CHEMICAL & PHARMACEUTICAL BULLETIN

Vol. 17, No. 9 September 1969

Regular Articles

[Chem. Pharm. Bull. 17(9)1757—1766(1969)]

UDC 547.722.5.04

Synthesis of Furan Derivatives. XLV.[1] A New Acid catalyzed Cyclization of sterically Hindered *cis* Alkenals[2]

HARUO SAIKACHI, HARU OGAWA, and KATUTOSHI SATO

Faculty of Pharmaceutical Sciences, Kyushu University[3]

(Received July 4, 1968)

Preparation of aryl 2,4-dialkyl-2,4-pentadienals (aryl is (5-nitro-2-furyl)- or (5-nitro-2-thienyl)-, alkyl is methyl or ethyl) by condensation of alkyl enol ether R–CH=CH–OR R≠H) with aryl-α-alkylated acrolein acetals gave stereoselectively 2-*cis*-4-*trans*-2,4-dialkylated pentadienals. Driving force leading to above configuration is overcrawding control of the sterically hindered chain. The stereoselective formation of *cis*-alkenals was found to be applicable for aryl 2-*cis*-4-*cis*-6-*trans*-trialkylated heptatrienal. All hindered *cis* alkenals prepared in this paper cyclized to five or seven membered cyclic ketones in the presence of HCl or some organic acids.

A mechanism for the cyclization was proposed, that involves initial formation of oxocarbonium ion, which is later transformed by two of successive processes, *i.e.*, the formation of bicyclo-[2.1.0] cyclopentanone derivative and its ring rupture by acid. Proposed mechanism was discussed from the result of deuterohydrochloric acid incorporated cyclization of IVa.

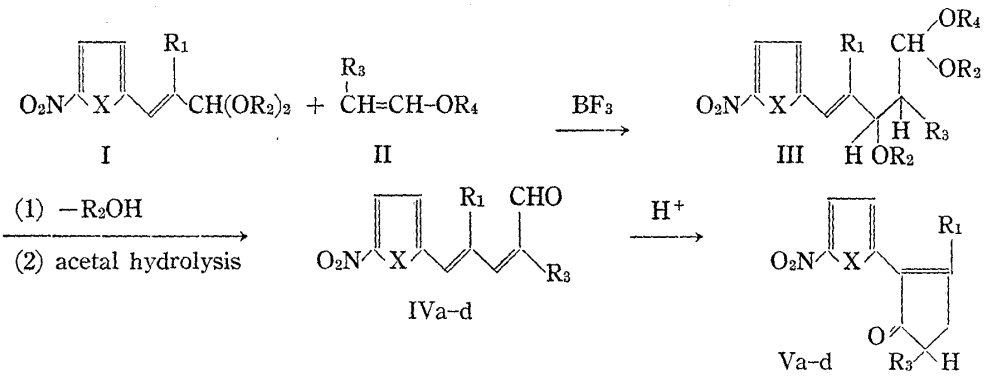
Earlier studies of the acid catalytic transformation[4] of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-2,4-pentadienal (IVa) with hydrochloric or hydrobromic acid have shown that the compound is readily transformed to five membered conjugated ketone, 2-(5-nitro-2-furyl)-3,5-dimethyl-pent-2-en-1-one (Va). The present studies have been undertaken to examine whether this type cyclization may generally occur in 5-(5-nitro-2-furyl)-2-*cis*-4-*trans*-2,4-dialkylated pentadienals (IVa—d) and 7-(5-nitro-2-furyl)-2-*cis*-4-*cis*-6-*trans*-2,4,6-trimethylheptatrienal (VI).

At the onset of this work, the first requisite for the cyclization of the pentadienal is that the pentadienal is to have 2-*cis*-4-*trans* arrangement, and the second is that the use of hydrochloric or hydrobromic acid should be essential to lead the reaction to completion.

In the preparation of several pentadienals possessing above configuration IV, it was found the first requirement was fulfilled by the previously reported method involving the

1) Part XLIV: H. Saikachi and J. Matsuo, *Chem. Pharm. Bull.* (Tokyo), 17, 1260 (1969).
2) Presented at the 88th Annual Meeting of the Pharmaceutical Society of Japan at Tokyo, April 1968.
3) Location: *Katakasu, Fukuoka.*
4) H. Saikachi and H. Ogawa, *Chem. Pharm. Bull.* (Tokyo), 17, 306 (1969).

condensation of aryl α-alkylated acrolein acetals ($R_1 \neq H$) (I) with alkyl enol ether (II) (R_3 =Me or Et) in the presence of boron trifluoride etherate, and subsequent dealkolation and acetal hydrolysis of the etheral acetal obtained III. The reaction scheme is shown in Fig. 1.



