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SYNTHESIS OF δ-HETARYL-α,α-DICARBONYLALKADIENES AND A STUDY OF THEIR ISOMERIZATION

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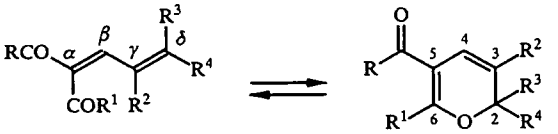
The reaction of β-hetarylacrolein and β-hetaryl-α-methylacroleins with esters of acetoacetic and malonic acids was studied. The structures of the products obtained were established using ^1H and ^{13}C NMR and UV spectroscopy. (E) and (Z) isomers of α,α-dicarbonylalkadienes, their mixtures with the corresponding 2H-pyrans or exclusively 2H-pyrans are formed depending on the substitution in the starting aldehyde and the ester used. 6-Methyl- and 3,6-dimethyl-5-carbalkoxy-2-(2-pyridyl)pyrans are converted upon heating to substituted 2-(pyrilidene)pyrans.

In previous work [1-5], we have shown that some α,α-dicarbonylalkadienes I are converted by valence isomerization to give the corresponding 2H-pyrans II and a dynamic equilibrium is established between I and II.



I II

There is a significant substituent effect on the capacity of dienes I to undergo this transformation and the manifestation of solvato-, thermo-, and photochromic properties related to these compounds. Thus, the substitution of the γ-proton in I (R = Me, OMe, R^1 = Me, R^2 = H, R^3 = H, R^4 = H, Me, Ph, cyclohexyl; R^3 = R^4 = Me) by a methyl group completely shifts the equilibrium toward the corresponding 2H-pyran II due to a strong steric interaction [3-5]. Conversion to the 2H-pyran is not found for dienes I (R^2 = H), which have an NMe_2 group in the δ-position, in contrast to the analogous compounds with an alkyl group in this position. However, a dynamic equilibrium is established between I and II (R^2 = Me, Ph, Cl, Br, OEt) [6, 7] or this equilibrium is completely shifted toward II (R^2 = *i*-Pr, NMe_2) [8] when substituents are present at the γ-position in such dienes.

The Knoevenagel reaction of β-hetaryl-α,β-unsaturated aldehydes (IIIa-IIIi) with the methyl and ethyl esters of acetoacetic (IV) or malonic acids (V) was carried out to study the effect of hetaryl substituents at the δ-position of these α,α-dicarbonylalkadienes on their valence isomerization and the structures of the products obtained were established.

The products, which may be formed in the condensation of aldehydes IIIa-IIIi with esters IVa, IVb, Va, and Vb, are shown in the general scheme on the following page.

Starting compounds IIIa, IIIb, and IIIf-IIIh, were obtained by the aldol condensation of the corresponding heterocyclic aldehydes with acetaldehyde or propionaldehyde according to reported procedures [9-11]. We should note that the recently developed method for aldol condensation in a phase transfer system [11] proved convenient for the synthesis of α-methyl-substituted aldehydes IIIg and IIIh and also IIIi. Unfortunately, this approach is not suitable for the synthesis of β-pyridylacroleins IIIc-IIIe and is very inefficient for obtaining previously unreported α-methyl-β-(4-pyridyl)acrolein (IIIj), which was prepared in only slight amounts and not used in further syntheses.

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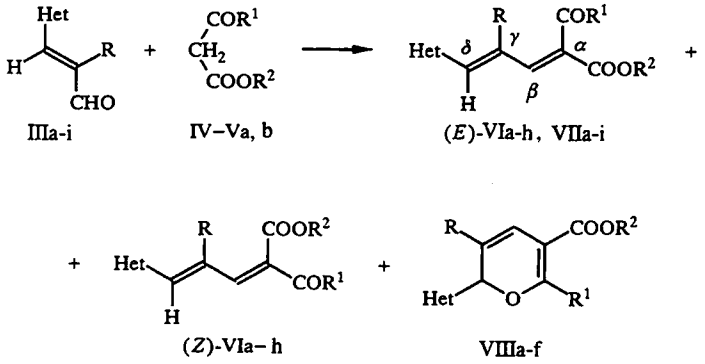
Scheme



