hz, NF H-4), 6.67 (2H, s, F H-3 and 4), 7.68 (1H, d, J=1.8 Hz, F H-5), 5.67 (1H, s, –CH=), 3.00—3.40, 3.70—4.10 (8H, each m, –N⟨ O⟩).

a) s: singlet, d: doublet, m, multiplet, F: furan ring, NF: nitrofuran ring.

Hydrolysis of IIa—c——Conc. HCl (2 ml) was added to 50 ml of MeOH solution of IIa, b, or c (0.01 mol), and the mixture was stirred for 5 hr at room temperature, then poured into ice-water. The precipitate was filtered and recrystallized from petroleum benzin to give IV in quantitative yield. This compound was identical with an authentic sample[6] (mixed melting point and some spectral data).

Addition of Ammonia——Ammonia gas was bubbled through a solution of 0.5 g (0.00246 mol) of I in 50 ml of MeOH, for 15 minutes under ice cooling; stirring was continued for 50 hr at room temperature, then the 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 red needles (III), mp 129—130°, 0.25 g (46%) and I (50% recovery). This compound was identical with an authentic sample[7] (mixed melting point and some spectral data).

Bromination——i) To a stirred solution of 0.5 g (0.00246 mol) of I in 20 ml of $CHCl_3$, 0.38 g (0.00246 mol) of Br_2 in 10 ml of $CHCl_3$ was added in small portions at room temperature. Stirring was continued for 1 hr, then the solvent was evaporated off. The residue was chromatographed on silica gel, eluting with benzene, to give 0.5 g of a viscid solid (V), and I (50% recovery). The viscid solid was rechromatographed on silica gel with petroleum benzin as an eluent to give 0.2 g of yellow needles (Va), mp 91—92°, and 0.25 g of pale yellow needles (Vb), mp 148—150°.

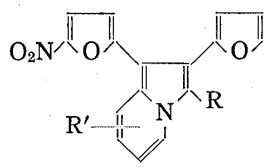
For Va; IR ν_{max}^{Nujol} cm^{-1}: 1020 (C–O–C); NMR (acetone-d_6) δ: 6.70 (1H, d, J=3.9 Hz, furan H-3), 6.95 (1H, d, J=3.9 Hz, furan H-4), 7.08 (1H, d, J=4 Hz, nitrofuran H-3), 7.67 (1H, d, J=4 Hz, nitrofuran H-4); MS *m/e*: 339, 441, 443, 445 (M^+); UV λ_{max}^{EtOH} nm (log ε): 300 (4.30), 375 (4.00). *Anal.* Calcd. for $C_{10}H_4Br_3NO_4$: C, 27.18; H, 0.91; N, 3.17. Found: C, 27.35; H, 1.13; N, 3.08.

For Vb; IR ν_{max}^{Nujol} cm^{-1}: 1035 (C–O–C); NMR (acetone-d_6) δ: 6.87 (1H, d, J=3.9 Hz, furan H-3), 7.40 (1H, d, J=3.9 Hz, furan H-4), 7.47 (1H, d, J=4 Hz, nitrofuran H-3), 7.73 (1H, d, J=4 Hz, nitrofuran H-4);

MS *m/e*: 339, 441, 443, 445 (M^+); UV λ_{max}^{EtOH} nm (log ε): 300 (4.30), 375 (4.08). *Anal.* Calcd. for $C_{10}H_4Br_3NO_4$: C, 27.18; H, 0.91; N, 3.17. Found: C, 27.55; H, 1.03; N, 3.00.

ii) 0.79 g (0.00492 mol) of Br_2 was used, and the procedure was identical with that used in method i). Va (0.3 g) and Vb (0.5 g) was obtained.

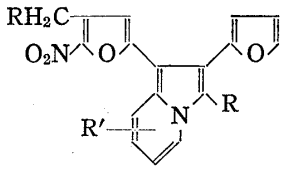
TABLE VII.