	R_1	R_3	X	
IVa	Me	Me	O	Va
IVb	Me	Et	O	Vb
IVc	Et	Me	O	Vc
IVd	Me	Me	S	Vd

Fig. 1. Preparation of Aryl-2,4-dialkylated-2-*cis*-4-*trans*-pentadienal

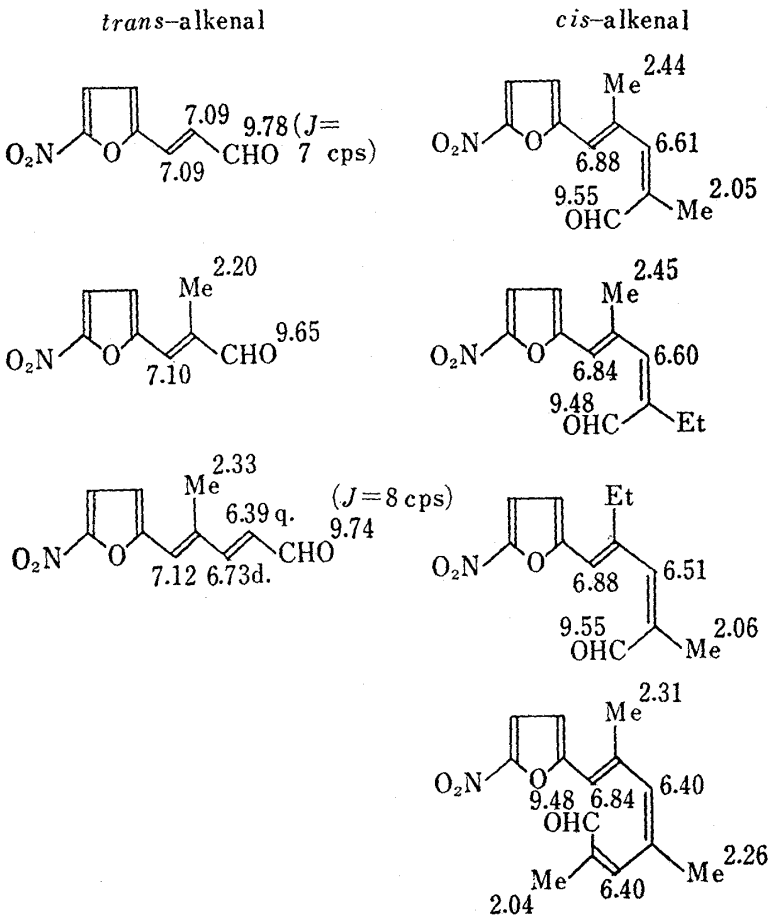


Fig. 2. Vinylic Chemical Shifts[a] of 5-Nitro-2-furyl-polyenals

a) in ppm from tetramethyl silane (60 Mc/s), solvent $CDCl_3$

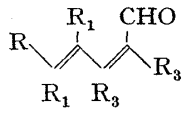
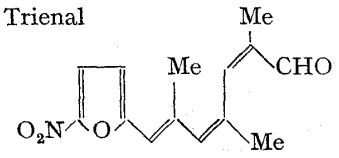
Although a number of pentadienals in furan derivatives[5] have been reported, no systematic preparation of 2,4-di-substituted-2,4-pentadienals which might be expected considerable overcrawding caused by two alkyl substituents have been carried out yet.

Pentadienals (IVa—d) obtained from above method were found to have 2-*cis*-4-*trans* configuration as shown in Fig. 1. Gaschromatographic analysis of the hydrolysis aliquote of the etheral acetal (III, X=O, $R_1=R_2=R_3=R_4$ =Me) did not show the appreciable amounts of other isomer than IVa. Substantiation of the configuration of IVa—d was drawn from the nuclear magnetic resonance (NMR) spectra, *i.e.*, high field shift of the signal of 5-hydrogen of IVa—c makes marked

5) M. Lipp and F. Dallacker, *Chem. Ber.*, **90**, 1730 (1957); F. Yoneda and Y. Nitta, *Chem. Pharm. Bull.* (Tokyo), **12**, 1264 (1964); S. Hillers, S. Pzaeva, K. Venters, L. N. Alekseeva, L. Krutzmetra, and S. Germane, *Akad. Nauk Latv. SSR*, **1965**, 187 (*Chem. Abstr.*, **63**, 16283 *h* (1965)).

contrast with the chemical shift of corresponding hydrogen in trans alkenals (see Fig. 2). The similar shift of 5-hydrogen of 2-*cis* pentadienal was already utilized to determine 2-*cis*-4-*trans* configuration of IVa,[4] which was also acertained by additional chemical evidence that dimethyl acetal of IVa easily eliminates one mole of methanol to give 1-methoxy-2-(5-nitro-2-furyl)-3,5-dimethylcyclopenta-2,4-diene.[4] Scale drawing of IVb—c may also suggest the preference of 3-(*S*)-*cis* than 3-(*S*)-*trans* configuration, because van der Waals radius of ethyl may be considered as same as methyl group. The NMR properties and physical properties of some new pentadienals are shown in Fig. 2 and Table 1, respectively.

Table I. Polyenals with *cis* Formyl Group

Dienal R				mp[a] (°C)	UV absorption λ_{max}^{EtOH}	$\varepsilon_{max.}$	IR absorption (cm^{-1}) $\nu_{C=O}$	$\nu_{C=C}$
(5-Nitro-2-furyl)-	Me	Me	(IVa)[b]	113—114	221 280 380	12000 9900 20800	1667	—
(5-Nitro-2-furyl)-	Me	Et	(IVb)	108—109	220 285 380—385	8800 10400 25300	1672	1612 1599
(5-Nitro-2-furyl)-	Et	Me	(IVc)	101—102	221.5 285 380—385	11600 10000 23700	1671	1600
(5-Nitro-2-thienyl)-	Me	Me	(IVd)	150—152	222 280 310 394	7700 9900 8600 24700	—	—
Trienal 			(VI)	117—118	242 312.5 400	11200 14700 28600	1671	1600 1620

Alkenal	Formula	Analysis Carbon (%) Calcd.	Found	Hydrogen (%) Calcd.	Found	Nitrogen (%) Calcd.	Found
IVb	$C_{12}H_{13}O_4N_1$	61.27	61.25	5.57	5.50	5.96	5.90
IVc	$C_{12}H_{13}O_4N_1$	61.27	61.20	5.57	5.51	5.96	5.96
IVd	$C_{11}H_{11}O_3N_1S_1$	55.69	55.47	4.67	4.41	5.91	5.73
VI	$C_{14}H_{15}O_4N_1$	64.36	63.96	5.79	5.62	5.62	5.60

a) Recrystallized from 75% ethanol.
b) H. Saikachi and H. Ogawa, *Chem. Pharm. Bull.* (Tokyo), **17**, 306 (1969)

The 2-*cis*-4-*trans* configuration of obtained 2,4-di-alkyl-substituted pentadienal was also presented by the Wittig reaction, *i.e.*, (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-pentadienal (IVa) was obtained in approximately 5% yield, when (5-nitro-2-furyl)-α-methyl-acrolein (X) was treated with three molar formylethylidene triphenylphosphorane[6] (XI) in acetonitrile at 85° for 8 hours. Mixed melting point determination of the product with authentic IVa did not show any depression and both of them gave same Infrared (IR) spectrum. In this preparation, again no other appreciable stereoisomer have been detected.