IIIa,f,VIa,c,VIIa,b,VIIIa Het = furyl-2; IIIb,g, IVb,d,VIIc-f,VIIIb Het = thienyl-2; IIIc,h,VIe,VIIg-i,VIIIc,e Het = pyridyl-2; IIIg,i,VIf,g,VIIj-k,VIIIf Het = pyridyl-3; IIIe,VIh,VII*l* Het = pyridyl-4; IIIa-e,VIa,b,e,f,h,VIg,j,*l* R = H; IIIf-i,VIc,d,g,VIIh,i,k,VIIIa-d,f R = Me; IVa,VIa-h,VIIIa-c,f, $R^1 = R^2 = Me$; IVb,VIIId, $R^1 = Me$, $R^2 = Et$; Va,VIIa-c,e,g,h,j-*l*, $R^1 = OMe$, $R^2 = Me$, Vb,VIId,f,i, $R^1 = OEt$, $R^2 = Et$

. It has been repeatedly reported that the condensation of acetaldehyde with pyridine aldehydes proceeds with very low yields [12, 13]. The Wittig reaction between the corresponding β-pyridylaldehydes and (formylmethylene) triphenylphosphorane proved a better method for the synthesis of β-pyridylacroleins [14] despite the necessity of preparing this phosphorane derivative. β-(2-Pyridyl)acrolein IIIc was obtained in 15% yield by a rather simple method, which has been proposed for the synthesis of β-(4-pyridyl)acrolein IIIe [13], by the direct aldol condensation of 2-pyridinaldehyde with acetaldehyde in benzene in the presence of morpholine acetate (see Experimental). An attempt to obtain this compound by the condensation of 2-pyridinaldehyde with the lithium derivative of Schiff base $CH_3CH{=}NBu\text{-}t$ [15] proved unsuccessful.

The spectral indices of aldehydes IIIa-IIIj are given in Table 1. The PMR data indicate that IIIa-IIIe are (*E*) isomers ($J_{\alpha,\beta}$ = 15-16 Hz).

The condensation of aldehydes IIIa-IIIi with esters IVa, IVb, Va, and Vb was carried out in the presence of piperidine or a mixture of piperidine and glacial acetic acid as the catalyst. The indices of these products are given in Tables 2 and 3. Their structures were established by UV (Tables 2 and 3), PMR (Tables 4 and 6), and ^{13}C NMR spectroscopy (Tables 5 and 7).

The assignment of the signals in the ^1H and ^{13}C NMR spectra of these products to either diene (VI) or 2H-pyran (VIII) was made by comparing their chemical shifts and coupling constants with those of aliphatic dienes and 2H-pyrans studied in our previous work [3, 16]. Assignment to the (*E*) or (*Z*) isomers was made using our data on the stereospecificity of the $^3J_{CO,H\beta}$ constants and ^{13}C NMR chemical shifts of the carbonyl groups in conjugated carbonyl compounds: $^3J_{CO,H\beta(cis)} < {}^3J_{CO,H\beta(trans)}$ [17], δCO *(cis)* < δCO*(trans)* [18]. The corresponding dienic ketoesters VIa and VIb were formed from β-furyl- (IIIa) and β-thienylacroleins (IIIb) and ketoester IVa as an equilibrium mixture of *(E)* and *(Z)* isomers at the α,β double bond with 54% *(Z)* in the case of VIa and 60% *(Z)* in the case of IVb.

X = O, S

Pure crystalline *(Z)* isomers were isolated upon prolonged standing or cooling of these mixtures, while equilibrium mixtures of *(Z)* and *(E)* isomers as indicated by PMR spectroscopy were reobtained upon maintenance in $CDCl_3$ at room temperature for several days.

