[Chem. Pharm. Bull. 17(2) 306—314 (1969)]

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Synthesis of Furan Derivatives. XL.[1] Synthesis of (5-Nitro-2-furyl)-methylated Polyenals[2]

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Seven (5-nitro-2-furyl)-methylated polyenals (I, $n=2$ to 3, n is the number of vinyl or propenyl group) were prepared from aldehyde dimethyl acetal ($n=1$ and 2) by alternate or repeated condensation with methyl vinyl ether or methyl propenyl ether in the presence of boron trifluoride etherate.

Excepting the formation of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (V), the chain extension reaction gave higher homologs of methylated polyenal with *trans* formyl group. The chemical evidence showing V must be above configuration was clearly given by the cyclization of its dimethyl acetal to 1-methoxy-2-(5-nitro-2-furyl)-3,5-dimethyl–cyclopenta–2,4-diene.

From the van der Waals projection diagram of V, it was suggested that 3-*S-cis* spatial configuration is more favored than 3-*S-trans* conformation. Nuclear magnetic resonance (NMR) spectrum of V supported this suggestion from its chemical shift of the proton adjacent to 5-nitrofuran ring.

In the presence of HX (X=Cl or Br), V was easily rearranged to five membered conjugated ketone, 2-(5-nitro-2-furyl)-3,5-dimethyl-cyclopent-2-en-1-one. This acid catalyzed ring closure of the *cis* dienal is a new type of rearrangement, which promises to have some synthetic utility.

(5-Nitro-2-furyl)-polyenals are not only characteristic in their chemical structures, but also in antibacterial activities. Several compounds of this series have been reported in the past in our laboratory[4,5] and others.[6] From our earlier work following two informations were obtained, *i.e.*, (1) interporation of the chain of conjugated double bond between the nitrofuran ring and aldehyde group plays an important role on the antibacterial activity, (2) higher vinylog of 5-nitrofurfural such as (5-nitro-2-furyl)-2,4,6-heptatrienal or (5-nitro-2-furyl)-2,4,6,8-nonatetraenal exhibits so high antibacterial activity that derivation to the nitrogenous derivatives from the parent aldehyde is unneccessarily.[7]

From the microbiological tests of methyl substituted early homolog of this series (n=1), the considerable antituberculostatical activity has been observed,[4,5] and this prompted us to prepare some of (5-nitro-2-furyl)-methylated polyenals (n=2 and 3).

Using the method previously reported,[4] the methylated polyenals were stepwise prepared from (5-nitro-2-furyl)-α-methyl-acrolein dimethyl acetal (IIa: R=propenyl) or (5-nitro-2-furyl)-acrolein dimethyl acetal (IIb: R=vinyl) as a precursor, which was repeatedly or alternatively condensed with methyl vinyl ether (IIIa) or methyl propenyl ether (IIIb) in the presence of boron trifluoride etherate. The intermediate etheral acetals (IV), without being

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[1] Part XXXIX: H. Saikachi and K. Takai, *Yakugaku Zasshi*, **88**, 1189 (1968).
[2] Some parts of this work were presented at the meeting of *Am. Chem. Soc.* (136 th Meeting Abstract papers, 40P–63, Sept. 1959).
[3] Location: *Katakasu, Fukuoka.*
[4] H. Saikachi and H. Ogawa, *J. Am. Chem. Soc.*, **80**, 3642 (1958).
[5] H. Saikachi, H. Ogawa, I. Furukawa and H. Hoshida, *Chem. Pharm. Bull.* (Tokyo), **3**, 407 (1955).
[6] F. Yoneda and Y. Nitta, *Chem. Pharm. Bull.* (Tokyo), **12**, 1264 (1964); S. Hillers, S.P. Zaeva, K. Venters, L.N. Alekseeva, L. Kruzmetra and S. Germene, *Geterotsikl Soedin., Akad. Nauk. Latv. SSR*, **1965**, 187 [*Chem. Abstr.*, **63**, 16283 h (1965)].
[7] T. Tokunaga, *Acta Medica Fukuoka*, **49**, 2368 (1958). The summary of the antibacterial activities of (5-nitro-2-furyl)-methylated polyenals prepared in this paper was described.

isolated, were followed by demethanolation and hydrolysis with dilute hydrochloric acid in acetic acid to produce corresponding methylated polyenals. Reaction schema and combination of reagents are shown in Fig. 1.