6) S. Trippett and D. M. Walker, *J. C. S.*, **1961**, 1266.

From this result, stereochemistry of the formyl olefination is seemed to be determined by the stability of the betaine intermediate (XII). The initial conbination of (5-nitro-2-furyl)-α-methyl-acrolein (X) with the phosphorane (XI) can occur in two ways to give either the *erythro* (XIIa) or *threo* (XIIb) betaine, which subsequently collapses with the formation of the 2-*cis*-4-*trans* isomer and 2,4-all *trans* isomer, respectively. In these conformations the *erythro* betaine (XIIa) is less sterically hindered than the *threo* betaine (XIIb), because in former conformation smaller formyl group is to place at the same side with larger 1-methyl-2-(5-nitro-2-furyl)vinyl group, and thus XIIa seems to more likely to form. As the phosphorane (XI) is resonance stabilized ylid[7] owing to electron withdrawing effect of formyl group, betaine formation with aldehyde (X) is seemed to be reversible. Therefore the subsequent reaction would then be expected to proceed entirely through the *erythro* betaine (XIIa), and 2-*cis*-4-*trans* configuration favored for the resulting olefin (IVa). The stereochemical course above mentioned is shown in Fig. 3.

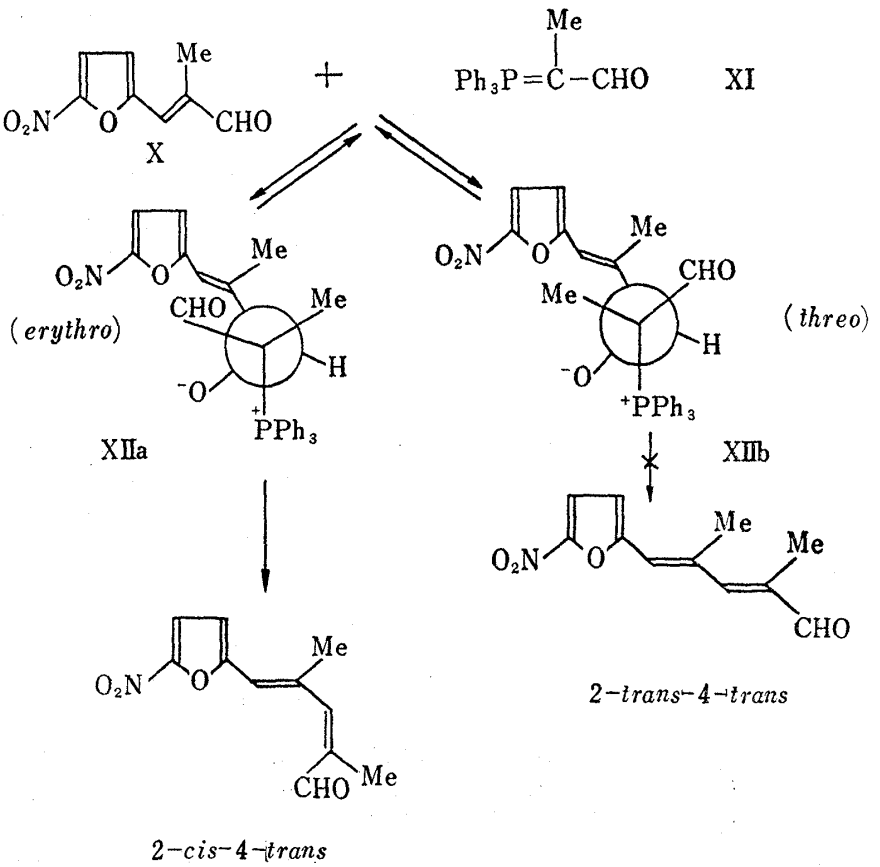
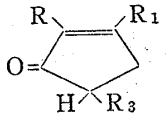


Fig. 3. Wittig Reaction of α-Formylethylidenetriphenylphosphorane with (5-Nitro-2-furyl)-α-methylacrolein

The 2-*cis*-4-*trans* pentadienals were now heated with dilute hydrochloric acid (0.5N) in acetonitrile to see expected cyclization would generally take place. As the result of these experiment, the cyclization is found to occur entirely in good yields (70—80% yields) to give 2-(5-nitro-2-furyl)-3,5-alkyl substituted-cyclopent-2-en-1-one (V). Structures of Va—d were shown in Table II.

7) A.J. Speziale and D.E. Bissing, *J. Am. Chem. Soc.*, **85**, 3878 (1963); I.U.P.A.C. (ed.), Organo-Phosphorus Compounds, Butterworths, London, 1964, pp. 255—269.