TABLE 1. PMR and UV Spectral Data for β-Hetarylacroleins

Compound	UV spectrum λ_{max}, nm (ε), EtOH	PMR spectrum, chemical shifts, δ, ppm, $CDCl_3$, coupling constants (J), Hz												
		CHO (1H)	α-H (1H, d.d)	β-H (1H)	Me (3H)	heterocycle (Het)								Coupling constant
						furyl/thienyl			pyridyl					
						3-H (1H, d)	4-H (1H)	5-H (1H, d)	2-H (1H, d)	3-H (1H, d)	4-H (1H)	5-H (1H)	6-H (1H)	
IIIa	322 (27000)	9,62 (d)	6,58	7,22 (d)	—	6,77	6,53 (m)	7,57	—	—	—	—	—	$J_{\alpha\beta}$ = 16; $J_{CHO,\alpha\text{-}H}$ = 8
IIIb	325 (18900)	9,76 (d)	6,50	7,57 (d)	—	7,35	7,09 (d,d)	7,49	—	—	—	—	—	$J_{\alpha\beta}$ = 16; $J_{CHO,\alpha\text{-}H}$ = 8
IIIc	295 (13900), 255 (11400)	9,80 (d)	7,10	7,55 (d)	—	—	—	—	—	7,53	7,78 (m)	7,30 (м)	8,70 (d)	$J_{\alpha\beta}$ = 16; $J_{CHO,\alpha\text{-}H}$ = 8
IIId	270 (18500)	9,75 (d)	6,78	7,50 (d)	—	—	—	—	8,80	—	7,90 (m)	7,39 (d,d)	8,65 (d,d)	$J_{\alpha\beta}$ = 16; $J_{CHO,\alpha\text{-}H}$ = 8
IIIe	265 (19700)	9,76 (d)	6,83	7,43 (d)	—	—	—	—	8,71	7,40	—	7,40 (d)	8,71 (d)	
IIIf	320 (28000)	9,40 (s)	—	6,95 (d)	2,02 (d)	6,71	6,48 (d,d)	7,56	—	—	—	—	—	$J_{CH_3\beta\text{-}H}$ = 1,5
IIIg *	320	9,45 (s)	—	7,40 (s)	2,05 (d)	7,35	7,12	7,57	—	—	—	—	—	$J_{CH_3\beta\text{-}H}$ = 1,5
IIIh*	295; 255	9,55 (s)	—	7,18 (s)	2,18 (d)	—	—	—	—	7,42	7,70	7,20	8,65	$J_{CH_3\beta\text{-}H}$ = 1,5
IIIi	275 (18800)	9,63 (s)	—	7,25 (s)	2,09 (d)	—	—	—	8,77	—	7,85 (d)	7,39 (d,d)	8,62 (d)	—
IIIj	—	9,54 (s)	—	7,15 (s)	1,97 (s)	—	—	—	8,58	7,30	—	7,30 (d)	8,58 (d)	—

*PMR spectral data from work of Kryshtal' [11].

TABLE 2. Physical Indices of Products of the Knoevenagel Reaction of Ketoester IVa and Aldehydes IIIa-IIIg and IIIi*

Starting aldehyde	Reaction products vol. % of mixture (according to PMR data)					mp, °C of (Z) isomer VI*2	bp, °C (mm Hg)*3	UV spectrum, λ_{max} (ε) EtOH	Mass spectrum, m/z	Yield, % (rel. to starting reagents)
	diene	(E) isomer	(Z) isomer	pyron						
IIIa	VIa	46	54	—	—	72...75	143...150 (0,47)	365 (52000)	220	45
IIIb	VIb	40	60	—	—	77...83	140...143 (0,09)	365 (27100)	236	48
IIIf	VIc	40	48	VIIIa	12	57...60	125...130 (0,37)	360 (38500)	234	23
IIIg	VId	9	78	VIIIb	13	89...94	—	355 (32100)	250	24
IIIc	VIe	40	60	—	—	Oil	—	330 (20800)	—	*4
IIId	VIf	45	55	—	—	102...108	—	325 (27700)	—	25
IIIi	VIg	—	14	VIIIf	86	—	130...140 (0,3)	208 (16800), 310 (8400)	245	28
IIIe	VIh	38	62	—	—	Oil	—	315 (15400)	—	20

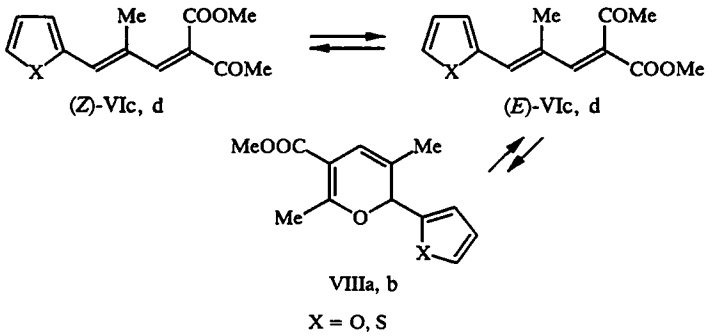
*Elemental analysis data given in Experimental. These data are lacking for some compounds due to difficulties in purifying small amounts.

*2Indistinct mp related conversion of (Z) isomer to (E) isomer and pyran VIII upon melting.

*3n_D^{20} = 1.6348 for this mixture of *(E)*- and *(Z)*-(VIa), 1.5945 for mixture of *(E)*- and *(Z)*-VIc and VIIIa, and 1.5723 for mixture of *(Z)*-VIg and VIIIf.

*4See Experimental.