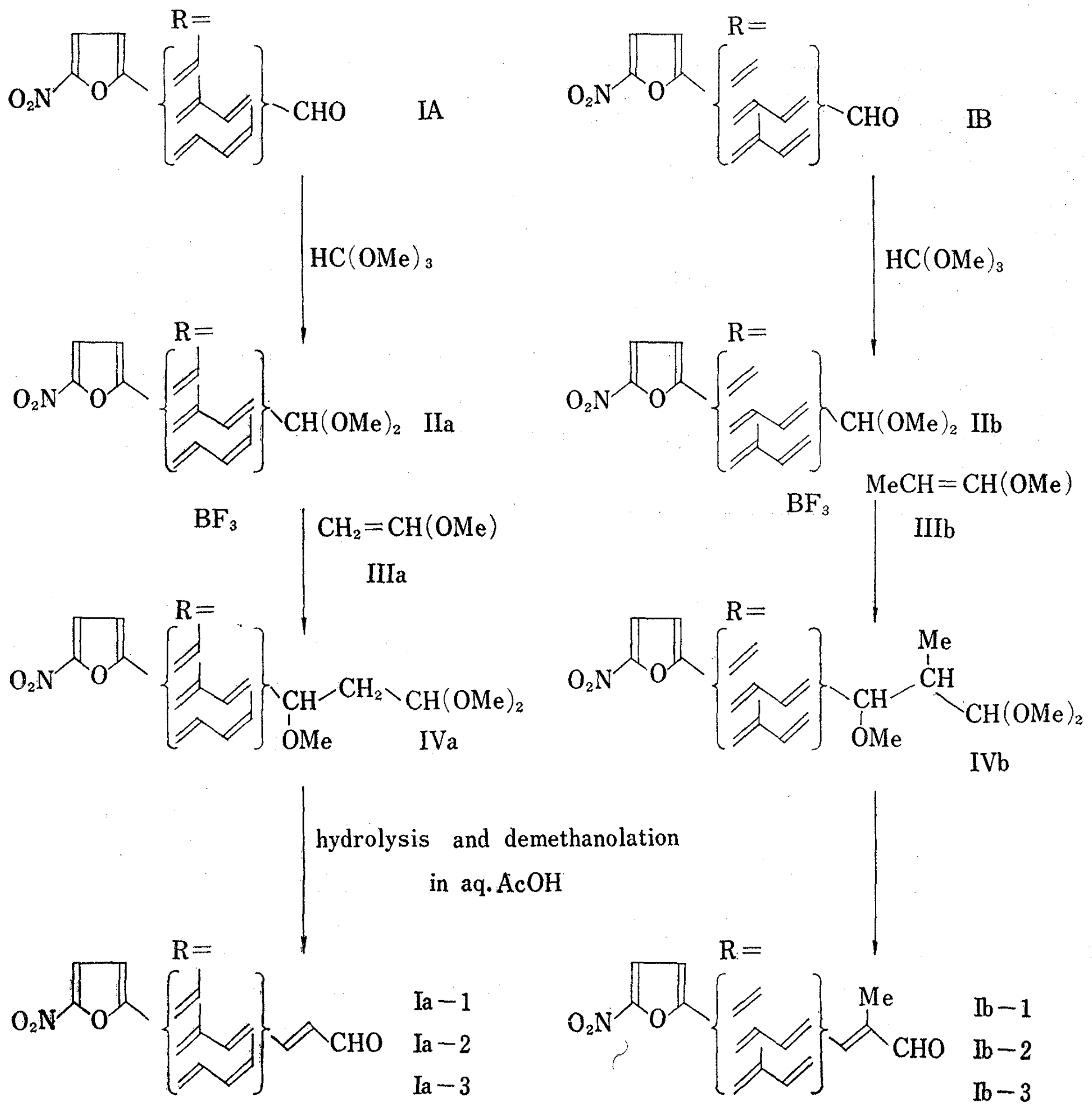

Fig. 1. Reaction Schema of Preparation of (5-Nitro-2-furyl)-methylated Polyenals

Two of methylated (5-nitro-2-furyl)-2,4-pentadienals and four of (5-nitro-2-furyl)-methylated-2,4,6-heptatrienals were obtained. Combinations of reactants, yields and melting points of resulted methylated polyenals including ultraviolet (UV) and infrared (IR) spectral data are shown in Table I. The geometry of their unsaturated aldehyde group can be assigned *trans* from the reaction mode in common with a similar formyl olefination.[8]

It can be seen from Table I and Fig. 2 that the introduction of one methyl group on the side chain of parent (5-nitro-2-furyl)-2,4-pentadienal results in a bathochromic displacement of the $\pi \rightarrow \pi^*$ transition band. Since the comparable absorption maximum of $\pi \rightarrow \pi^*$ transition band of non-methylated (5-nitro-2-furyl)-2,4-pentadienal was observed at 376.5 mμ, the

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[8] This formyl olefination was elegantly applied for carotinoid synthesis by O. Isler, H. Lindler, M. Montavon, R. Rüegg and P. Zeller, *Helv. Chim. Acta*, 39, 249; *ibid.*, 39 259 (1956), and was shown to give all *trans* $n+1$ unsaturated aldehydes.

Table I. (5-Nitro-2-furyl)-methylated Polyenals

Acetal	Alkyl enol ether$^{a)}$	Polyenal	Yield (%)	mp$^{b)}$ (°C)	UV absorption max. (mμ) and ε max.	IR absorption $\nu_{C=O}$ (cm^{-1})
(5-Nitro-2-furyl)-α-methylacrolein dimethyl acetal	v	(5-nitro-2-furyl)-4-methyl-2,4-pentadienal (Ia–1)	92	145—147	275$^{c)}$ (12200) 380 (27800)	1678 (KBr)
(5-Nitro-2-furyl)-acrolein dimethyl acetal	p	(5-nitro-2-furyl)-2-methyl-2,4-pentadienal (Ib–1)	80	153—154	285$^{c)}$ (15700) 383.5 (28600)	1659 (KBr)
(5-Nitro-2-furyl)-4-methyl-2,4-pentadienal dimethyl acetal	v	(5-nitro-2-furyl)-6-methyl-2,4,6-heptatrienal (Ia–2)	43	138—139	235$^{d)}$ (9700) 311.5 (21000) 399 (47000)	1670 (Nujol)
(5-Nitro-2-furyl)-2-methyl-2,4-pentadienal dimethyl acetal	v	(5-nitro-2-furyl)-4-methyl-2,4,6-heptatrienal (Ia–3)	53	140—141	233$^{d)}$ (8400) 311 (20200) 403.5 (43600)	1667 (Nujol)
(5-Nitro-2-furyl)-2,4-pentadienal dimethyl acetal	p	(5-nitro-2-furyl)-2-methyl-2,4,6-heptatrienal (Ib-2)	68	158—159	230$^{d)}$ (6600) 308.5 (23900) 401.5 (44100)	{1669 1686 (Nujol)
(5-Nitro-2-furyl)-4-methyl-2,4-pentadienal dimethyl acetal	p	(5-nitro-2-furyl)-2,6-dimethyl-6-heptatrienal (Ib-3)	82	216—217	238$^{d)}$ (8120) 316 (21600) 403 (48600)	1660 (Nujol)

a) v=methyl vinyl ether, p=methyl propenyl ether *b*) Recrystallized from EtOAc. *c*) in EtOH *d*) in dioxane

bathochromic shifts were found to be 7 mμ for (5-nitro-2-furyl)-2-methyl-2,4-pentadienal (1b-1) and 3.5 mμ for (5-nitro-2-furyl)-4-methyl-2,4-pentadienal (1a-1), respectively (see Table I).