Compd. No.	MS (M^+)	UV λ_{max}^{EtOH} nm (log ε)	NMR[a] δ (in $CDCl_3$)
VIIb	380	449(4.20)	5.91 (1H, d, J=4 Hz, NF H-3), 7.37 (1H, d, J=4 Hz, NF H-4), 6.65 (2H, broad s, F H-3 and 4), 7.73 (1H, d, J=1.8 Hz, F H-5), 6.90 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 7.20—7.50 (1H, m, I H-7), 8.43 (1H, d-d, J=9 Hz, J=2 Hz, I H-8), 4.30 (2H, q, J=7 Hz, CH_2), 2.67 (3H, t, J=7 Hz, CH_3).
VIIc	380	447(4.31)	5.78 (1H, d, J=4 Hz, NF H-3), 7.40 (1H, d, J=4 Hz, NFH-4), 6.50—6.77 (2H, m, F H-3 and 4), 7.72 (1H, d, J=1.8 Hz, F H-5), 9.57 (1H, d, J=7 Hz, I H-5), 6.98 (2H, d-d, J=7 Hz, J=2 Hz, I H-6), 8.28 (1H, d, J=2 Hz, I H-8), 4.27 (2H, q, J=7 Hz, CH_2), 1.15 (3H, t, J=7 Hz, CH_3).
VIId	336	380(4.25) 429(4.32)	5.70 (1H, d, J=4 Hz, NF H-3), 7.33 (1H, d, J=4 Hz, NF H-4), 6.53—6.77 (2H, m, F H-3 and 4), 7.73 (1H, d, J=1.8 Hz, FH-5), 10.08 (1H, d-d, J=7 Hz, J=2 Hz, I H-5), 6.90—7.80 (2H, m, I H-6 and 7), 8.46 (1H, d-d, J=9 Hz, J=2 Hz, I H-8), 2.13 (3H, s, CH_3).
VIIe	350	380(4.14) 443(4.32)	5.83 (1H, d, J=4 Hz, NF H-3), 7.40 (1H, d, J=4 Hz, NF H-4), 6.60—6.80 (2H, m, F H-3 and 4), 7.80 (1H, d, J=1.8 Hz, F H-5), 6.98 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 7.30—7.63 (1H, m, I H-7), 8.37 (1H, d, J=9 Hz, I H-8), 2.50 (3H, s, CH_3), 2.25 (3H, s, CH_3).
VIIf	350	385(4.25) 441(4.33)	5.74 (1H, d, J=4 Hz, NF H-3), 7.44 (1H, d, J=4 Hz, NF H-4), 6.63—6.87 (2H, m, F H-3 and 4), 7.88 (1H, d, J=1.8 Hz, F H-5), 10.03 (1H, d, J=7 Hz, I H-5), 7.08 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 8.33 (1H, d, J=1.8 Hz, I H-8), 2.58 (3H, s, CH_3), 2.14 (3H, s, CH_3).
VIIg	398	431(4.39)	5.80 (1H, d, J=4 Hz, NF H-3), 5.96—6.20 (2H, m, F H-3 and 4), 9.55 (1H, d-d, J=7 Hz, J=2 Hz, I H-5), 8.53 (1H, d-d, J=9 Hz, J=2 Hz, I H-8), 6.90—7.70 (8H, m, NF H-4, I H-6 and 7, and phenyl H).
VIIh	412	448(4.20)	5.93 (1H, d, J=4 Hz, NF H-3), 6.20—6.30 (2H, m, F H-3 and 4), 6.95 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 8.53 (1H, d-d, J=9 Hz, J=2 Hz, I H-8), 2.47 (3H, s, CH_3), 7.30—8.00 (7H, m, NF H-4, I H-7, and phenyl H).
VIIi	412	448(4.20)	5.78 (1H, d, J=4 Hz, NF H-3), 5.95—6.23 (2H, m, F H-3 and 4), 9.65 (1H, d, J=7 Hz, I H-5), 7.33 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 7.17—7.70 (6H, m, NF H-4 and phenyl H), 2.59 (3H, s, CH_3), 8.30 (1H, d, J=2 Hz, I H-8).
VIIj	415	—	5.97 (1H, d, J=4 Hz, NF H-3), 6.29 (1H, d, J=3.8 Hz, F H-3), 6.50 (1H, d-d, J=3.8 Hz, J=1.8 Hz, F H-4), 6.67—7.20 (1H, m, I H-6), 7.20—7.80 (4H, m, NF H-4, I H-7, and nitrophenyl H), 8.00—8.50 (4H, m, I H-6 and 7, and nitrophenyl H).