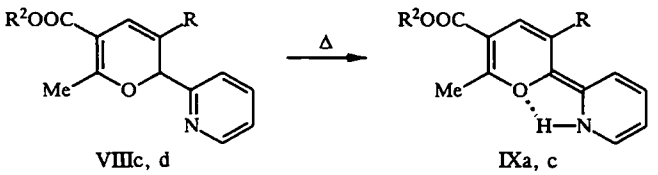
2H-Pyrans VIIIa and VIIIb were also formed from α-methyl-substituted β-furylacrolein IIIf and β-thienylacrolein IIIg and ketoester IVa along with the *(Z)* and *(E)* isomers of dienes VIc and VId. The ratios of these products determined using PMR spectroscopy are given in Table 2.



The (Z) isomers VIc and VId isolated in crystalline form undergo isomerization upon prolonged maintenance in solution in $CDCl_3$ or CD_3OD and PMR spectroscopy indicated formation of equilibrium mixtures of the (Z) and (E) isomers of VIc and VId and pyran VIIIa and VIIIb (see Table 2). We should note that the (E)-VI:VIII ratio in these mixtures was the same as in the condensation product. These findings are in accord with the results obtained in a study of the temperature dependence of the isomer composition of α,α-dicarbonylalkadienes, indicating that (E)-I, (Z)-I, and II are in equilibrium. This equilibrium between the geometric isomers is established much more slowly than between structures (E)-I and II.

The reactions of dimethyl malonate Va with aldehydes IIIa, IIIb, IIIf, and IIIg and of diethyl malonate Vb with aldehydes Vb with aldehydes IIIb and IIIg gave only dienic diesters VIIa-VIIf (see scheme), not containing the corresponding 2H-pyrans as indicated by ^1H and ^{13}C NMR spectroscopy.

On the other hand, only pyran VIIIc is formed in the condensation of α-methyl-β-(2-pyridyl)acrolein IIIh with ketoester IVa.



VIIIc,, IXa R = R^2 = Me; VIIId, IXb R = Me, R^2 = Et

Distillation of pyran VIIIc was unexpectedly accompanied by its conversion to 3,6-dimethyl-5-carbomethoxy-2-(pyridylidene)pyran (IXa). PMR spectroscopy indicated that the distilled product was an 82:18 mixture of IXa and VIIIc. Crystallization of this mixture gave pure pyran IXa. This pyran is formed not only upon distillation but also upon heating pyran VIIIc. Maintaining pyran VIIIc at 80°C for 40 min led to 40% conversion to pyran IXa. The structure of pyran IXa was established by ^1H and ^{13}C NMR, and UV spectroscopy and mass spectrometry (Tables 2, 6, and 7) and elemental analysis. The PMR spectrum of IXa in $CDCl_3$ lacks the signal at 5.71 ppm, corresponding to 2-H in pyran VIIIc. The signal for the NH group proton is seen at 13.42 and 13.36 ppm in the same spectrum taken in DMSO-d_6. This signal is lacking upon replacement of the solvent by CD_3OD. Hence, pyran IXa is a chelate with intramolecular hydrogen bonding. The chemical shifts and coupling constants of the protons of the pyrilidene ring in pyran IXa are similar to those in compounds with pyrilidene structure and existing as chelates with intramolecular hydrogen bonding [19, 20].

The ^{13}C NMR spectrum of IXa in $CDCl_3$ shows singlets at 132.51 and 124.61 ppm assigned to the $C_{(2)}$ atoms in the pyran and pyrilidene rings, respectively.

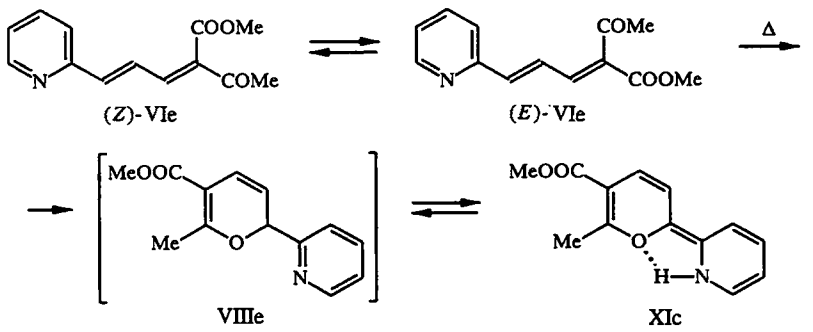
The reaction of aldehyde IIIh with ketoester IVb proceeds similarly. Ylidenic pyran IXb is formed upon distillation of the reaction product. In this case, pyran VIIId was not isolated but its formation was indicated by the UV spectrum of the undistilled product (λ_{max} 210, 250, 320 nm), which is analogous to the spectrum of pyran VIIIc.