Above formyl olefination was shown to give *trans* higher polyenals. On the contrary, it became clear that (5-nitro-2-furyl)-α-methylacrolein dimethyl acetal afforded stereoselectively (5-nitro-2-furyl)-2-*cis*-4-*trans*-2,4-pentadienal (V), mp 113—114°, by analogous condensation with methyl propenyl ether (IIIb) followed by the demethanolation and hydrolysis of the obtained etheral acetal (IVc) with oxalic acid or *p*-toluenesulfonic acid (see Fig. 3).

In this reaction, the above selection of the acid is important to obtain the *cis* pentadienal, since the use of the hydrochloric acid should bring the reaction to quite another course. (This is discussed later.)

As showned in Fig. 3, the configuration of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal was firmly established by the occurence of cyclization of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal dimethyl acetal. The acetal easily eliminated one mole of methanol by the gentle refluxing with a small amount of *p*-toluenesulfonic acid in methanol to give deep red, 1-methoxy-2-(5-nitro-2-furyl)-3,5-dimethy-lcyclopenta-2,4-diene (IId), mp 103—104°. The structure of

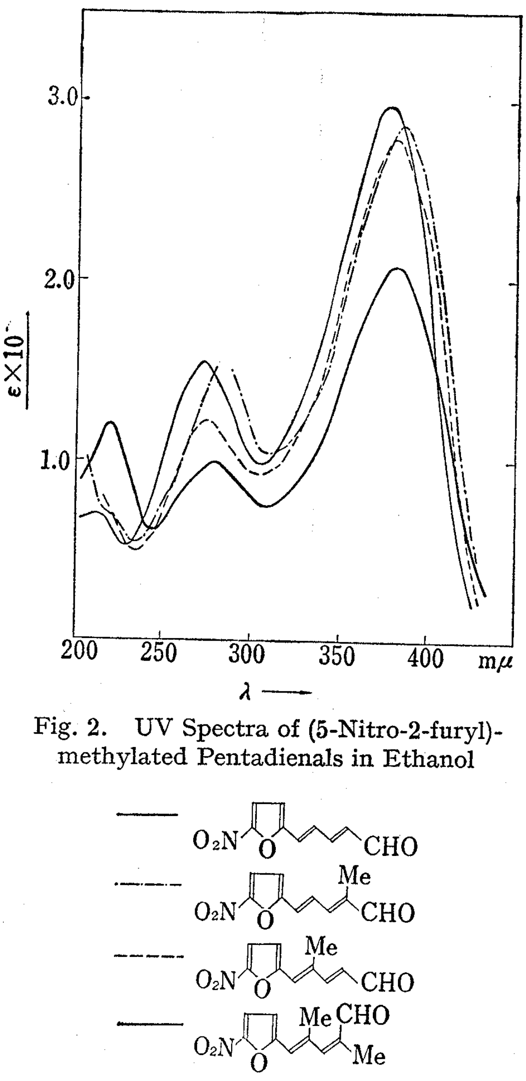


Fig. 2. UV Spectra of (5-Nitro-2-furyl)-methylated Pentadienals in Ethanol

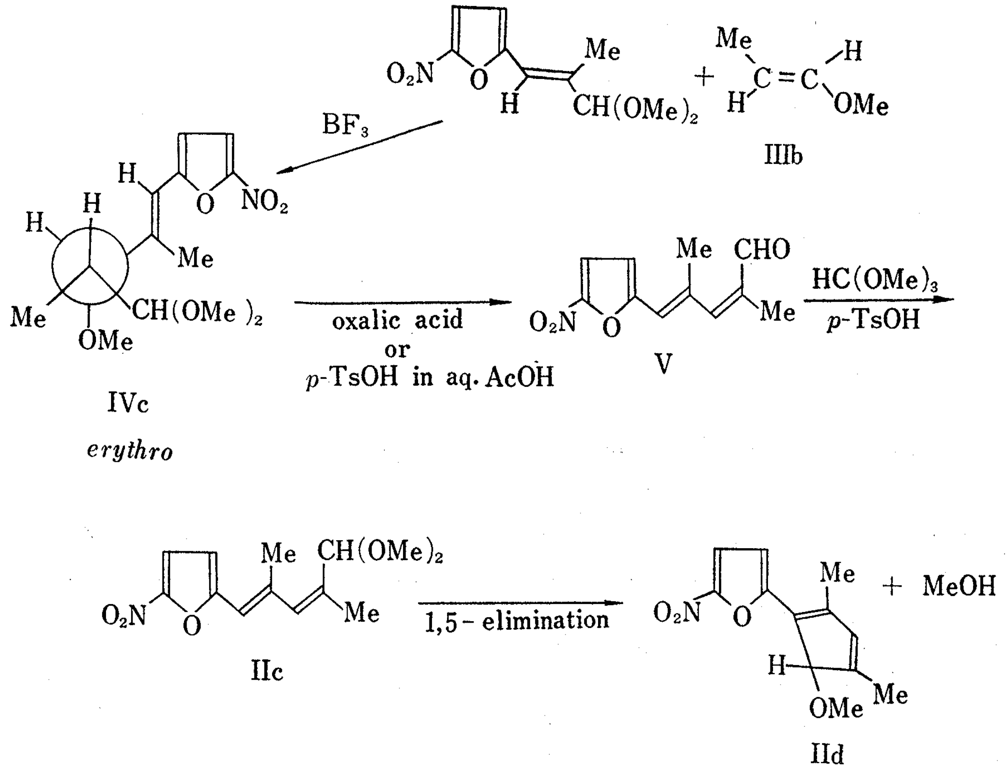
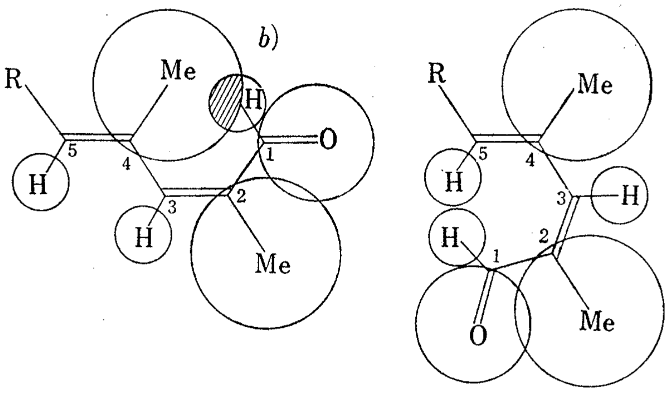