Table II. Physical Properties of Cyclopentenone Derivatives

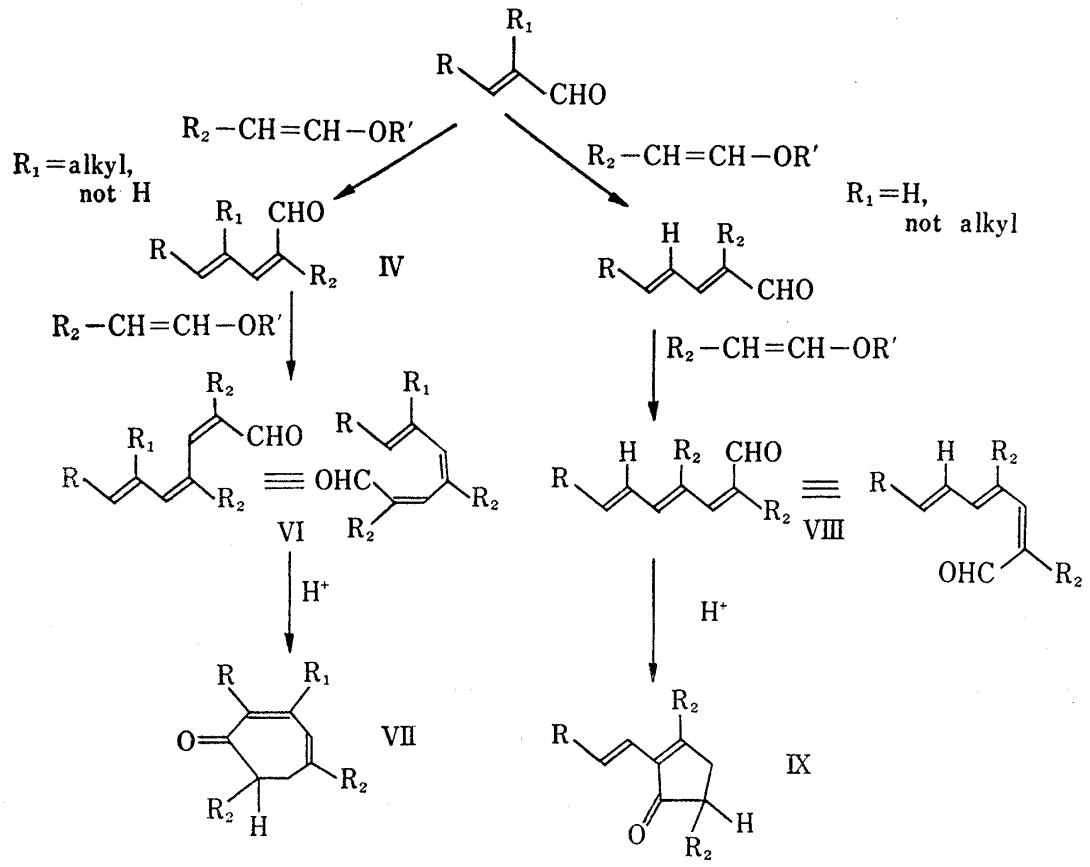


Cyclopentenone derivative substitutent R	R_1	R_3		mp (°C)	UV absorption λ_{max}^{EtOH} mμ	$\varepsilon_{max.}$	IR absorption (cm^{-1}) $\nu_{C=O}$	$\nu_{C=C}$
5-Nitro-2-furyl-	Me	Me	(Va)	108—109	228	14000	1718	1645
					272	5400		
					353	13800		
5-Nitro-2-furyl-	Me	Et	(Vb)	61— 62	225—227	14100	1705	1640
					270	5700	1694	
					350	13900		
5-Nitro-2-furyl-	Et	Me	(Vc)	79— 80	227	15200	1719	1639
					272	6500		
					352	15000		
5-Nitro-2-thienyl-	Me	Me	(Vd)	136—137	230	7700	1708	
					360	17500		
(5-Nitro-2-furyl)-acryl-	Me	Me	(IX)	142—143	220	7800	1693	1631
					265	17600		1601
					383	18300		

Compound	Formula	Carbon (%) Calcd.	Found	Hydrogen (%) Calcd.	Found	Nitrogen (%) Calcd.	Found
Vb	$C_{12}H_{13}O_4N_1$	61.27	61.20	5.57	5.41	5.96	5.93
Vc	$C_{12}H_{13}O_4N_1$	61.27	61.11	5.57	5.36	5.96	5.98
Vd	$C_{11}H_{11}O_3N_1S_1$	55.69	55.59	4.67	4.41	5.91	5.80
IX	$C_{13}H_{13}O_4N_1$	63.15	63.28	5.30	5.34	5.67	5.60

It was obtained that the condensation of aryl-α-alkyl-acrolein acetal (I) with alkenyl ether (II) (R–CH=CH–OR, R≠H) never failed to give aryl 2-*cis*-4-*trans*-2,4-alkylated pentadienal (IV). If this stereochemical outcome is exactly retained in the attempted preparation of (5-nitro-2-furyl)-2,4,6-trimethylheptatrienal (VI), the configuration of this highyl hindered trienal should be 2-*cis*-4-*cis*-6-*trans* arrangement, and its zig–zag type conjugation might have a cyclization possibility which lead to seven membered cyclic ketone by acid (see Fig. 4). On the other hand, if R_1 is hydrogen, in stead of alkyl, expected stereochemistry of this trienal would be 2-*cis*-4-*trans*-6-*trans* arrangement, and subsequent cyclization might give five membered cyclic ketone.