a) s: singlet, d: doublet, d-d: double doublet, m: multiplet, q: quartet, t: triplet, F: furan ring, NF: nitrofuran ring, I: indolizine ring.

TABLE VIII.



Compd. No.	MS (M^+)	IR ν_{max}^{Nujol} cm^{-1}: C=O	NMR[a] δ (in $CDCl_3$)
VIIIc	466	1680, 1735	5.82 (1H, s, NF H-3), 6.50—6.78 (2H, m, F H-3 and 4), 7.73 (1H, d, J=1.8 Hz, F H-5), 9.56 (1H, d, J=7 Hz, I H-5), 6.98 (1H, d-d, J=7 Hz, J=2 Hz, I H-6), 8.28 (1H, d, J=2 Hz, I H-8), 3.94 (2H, s, CH_2), 4.26 (4H, q, J=7 Hz, $CH_2\times2$), 2.56 (3H, s, CH_3), 1.14, 1.29 (6H, each t, J=7 Hz, $CH_3\times2$).
VIIId	392	1640, 1720	5.37 (1H, s, NF H-3), 6.60—6.90 (2H, m, F H-3 and 4), 7.83 (1H, d, J=1.8 Hz, F H-5), 10.05 (1H, d-d, J=7 Hz, I H-5), 7.00—7.80 (2H, m, I H-6 and 7), 8.58 (1H, d-d, J=10 Hz, J=2 Hz, I H-8), 4.25 (2H, s, CH_2), 2.15, 2.30 (6H, each s, $CH_3\times2$).

a) s: singlet, d: doublet, d-d: double doublet, m: multiplet, q: quartet, t: triplet, F: furan ring, NF: nitrofuran ring, I: indolizine ring.

Indolizine Synthesis in Dioxane——i) A solution of 0.5 g (0.00246 mol) of I, VIa, and 50% NaH (0.00246—0.0246 mol) in 50 ml of dioxane was stirred for 50 hr at room temperature then filtered. The filtrate was concentrated and the residue was chromatographed on silica gel with benzene as an eluent to give VIIa. This compound was identical with an authentic sample[10] (mixed melting point and IR spectrum).

ii) The reactions of VIb—j and 50% NaH (0.0123 mol) with I were carried out as described for VIa, giving VIIb—j, respectively.

iii) A mixture of 0.5 g (0.00246 mol) of I, 1.8 g (0.00738 mol) of VIa and 0.12 g (0.00738 mol) of 50% NaH in 50 ml of dioxane was heated at 80—90° for 2 hr, then filtered. Work-up as described in i) gave VIIa, 0.5 g (56%).

Indolizine Synthesis in DMF——Fifty percent NaH (0.0123 mol) was added to a solution of 0.5 g (0.00246 mol) of I and 0.0123 mol of VIb, c, d, g, or j in 50 ml of DMF under ice cooling. Stirring was continued for 4 hr at room temperature, then the 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 concentrated. The residue was chromatographed on silica gel with benzene as an eluent to give VIIb, c, d, g, or j (10—30% yield) and VIIIc and d.

Acknowledgement The authors are greatly indebted to the staff of the central analytical center of this university for elemental analyses and spectral measurements.