Fig. 3. Cyclization of (5-Nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal Dimethyl Acetal (IIc)

the cyclic diene was deduced from the NMR signals for three methoxy protons singlet at 2.97 ppm, methine proton singlet at 4.79 ppm and two olefinic methyl proton at 2.35 and 2.03 ppm, and one olefinic proton at 6.09 ppm as a singlet. Light absorption spectrum of (IId) is shown in Fig. 7.

From easy cyclization of the *cis* pentadienal dimethyl acetal (IIc) steric overcrowding of the parent *cis* dienal must be expected. Van der Walas projection diagram of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (V) shows that steric hindrance presents in both of the 3-*S*-*cis* and 3-*S*-*trans* spatial configuration as shown in Fig. 4. It may strongly suggest that 3-*S*-*cis* configuration, though its coplanarity is to some extent twisted because of hindrance between two hydrogens at 1 and 5 position, would be favorable than 3-*S*-*trans*, since 3-*S*-*trans* configuration would have much strict deviation from coplanarity by methyl–hydrogen interaction between 1 and 4 position.



3-*S*-*trans* 3-*S*-*cis*

Fig. 4. The Two In-plane Conformation of V

bond lengths			bond angles		
	C=C	1.39Å		C=C-C	125°
	C-C	1.46		C=C-H	122
	C-C$^{a)}$	1.54		C=C-C=O	120
	C-H	1.09	interaction radii[9]		
	C=O	1.21		Me	1.70Å
				O	1.32
				H	0.62

R=5-nitro-2-furyl-
a) none conjugated C-C
b) shaded portion represents methyl↔hydrogen interaction

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9) E.A. Braude, and F. Sondheimer, *J. Chem. Soc.*, **1955**, 3754.

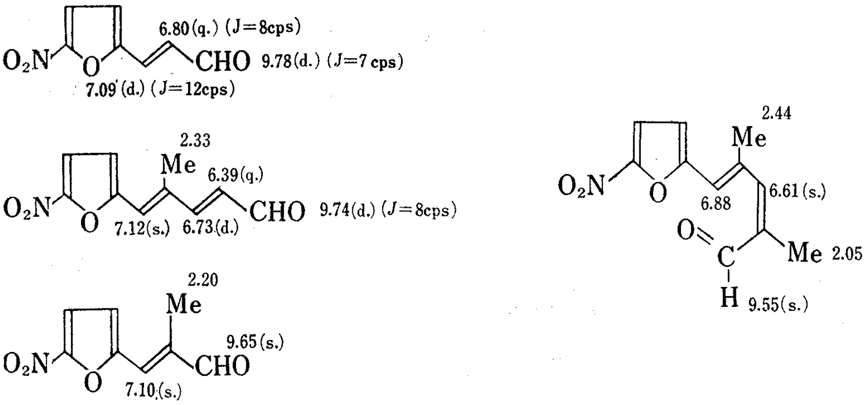

Fig. 5. Proton Chemical Shifts (ppm) of (5-Nitro-2-furyl)-polyenals (in $CDCl_3$)
(s)=singlet (d)=doublet (p)=quartet

Comparing the UV spectrum of (V) with those of other *trans* methylated polyenals (see Fig. 2), a characteristic band with appreciably high intensity was observed at 221 mμ. Another characteristics of the spectrum were large decreased intensities in both of the bands at 279 and 381 mμ with increasing methyl substitution. It is not clear whether these decreases of absorption intensities are due entirely to steric hindrance to coplanarity or partily to changes in spatial conformation. Electronic spectra appear to be relatively insensitive to changes in conformation, because considerable noncoplanarity can be tolerated without changes in absorption maxima, although the intensities of the absorption may vary.[10]

By contrast, NMR spectrum of V appears to be particularly instructive regarding to the conformation of the molecule. As can be seen from Fig. 4, the olefinic hydrogen adjacent to nitrofuran ring of the *cis* dienal (V) is to place different environment according to its spatial configuration. If (V) takes 3-*S*-*cis* configuration it must be expected that the olefinic hydrogen adjacent to nitrofuran ring is in the shielding zone of carbonyl group and results in high field shift of the proton. As a strong support of this expectation, the proton absorption occurred at 6.88 ppm, which exerts 0.22±0.02 ppm shielding influence relative to 7.10±0.02 ppm, which is the average value of corresponding hydrogen in those of *trans* unsaturated aldehydes (see Fig. 5). From the observation of NMR spectroscopy 3-*S*-*trans* conformation of (V) thus may be precluded.