(5-Nitro-2-furyl)-2,4,6-trimethyl-2-*cis*-4-*cis*-6-*trans*-heptatrienal (VI) was obtained in the yield of 3—5% from concomitant reddish oily mixture which showed two peaks in gaschromatography. The configuration of the molecule was acertained by its NMR spectrum, *i.e.*, upfield shift of 7-vinylic proton appeared at 6.84 ppm gave a strong support to the configuration, whereas two hydrogens at 3 and 5 position showed singlet at 6.40 ppm. Assignable peaks for vinylic methyl at 2, 4 and 6 position were shown at 2.04, 2.26 and 2.31 ppm, respectively (see Fig. 2). VI showed carbonyl streching band at 1671 cm^{-1}, and its UV and light absorption maxima showed at 242 mμ (11200), 312.5 mμ (14720) and 400 mμ (28600). Low yield of VI is ascribed to the fact that facile cyclization of VI to give 2-(5-nitro-2-furyl)-3,5,7-trimethyl-cyclo-hepta-2,4-dien-1-one (VII) took place together with the hydrolysis of VI's precursor, 7-(5-nitro-2-furyl)-1,1,3-trimethoxy-2,4,6-trimethylhepta-4,6-diene under the similar condition used in the hydrolysis of etheral acetals (III). VII was obtained as red viscous oil, and its



R=5-nitro-2-furyl, R′=methyl, R_2=methyl or ethyl, not hydrogen

Fig. 4. The Acid Catalyzed Cyclization of Hindered Alkenals

structure was affirmed by its NMR spectrum, which showed doublet at 1.26 ppm (J=7 cps) due to 7-position secondary methyl group, and two singlets assigned for 3- and 5-vinylic methyl at 2.06 and 2.00 ppm, respectively. No other vinylic protons appeared except a singlet at 6.36 ppm which was assigned for 4-vinyl hydrogen, and another complex multiplets were appeared in the range of 2.0—3.2 ppm with three proton integration. Carbonyl stretching occurred at 1693 cm^{-1} and UV absorption maximum occurred at 230 mμ (20700) and 370 mμ (12300) in ethanol. These values gave a reliable evidence of cyclization by losing one double bond from mother aldehyde (VI).

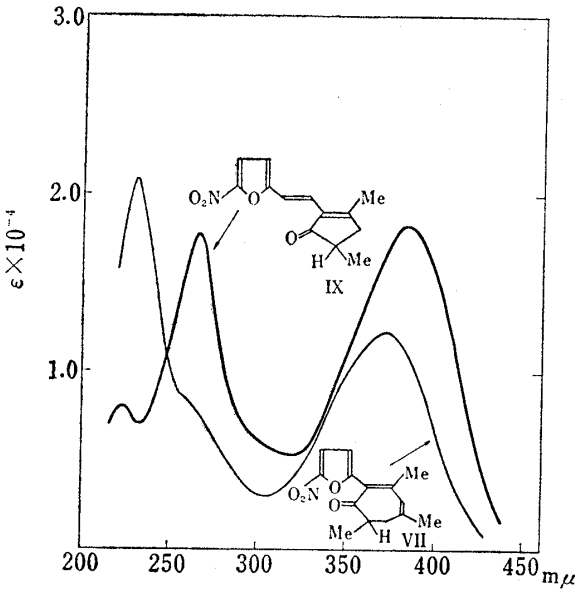


Fig. 5. The UV and Light Absorption Spectra of VII and IX in Ethanol

In contrast, cyclization of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-6-*trans*-heptatrienal (VIII) proceeded so easily that the alkenal could not isolated as pure form even in the use of weaker acid such as oxalic acid or *p*-toluenesulfonic acid. Hydrolysis of the corresponding etheral acetal which leads to VIII gave 2-(5-nitro-2-furyl)-acryl-3,5-dimethyl-cyclopenta-2-en-1-one (IX). NMR spectrum of (IX) showed the presence of *trans* vinyl