To our interest, carbonyl group of the *cis* pentadienal (V) was shown to come very closely to the olefinic hydrogen adjacent to 5-nitrofuran ring. Thus, it may be expected that the

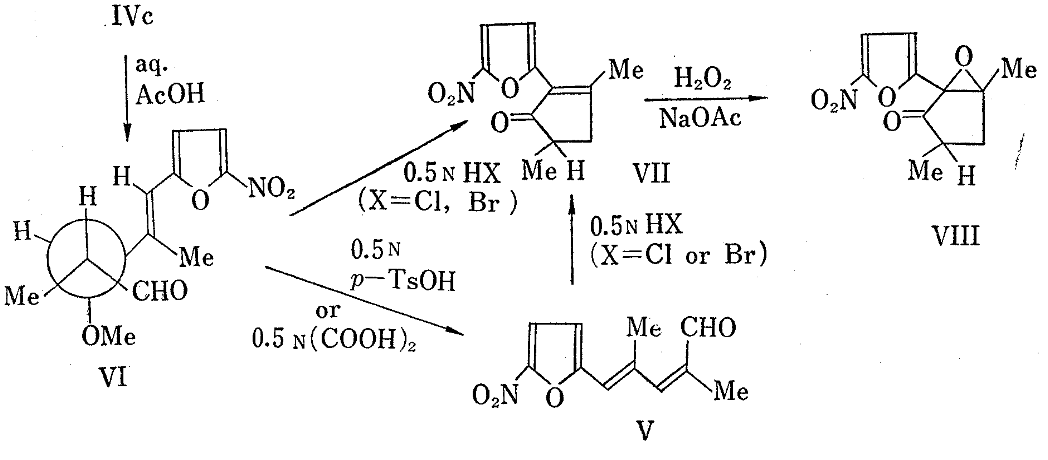

Fig. 6. Formation of (5-Nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (V)

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[10] E.A. Braude and C.J. Timmons, *J. Chem. Soc.*, **1955**, 3766; F.H. Cottee, B.P. Straughan and C.J. Timmons, *J. Chem Soc.* (B), **1967**, 1146.

cis denal (V) shows different chemical reaction in regard to its conjugated diene system from other less hindered pentadienals. It was already shown that (V) was not produced by hydrolysis and demethanolation of the corresponding etheral acetal (IVc) in the presence of dilute hydrochloric acid, but obtained by the use of *p*-toluenesulfonic acid or oxalic acid. To clarify this descrepance of the acid action, the formation of (V) was examined according to following sequence (see Fig. 6).

By heating of aqueous acetic acid solution of the etheral acetal (IVc) which obtained from condensation of (5-nitro-2-furyl)-α-methylacrolein dimethyl acetal with methyl propenyl ether, (5-nitro-2-furyl)-2,4-dimethyl-3-methoy-4-penten-1-al (VI), mp 113—115°, was obtained, which showed absorption band at 1721 cm^{-1} (nonconjugated aldehyde C=O stretch), and showed methoxy protons singlet at 3.35 ppm.

(5-Nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (V) was obtained by heating of (VI) with 0.5N *p*-toluenesulfonic acid or oxalic acid in ethyl alcohol at 100° (in sealed tube), along with a small amount of 2-(5-nitro-2-furyl)-3,5-dimethyl–cyclopent-2-en-1-one (VII), mp 108—109°, which was identified by gaschromatography, IR spectrum and mixed melting point test with an authentic sample. Gaschromatographic analysis of the reaction mixture contradicted the presence of another stereoisomer of (V) (see Fig. 6).

Heating of tetrahydrofuran solution of (VI) in the presence of hydrochloric or hydrobromic acid (0.5N) in a sealed tube was found to give (VII) as the cyclization product of (VI) in good yield.

The structure of (VII) was affirmed by the following spectral data, *i.e.*, (VII) shows absorption bands at 1635 cm (C=C strech), 1710 cm^{-1} (C=O stretch characteristic for five membered conjugated ketone), the UV spectrum in ethanol showed bands (max. 352.5 mμ and ε 13700, 271 mμ and 5400, and 227 mμ and 1400) (see Fig. 7). The NMR spectrum lacked in aldehyde proton and showed doublet centered at 1.24 ppm (J=8 cps) characteristic for secondary methyl protons. Mass spectrum of the molecule revealed *m/e* 221 as a parent peak. The failure of semicarbazone or oxime derivation from (VII) may suggest the presence of ortho effect of two substituents adjacent to the carbonyl group. Epoxydation of (VII) was carried out by hydrogen peroxide in the presence of sodium acetate to produce 2-(5-nitro-2-furyl)-2,3-epoxy-3,5-dimethylcyclopentanone (VIII), mp 157°. The epoxy ketone showed characteristic carbonyl stretching band at 1763 cm^{-1} which was good accordance with the value reported for five membered epoxy ketone.[11]

It is considerable of interest that, under the action of hydrochloric or hydrobromic acid, sterically hindered (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal cyclized to five membered ketone. This acid catalytic ring closure of the *cis* pentadienal is a new type of rearrangement, which promises to have some synthetic utility. Investigation of mechanism and scope of this reaction are in progress in our laboratories.