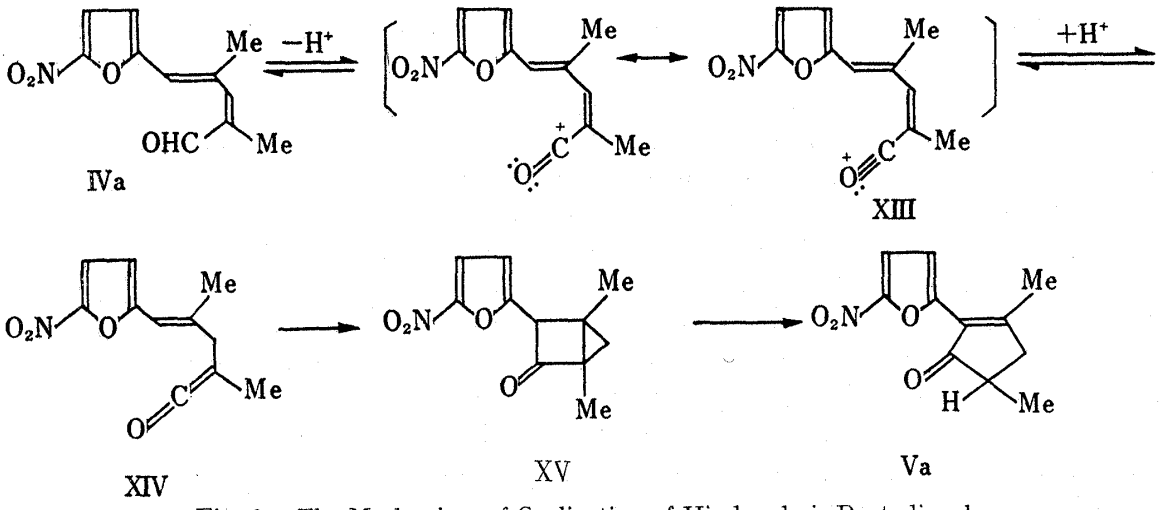


Fig. 6. The Mechanism of Cyclization of Hindered *cis*-Pentadienal

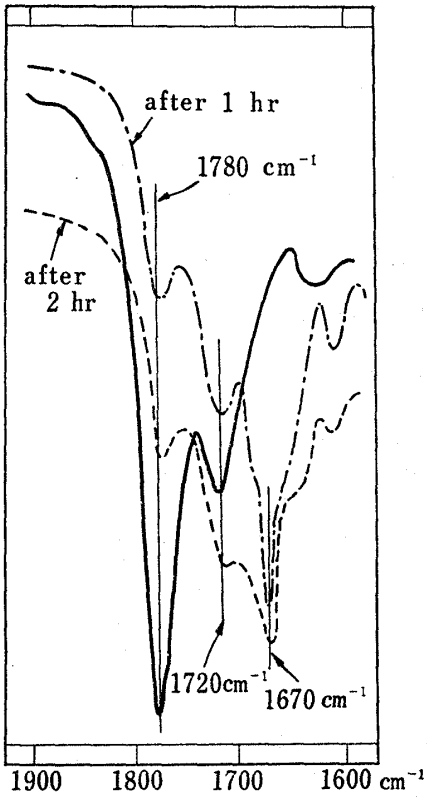


Fig. 7. Infrared Spectra of Cyclization Mixture of 5-(5-Nitro-2-furyl)-2,4-dimethyl-3-methoxypent-4-en-1-al in THF at 65°

The spectrum showed in solid line is obtained from oily residue which is obtained by evaporation of benzene elute in silicagel chromatograph of cyclization mixture after 4 hr.

cyclization condition: 100 mg of 5-(5-nitro-2-furyl)-2,4-dimethyl-3-methoxypent-4-en-1-al in 1 ml of THF is refluxed with 0.11 ml of 0.5 N HCl, in each run the reaction was stopped by the addition of sodium bicarbonate solution and the mixture was extracted with chloroform and dried with sodium sulfate. Evaporation of solvent yielded reddish oil, which was presented for analytical sample.

protons, which appeared as two doublets each centered at 7.00 (J=17 cps) and 7.70 ppm (J=17 cps). This is a strong support that (IX) is not seven membered but five membered cyclic ketone. The IR spectrum of (IX) showed carbonyl stretching at 1693 cm^{-1} and double bond streching at 1601 cm^{-1}. The UV maxima showed at 220 mμ (7800), 265 mμ (17600) and 383 mμ (18300) in ethanol (see Fig. 5).

The next step of this work was to investigate the reaction mechanism of the above cyclization. The reaction appeares to involve initial ionization of carbonyl to form linear oxocarbonium ion (XIII). Ready loss of a proton from formyl group relieves the overcrawding of the molecule as shown in Fig. 6. Then the ion rearranged to the ketene intermediate (XIV) which is probably in equilibrium with oxocarbonium ion,[8] and then the intermediate transformed successively to bicyclo[2.1.0]pentanone

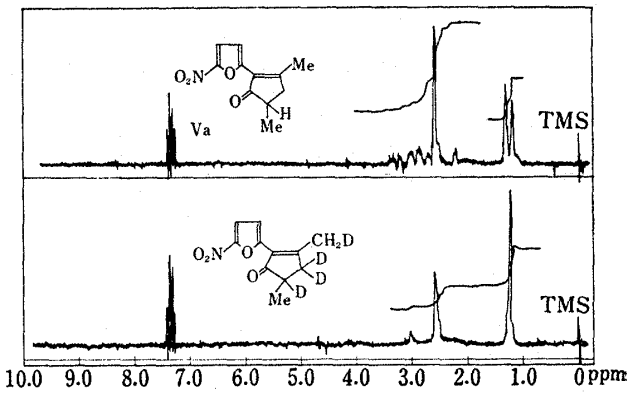


Fig. 8. The Comparison of NMR Spectrum of Va with that Deutrated 2-(5-Nitro-2-furyl)-3,5-dimethylpent-2-en-1-one

8) N.C. Deno, C.U. Pittman, and M.J. Wisotsky, *J. Am. Chem. Soc.*, **86**, 4370 (1964).

derivative (XV), which was converted to the cyclic ketone by subsequent acid cleavage of cyclopropane ring.

As one of the indirect supports of the intermediacy of above bicyclic ketone(XV), we can point out the presence of 1780 cm^{-1} carbonyl streching absorption which is assignable for cyclobutanone or ketene carbonyl from the cyclization reaction mixture of (5-nitro-2-furyl)-2,4-dimethyl-3-methoxy-pent-4-en-1-al (XVI) as shown in Fig. 7.

In order to examine the above reaction mechanism, deuterohydrochloric acid incorporated cyclization of IVa was then carried out in acetonitrile. Comparing with the NMR spectrum of the undeutrated ketone, the spectrum of the deutrated ketone showed following characteristics, *i.e.*, (1) disappearance of complex multiplets in 2.0—3.3 ppm, (2) a singlet at 1.25 ppm ascribed to $CH_3C\leqslant D$, and (3) a singlet at 2.57 ppm having two proton integration due to vinylic CH_2D. The comparison of both spectrum is shown in Fig. 8.

The finding that all the moving hydrogens participated in the cyclization are readily replaced by deutrium is not inconsistent with above mechanism. The further examination of the proposed mechanism must be done from kinetic view point. This is in progress in our laboratories.

Experimental[9]

Alkyl Enol Ethers

Methyl propenyl ether was prepared by the catalytic vapor phase decomposition of propionaldehyde dimethyl acetal by our previous paper.[4]

Ethyl butenyl ether was prepared according to M.G. Voronkov's procedure,[10] which boiled at 94—96.5°, n_D^{20} 1.40627.