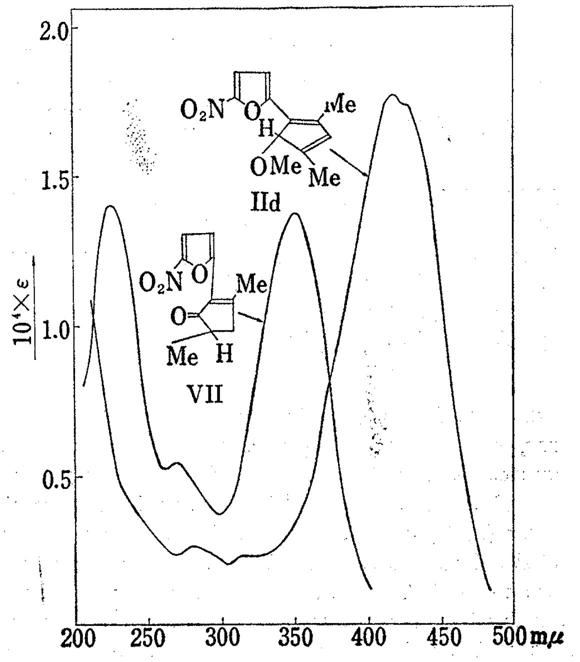

Fig. 7. UV Spectra of 2-(5-Nitro-2-furyl)-3,5-dimethyl-cyclopent-2-en-1-one(VII) and 1-Methoxy-2-(5-nitro-2-furyl)-3,5-dimethyl-cyclopenta-2,4-diene (IId) in Ethanol

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[11] H.O. House and R.L. Wasson, *J. Am. Chem. Soc.*, **79**, 1488 (1957).

Experimental

Melting points were not corrected. IR spectra were measured on a Koken DS–301 spectrophotometer. NMR spectra were determined in $CDCl_3$ at 60 Mc on a Varian Associates A–60 recording spectrophotometer using TMS as the internal standard. UV spectra were determined on a Hitachi–Perkin Elmer UV–Vis spectrophotometer Model 139. The low resolution mass spectrum was obtained on a Hitachi 6E–3 instrument, with visicorder recording.

Methyl Propenyl Ether——The unsaturated ether was prepared by the catalytic vapor phase decomposition of propionaldehyde dimethyl acetal. This method gave an excellent yield compared with the liquid phase dealcoholation of the acetal reported by M.G. Voronkov.[12]

For the catalyst of dealcoholation tone plates (manufactured by Nihon Chemical Ceramic Co.) was broken into pieces (8—15 mesh). The prepared catalyst was packed into 30 cm × 2.5 cm Pyrex tube, vertically arranged, which was surrounded by automatically controlled 300 watts electric ribbon heater to maintain the reaction temperature at 300° ± 10°. To prevent the radiation loss, the column was covered with several sheets of aluminum foils and finally insulated about 1 cm thickness of absestos. This packed column was then heated at the reaction temperature in a stream of nitrogen to dry the catalysts. After one hour 113 g (1.085 mole) of propionaldehyde dimethyl acetal which was prepared by modified Adkins, Nissen procedure[13] was constantly introduced from dropping funnel at the rate of 60 ml/hr. The vapor of the unsaturated ether was cooled to moderate temperature by passing it through about 20 cm connected glass lines and then condensed perfectly in cold traps dipped into a dry ice–acetone bath (−55°). After the addition of the acetal, nitrogen was continued to pass for additional half an hour in order to sweep remaining products. Condensate was washed with water to remove methanol and dried on sodium carbonate. Fractionation using small Widmer column gave 57.3 g of methyl propenyl ether in 73.3% yield, bp 42—43°.

(5-Nitro-2-furyl)-methylated Alkenal Dimethyl Acetals (II)——In the usual method, (5-nitro-2-furyl)-methylated alkenal dimethyl acetal was prepared by the acid catalyzed reaction of the appropriate aldehyde with methyl orthoformate in absolute methanol.

General Method: In a flask were placed 0.2 mole of (5-nitro-2-furyl)polyenealdehyde, 26.8 g (0.252 mole) of methyl orthoformate, 40 ml of absolute methanol and 0.05 g of *p*-toluenesulfonic acid. After being refluxed for 30 minutes, the mixture was neutrallized with a methanolic solution of sodium acetate, and the solution was cooled in an ice–salt bath. Resulting crystals were filtered and recrystallized from methanol. The acetals obtained were listed in Table II.

TABLE II. (5-Nitro-2-furyl)-methylated Alkenal Dimethyl Acetals

Acetal	Yield (%)	mp (°C)	Carbon(%)		Hydrogen(%)		Nitrogen(%)	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
(5-Nitro-2-furyl)-α-methylacrolein dimethyl acetal	81	51.5— 53	52.85	53.12	5.77	5.50	6.17	6.48
(5-Nitro-2-furyl)-2-methyl-2,4-pentadienal dimethyl acetal	88	111 —112	56.91	57.07	5.97	5.93	5.53	5.33
(5-Nitro-2-furyl)-4-methyl-2,4-pentadienal dimethyl acetal	*ca.* 80	without isolation	56.91	—	5.97	—	5.53	—

(5-Nitro-2-furyl)-methylated Polyenals (I)——General Method: In a three necked flask fitted with stirrer, reflux condenser, thermometer and dropping funnel (where methyl vinyl ether (bp 5°) was used vapour diffuser was fitted in stead of dropping funnel), 0.172 mole of dry appropriate unsaturated aldehyde dimethyl acetal and 50 ml of dry chloroform were placed and stirred. A solution of 0.1 g of borontrifluoride etherate (0.2% of borontrifluoride based on the weight of the acetal) in 20 ml of absolute chloroform was added to the acetal solution dropwise during the addition of 0.206 mole of appropriate unsaturated ether at 40—45°. The rate of addition was so controlled that the temperature of the reaction mixture was maintained nearly constant. After the addition was completed, the reaction mixture was continued to stirr for an additional 1 hr at this temperature. Entire contents of the flask were then transferred to a separatory funnel, and washed with 2% of aq. sodium acetate solution to remove the acidic catalyst. The lower layer was separated, washed with water two times and dried over anhydrous sodium sulfate. Then chloroform was removed *in vacuo* to give a dark reddish residue, to which 200 ml of acetic acid and 100 ml of 3% of hydrochloric acid were added. The mixture was stirred and heated on a steam bath at 80—90° for 1.5 hr, and

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12) M.G. Voronkov, *J. Gen. Chem., U.S.S.R.*, **20**, 2060 (1950) [*Chem. Abstr.*, **45**, 5607h (1950)].