(5-Nitro-2-furyl)-α-methyl-acrolein and (5-nitro-2-furyl)-α-ethyl-acrolein was prepared by our previous paper.[4]

(5-Nitro-2-thienyl)-α-methylacrolein——(5-Nitro-2-thienyl)-α-methylacrolein was prepared by following modification of G. Carrara, *et al.*'s procedure.[11]

Ten grams of dry 5-nitro-2-thiophenealdehyde was placed in a flask fitted with a stirrer, dropping funnel, reflux condenser and thermometer. After cooling in an ice bath 30 ml of freshly distilled propionaldehyde was added all at once with stirring. With caution, a 20% methanol solution of potassium hydroxide added dropwise until the temperature of the reaction mixture reaches to 30—35°. After rapid cooling 20 ml of acetic anhydride was added in one portion, the solution was boiled for 20 minutes and then cooled to 0°. After the addition of 50 ml of water and 3 ml of hydrochloric acid, the mixture was carefully warmed to prevent sudden flashing of the contents and refluxed for 30 minutes, cooled, and the precipitates was collected and recrystallized from ethanol. It yielded 7.0 g of yellow prisms, mp 134°. UV $\lambda_{max}^{ethanol}$ mμ (ε): 249 (10200), 362 (22800). *Anal.* Calcd. for $C_8H_7O_3N_1S$: C, 48.74; H, 3.58; N, 7.11. Found: C, 48.55; H, 3.42; N, 6.98.

Aryl-2,4-di-alkylated-2-*cis*-4-*trans*-pentadienals

Since all preparations were essentially carried out in the same way, a typical experiment in the preparation of (5-nitro-2-furyl)-2-ethyl-4-methyl-2-*cis*-4-*trans*-pentadienal (IVb) is described.

(5-Nitro-2-furyl)-2-ethyl-4-methyl-2-*cis*-4-*trans*-pentadienal (IVb)——To a solution of 22.7 g (0.1 mole) of (5-nitro-2-furyl)-α-methylacrolein dimethyl acetal (mp 52—54°)[4] in 50 ml of anhydrous chloroform was added a solution of 0.05 g of boron trifluoride etherate in 20 ml of anhydrous chloroform dropewise during the addition of 11 g (0.11 mole) of ethyl butenyl ether at 40—45°. The rate of addition was so controlled that the reaction temperature was maintained nearly constant. After the addition, the mixture was neutrallized with a 2% aq. sodium acetate solution. The chloroform layer was separated and washed with water and dried over sodium sulfate. After evaporation a dark reddish oily residue was obtained, on which 100 ml of acetic acid, 35 ml of water and 3 gram of *p*-toluenesulfonic acid were added, and the mixture was heated on a steam bath at 85—90° for 1 hr. On cooling, yellow crystals were deposited, which were washed with water and recrystallized from 80% ethanol to give 19.5 g. of yellow prisms, mp 108—109°. Analysis and spectral data are shown in Table I.

Reaction of α-Formylethylidenetriphenylphosphorane (XI) with (5-Nitro-2-furyl)-α-methylacrolein (X)——A solution of (5-nitro-2-furyl)-α-methylacrolein (1.0 g, 5.5 mmole) and the phosphorane[6] (5.2 g, 16.5 m

9) All melting points were not corrected.
10) M.G. Voronkov, *J. Gen. Chem., U.S.S.R.*, **20**, 2060 (1950) [*Chem. Abstr.*, **45**, 5607 *h* (1951)].
11) G. Carrara, R. Ettorre, F. Fava, G. Rolland, E. Testa, and A. Vecchi, *J. Am. Chem. Soc.*, **76**, 4391 (1954).

mole) in acetonitrile was refluxed for 8 hr. The solvent was removed under reduced pressure, and the residue was extracted with three 25 ml portions of benzene. The combined extracts were evaporated up to give reddish oily gum which was adsorbed on to a column of silicagel (diameter 20 mm, height of packing 130 mm). The column was developed with benzene, and yellow prisms (50 mg) were obtained, which does not show any depression by mixed melting point determination with authentic (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-pentadienal (IVa).

Cyclization of Aryl-2,4-dialkylated 2-*cis*-4-*trans*-Pentadienal

As the cyclization experiments were carried out in the same way, a typical experiment in the cyclization of (5-nitro-2-furyl)-2-methyl-4-ethyl-2-*cis*-4-*trans*-pentadienal is shown.

2-(5-Nitro-2-furyl)-3-ethyl-5-methyl-cyclopent-2-en-1-one (Vc)——In a flask, 2.3 g of (5-nitro-2-furyl)-2-methyl-4-ethyl-2-*cis*-4-*trans*-2,4-pentadienal, 30 ml of tetrahydrofuran and 5 ml of 0.5N hydrochloric acid were placed. The mixture was heated for 2 hr on a water bath. After cooling, the solvent was evaporated *in vacuo*. The residue obtained was recrystallized from 80% ethanol, it yielded 1.2 g of pale yellow needles, mp 79—80°. UV $\lambda_{max}^{ethanol}$ mμ (ε): 227 (15200), 272 (6500), 352 (15000). IR cm^{-1}: νC=O 1719 (KBr); νC=C 1639 (KBr). Analysis was shown in Table II.

Cyclization of (5-nitro-2-furyl)-2,4-dialkyl-2-*cis*-4-*trans*-pentadienals were carried out in the similar way, and corresponding cyclic ketones were obtained in 70—80% yields.