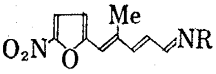
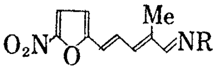
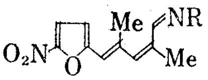
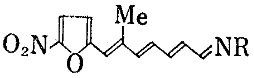
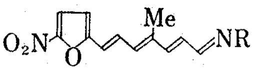
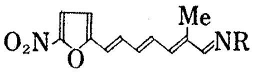
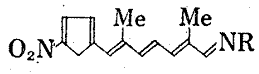
13) "Organic Syntheses," Coll. Vol. I, ed. By A.H. Blatt, John Wiley and Sons, Inc., New York, N.Y., 1948, p.1.

then cooled to 0°. The crystals of higher vinylog of starting unsaturated aldehyde were obtained, which were washed with 250 ml of water and recrystallized from proper solvent. The melting points, yields and UV and IR spectral data of these (5-nitro-2-furyl)-methylated polyenals were listed in Table I. Analytical data of those of methylated polyenals and their nitrogenous derivatives such as semicarbazones or oximes were also listed in Table III and IV, respectively.

Table III. Analytical Data of (5-Nitro-2-furyl)-methylated Polyenals

Polyenal	Formula	Carbon(%) Calcd.	Carbon(%) Found	Hydrogen(%) Calcd.	Hydrogen(%) Found	Nitrogen(%) Calcd.	Nitrogen(%) Found
Ia-1	$C_{10}H_9O_4N_1$	57.97	57.86	4.38	4.40	6.76	6.49
Ib-1	$C_{10}H_9O_4N_1$	57.97	57.99	4.38	4.66	6.76	6.50
V	$C_{11}H_{11}O_4N_1$	59.72	59.75	5.01	5.27	6.33	6.09
Ia-2	$C_{12}H_{11}O_4N_1$	61.80	61.99	4.75	4.85	6.01	6.19
Ia-3	$C_{12}H_{11}O_4N_1$	61.80	61.43	4.75	4.59	6.01	5.65
Ib-2	$C_{12}H_{11}O_4N_1$	61.80	61.74	4.75	4.83	6.01	6.15
Ib-3	$C_{13}H_{13}O_4N_1$	63.15	62.92	5.30	5.60	5.67	5.55

Table IV Nitrogenous Derivtives of (5-Nitro-2-furyl)-methylated Polyenals

	R	mp (decomp.)	Nitrogen(%) Calcd.	Nitrogen(%) Found
	–OH	170	12.61	12.45
	–NHCONH₂	244	21.20	21.18
	–NHCSNH₂	234	19.99	19.90
	–NHC(=NH)NH₂·HCl	266	23.37	23.21
	–OH	221—223	12.61	12.46
	–NHCONH₂	265	21.20	21.15
	–NHCSNH₂	252—255	19.99	20.05
	–NHC(=NH)NH₂·HCl	284—286	23.37	23.29
	–NOH	180—184	11.86	11.85
	–NHCONH₂	215—217	20.14	20.05
	–OH	192—193	11.29	10.91
	–NHCONH₂	247—248	19.30	19.28
	–NHCSNH₂	245	18.29	18.21
	–NHC(=NH)NH₂·HCl	279—280	21.50	21.30
	–OH	199	11.29	11.14
	–NHCONH₂	244	19.30	18.99
	–NHCSNH₂	231—232	18.29	17.99
	–NHC(=NH)NH₂·HCl	258—259	21.50	21.27
	–OH	225	11.29	11.28
	–NHCONH₂	258	19.30	19.23
	–NHCSNH₂	265—270	18.29	18.10
	–NHC(=NH)NH₂·HCl	260	21.50	21.47
	–OH	238—239	10.68	10.89
	–NHCONH₂	263	18.41	18.30
	–NHCSNH₂	262	17.49	17.17
	–NHC(=NH)NH₂·HCl	270	20.61	20.55

1-Methoxy-2-(5-nitro-2-furyl)-3,5-dimethylcyclopenta-2,4-diene (IId)——To a solution contained 19 g (0.086 mole) of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal and 10.9 g (0.103 mole) of methyl orthoformate in 30 ml absolute methanol 10 mg of *p*-toluenesulfonic acid was added and the solution was refluxed for 1.5 hr. After cooling, the reaction mixture was neutrallized with a methanolic solution of sodium acetate, and then excess orthoformate and solvents were evaporated under reduced pressure. Reddish oily residue was obtained. After allowing to stand overnight at room temperature, red crystals were separated, which were filtered and washed with cold methanol. Recrystallization from methanol gave 3.0 g of (IId) as reddish prisms, mp 103—104°, in 15% yield. *Anal.* Calcd. for $C_{12}H_{13}O_4N_1$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.19; H, 5.63; N, 5.95. The NMR spectrum of (IId) supported its structure. There were assignable peaks for secondary methoxy protons (singlet at 2.97 ppm), methine proton at 1-position (singlet at 4.79 ppm) and two olefinic methyl protons at 3 and 5-position (each doublet at 2.35 (J=2 cps) and 2.03 ppm (J=1 cps), respectively. Olefinic proton at 4 position absorbed at 6.09 ppm as singlet. The UV spectrum of (IId) is shown in Fig. 7.

5-(5-Nitro-2-furyl)-2,4-dimethyl-3-methoxy-pent-4-en-1-al (VI)——Fifteen grams (0.05 mole) of the ethereal acetal (IVc) which was obtained from the reaction of methyl propenyl ether with (5-nitro-2-furyl)-α-methylacrolein dimethyl-cetal according to the above procedure was stirred with 70 ml of 80% aq. acetic acid, and warmed at 80° for 1 hr. After cooling, resulting yellowish addhesive crystals were filtered and washed several times with water and recrystallized from 80% aq. methanol. The crystals were filtered and dried under vaccum at 75° for 5 hrs to remove the crystal solvent. After cooling yellow prisms were obtained, mp 113—115 (9.0 g). *Anal.* Calcd. for $C_{12}H_{15}O_5N_1$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.96; H, 5.87; N, 5.49. IR cm^{-1} (KBr): $\nu_{C=O}$ 1721 (unconjugated aldehyde), 1650 ($\nu_{C=C}$ stretch). The NMR spectrum was strongly indicative ot its structure. There were assignable peaks for methoxy protons (singlet at 3.35 ppm), methyl protons at 4-position (singlet at 2.08 ppm), and aldehyde proton (singlet at 9.80 ppm).

(5-Nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (V)——Forty five grams (0.157 mole) of (5-nitro-2-furyl)-2,4-dimethyl-3-methoxy-pent-4-en-1-al dimethyl acetal which obtained from the condensation of methyl propenyl ether with (5-nitro-2-furyl)-α-methyl–acrolein dimethyl acetal, was dissolved into a mixture of 120 ml of acetic acid, 80 ml of water and 5.0 g of oxalic acid. The solution was heated for 4 hr in a boiling water bath. After cooling yellow needles were separated from the reaction mixture, filtered and washed with water to remove the acids. The crystals were recrystallized from 75% of aq. methanol, 16 g of yellow prisms were obtained, mp 113—114°, in 46% yield. UV $\lambda_{\max}^{\text{ethanol}}$ mμ (ε): 221 (12000), 279 (10000), 381 (20800). IR cm^{-1} (Nujol): $\nu_{C=O}$ 1670; $\nu_{C=C}$ 1600. The NMR spectrum showed assignable peaks to methyl protons at 2-position (2.05 ppm), methyl protons at 4-position (singlet at 2.44 ppm) and aldehyde proton (singlet at 9.55 ppm).

2-(5-Nitro-2-furyl)-3,5-dimethylcyclopent-2-en-1-one (VII)——In a 250 ml thick walled tube, 8.5 g (0.0336 mole) of 5-(5-nitro-2-furyl)-2,4-dimethyl-3-methoxypent-4-en-1-al (VI), 64 ml of tetrahydrofuran and 5 ml of 0.5 N hydrochloric acid were placed and sealed. The mixture was heated for 3 hrs in a boiling water bath. After cooling the sealed tube was opened and the solvent was evaporated under reduced pressure. The obtained residue was dissolved in 80% aq. ethanol and cooled. Needle crystals were separated from the solution, which were filtered and washed with water and recrystallized from 80% aq. ethanol. A yield of 5.6 g (75.5%) of 2-(5-nitro-2-furyl)-3,5-dimethyl-cyclopent-2-en-1-one (VII) was obtained as pale yellow needles, mp 108—109°. *Anal.* Calcd. for $C_{11}H_{11}O_4N_1$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.50; H, 4.95; N, 6.24. IR cm^{-1} (Nujol): $\nu_{C=O}$ 1710 (five membered conjugated ketone); $\nu_{C=C}$ 1635. UV $\lambda_{\max}^{\text{ethanol}}$ mμ (ε): 352.5 (13700), 271 (5400), 227 (14000). The main absorption band of this cyclic ketone was shown to shift about 30 mμ toward shorter wavelength compared with that of (5-nitro-2-furyl)-2,4-pentadienal. The UV spectrum of (VII) was shown in Fig. 7. The NMR spectrum lacked in aldehyde proton and showed peaks characteristic for secondary methyl protons at 5-position (doublet, centered at 1.24 ppm, J=8 cps) and another methyl protons at 3-position (2.57 ppm as singlet). Neither the semicarbazone nor oxime could be isolated from the reaction of this cyclopentenone with the corresponding carbonyl reagent.

2-(5-Nitro-2-furyl)-2,3-epoxy-3,5-dimethylcyclopentanone (VIII)——To a stirred solution of 1.0 g (4.52 mmole) of 2-(5-nitro-2-furyl)-3,5-dimethyl–cyclopent-2-en-1-one and 6 ml of 24% aq. hydrogen peroxide in 20 ml of ethanol was added at room temperature 10 ml of aq. solution of 0.5 g of sodium acetate. The mixture was stirred for further 30 minutes at 50°, and then cooled in an ice bath. Resulting nearly colorless crystals were filtered and washed with water. Recrystallization from 70% aq. ethanol yielded 0.4 g of colorless needles, mp 155—157°. *Anal.* Calcd. for $C_{11}H_{11}O_5N_1$: C, 55.69; H, 4.67; N, 5.91. Found: C, 55.20; H, 4.69; N, 5.63. IR cm^{-1} (KBr): $\nu_{C=O}$ 1763. UV $\lambda_{\max}^{\text{ethanol}}$ mμ (ε): 316 (10200). NMR spectrum showed peaks assignable to methyl protons at 5-position (doublet centered at 1.14 ppm, J=7 cps) and methyl proton at 3-position (singlet at 1.67 ppm) and multiplet absorptions centered at 2.62 ppm.

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