Cyclization of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-pentadienal in the Presence of Deutrohydrochloric Acid——The mixture of 1.5 g (6.8 mmole) of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-pentadienal (IVa), 25 ml of tetrahydrofuran and 2 ml of 20% deutrohydrochloric acid was heated for 2 hr on a steam bath. After cooling, the solvent was distilled off *in vacuo*. Yellow crystals thus obtained were collected, washed with several portions of small amount of carbon tetrachloride. Recrystallization from carbontetrachloride gave 1.0 g of deutrated 2-(5-nitro-2-furyl)-3,5-dimethylcyclopent-2-en-1-one, mp 108—109°. The NMR spectrum of this compound showed a characteristic peaks for secondary methyl protons ($\overset{Me}{\underset{D}{>}}C<$ 1.25 ppm) as a singlet with integrated intensity 3, vinyl methyl protons (2.57 ppm, integrated intensity 2). Complex multiplets which appeared in the spectrum of undeutrated (Va) were lost. The spectrum was contrasted with that of undeutrated cyclic ketone in Fig. 8.

(5-Nitro-2-furyl)-2,4,6-trimethyl-2-*cis*-4-*cis*-6-*trans*-hepta-2,4,6-trienal (VI)——15 g (0.068 mole) of (5-nitro-2-furyl)-2,4-dimethyl-2-*cis*-4-*trans*-pentadienal (IVa), 8.7 g (0.0815 mole) of methyl orthoformate, 12.8 g of absolute methanol and a few mg of *p*-toluenesulfonic acid were placed in a three necked flask fitted with a stirrer, thermometer and dropping funnel. To the mixture 160 g of anhydrous chloroform was added and the solution was refluxed on a water bath. After 30 minutes, the mixture was fractionated through a 15 cm × 2 cm Widmer column to remove methyl orthoformate and methanol. Some 30 ml portions of chloroform was added in the course of fractionation. When the reading of thermometer reached to 62°, the mixture was cooled to 45°. After the fractionation, about 100 ml of chloroform solution of the acetal was obtained. To this solution 4.9 g (0.068 mole) of methyl propenyl ether was added dropwise at 55° in the presence of 50 mg of borontrifluoride etherate. Addition of propenyl ether was so controlled that the temperature of the reaction mixture was kept nearly constant. After the addition, stirring was continued for additional 1 hr, and then the mixture was neutrallized with aqueous sodium bicarbonate and dried with anhydrous sodium sulfate. After evaporation of chloroform, 24 g of reddish oily substance obtained, and a half of the oil was dissolved into the mixture which contained 30 ml of acetic acid, 10 ml of water and 1 g of oxalic acid. The mixture was heated for 4 hours at 80°. After two days red prisms were separated, which were filtered, washed with water and recrystallized from 70% ethanol. It yielded 0.6 g of red prisms, mp 117—118°. *Anal.* Calcd. for $C_{14}H_{15}O_4N$: C, 64.36; H, 5.79; N, 5.36. Found: C, 63.96, H, 5.62, N, 5.20. The structural assignement for VI follows from their spectral data. IR cm^{-1}: ν C=O 1671 (KBr); νC=C 1620 and 1600 (KBr). UV $\lambda_{max}^{ethanol}$ mμ (ε): 242 (11200), 312.5 (14700), 400 (28600). The NMR spectrum was strongly indicative of its structure. Each vinylic methyl at 2,4 and 6 position showed singlet at 2.04, 2.26 and 2.31 ppm, respectively. Two vinyl protons at 2 and 4 position absorbed at 6.40 ppm as singlet, one proton adjacent to 5-nitro-furan ring absorbed at 6.84 ppm, its high field shift of the proton confirmed the 2-*cis*-4-*cis*-6-*trans* structure. Gaschromatographic analysis of the mother liquid showed four peaks. Contamination of 2-(5-nitro-2-furyl)-3,5-dimethyl-cyclopent-2-en-1-one and 1-methoxy-2-(5-nitro-2-furyl)-3,5-dimethyl-pent-2,4-diene was detected. From the solution oily 2-(5-nitro-2-furyl)-3,5,7-tri-methyl-cyclohepta-2,4-dien-1-one (VII) was obtained as a major product, beside with the minor formation of an uncharacterized red oil which showed relative retention volume of 1:2 based on the retension volume of (VII).

2-(5-Nitro-2-furyl)-3,5,7-trimethyl-cyclohepta-2,4-dien-1-one (VII)——0.6 g of (5-nitro-2-furyl)-2,4,6-trimethyl-2-*cis*-4-*cis*-6-*trans*-2,4,6-heptatrienal (VI) was dissolved in 10 ml of acetonitrile containing 1.5 ml of 0.5N hydrochloric acid and refluxed for 2.5 hr on a water bath. After cooling, the solution was evaporated *in vacuo*. An oily residue thus obtained was fractionated by preparative gaschromatograph (0.5% SE-30, Shimalite W, at 220°). From the first fraction, total 0.3 g of 2-(5-nitro-2-furyl)-3,5,7-trimethylcyclohepta-2,4-dien-1-one was obtained as a reddish oil, its structure was derived from the following spectral data. IR cm^{-1}: νC=O 1694: ν C=C 1654 and 1631. UV $\lambda_{max}^{ethanol}$ mμ (ε): 230 (20700), 370 (12300). The NMR

spectrum was strongly indicative of its structure. It showd two singlets at 2.00 and 2.06 ppm ascribes to vinylic methyl group, one secondary methyl at 1.26 ppm as doublet ($J=7$ cps), one vinylic proton at 6.36 ppm as singlet and complex multiplets in 2.0—3.4 ppm having intensity of three proton integration. Again, 0.1 g of uncharacterized reddish oil was obtained, and its UV spectrum in ethanol gave maxima at 228 mμ and 370 mμ which is nearly the same compared with that of VII. Whether the minor product is the stereoisomer of VII or double bond structural isomer of the cycloheptadienone is not fully certain.

Acknowledgment The authors wish to thank Dr. W. Kashihara, Ueno Chemical Research Laboratories and Department of Development, Mitsubishi Chemical Works, Kurosaki, for their contributions many helpful intermediates to this work.