TABLE 3. Physical Indices of Diesters VIIa-VII*

Reagents		Product	mp, °C	bp, °C (mm Hg)	UV spectrum, λ_{max}, nm (ε) EtOH	Mass spectrum, M^+	Yield, % (rel. to starting reagents)
aldehyde	diester						
IIIa	Va	VIIa	88...90	140...145 (0,47)	350 (47000)	236	60
IIIf	Va	VIIb	76...78	147...150* (0,5)	360 (32500)	250	35
IIIb	Va	VIIc	64...65	—	350 (42100)	252	20
IIIb	Vb	VIId	38...45	156...161 (0,37)	360 (31600)	—	48
IIIg	Va	VIIe	71...74	—	345 (35600)	266	14
IIIg	Vb	VIIf	—	152...156 (0,36)	345 (34600)	—	26
IIIc	Va	VIIg	70...72	—	323 (32200)	—	20
IIIh	Va	VIIh	61...63	—	315 (26100)	261	6
IIIh	Vb	VIIi	Oil	150...163 (0,35)	310 (14200)	289	3
IIId	Va	VIIj	61...65	—	320 (31100)	—	53
IIIi	Va	VIIk	73...76	—	305 (32000)	261	20
IIIc	Va	VII*l*	87...91	—	315 (25500)	—	54

*n_D^{20} = 1.6340.

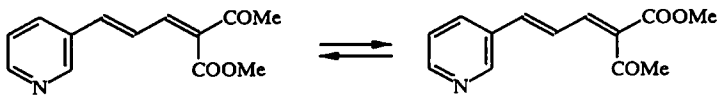
The reaction of β-(2-pyridyl)acrolein IIIc with ketoester IVa gives a 40:60 mixture of (*E*) and (*Z*) isomers of ketoester IVe (PMR spectral data, Table 6). The same isomer composition was found for the product purified by preparative chromatography on silica gel.



Distillation of ketoester VIe is accompanied by its cyclization to an ylidene derivative, namely, pyran IXc. PMR spectroscopy indicates that the distilled product contained 82% pyran IXc and 18% starting ketoester IVe as a 3:2 mixture of the (*Z*) and (*E*) isomers. Pyran IXc was isolated from this mixture by crystallization from methanol solution and its structure was confirmed by PMR and UV spectroscopy and mass spectrometry (Table 2 and 6) as well as by elemental analysis. The formation of ylidenic pyran IXc probably proceeds through pyran VIIIe, which arises in the cyclization of dienone (*E*)-VIe.

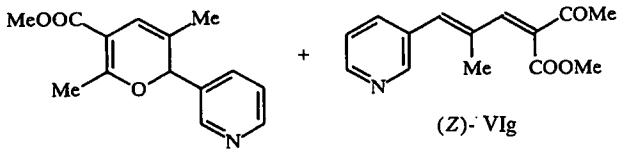
The condensation of β-(3-pyridyl)acrolein IIId with ketoester IVa gives VIf as an equilibrium mixture of (*Z*) and (*E*) isomers, from which the pure (*Z*) isomer was isolated by crystallization.

The (*Z*) isomer was reconverted to an equilibrium 55:45 mixture of the (*Z*) and (*E*) isomers upon brief heating at 100-110°C without solvent or upon standing for 1 h at 50°C in $CDCl_3$ solution.



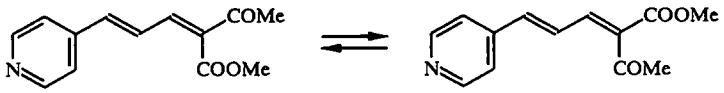
(*Z*)-VIf (*E*)-VIf

In contrast to aldehyde IIId, the reaction of its methyl derivative, IIIi, with ketoester IVa leads to 3,6-dimethyl-5-carbomethoxy-2-(3-pyridyl)pyran VIIIf containing 14% dienone (*Z*)-VIg.



VIIIf (*Z*)-VIg

The reaction product obtained by the condensation of β-(4-pyridyl)acrolein IIIe with ketoester IVa, similar to ketoester VIf, is also a mixture of (*Z*) and (*E*) isomers of VIh, which lacks an admixture of the corresponding pyran.



(*Z*)-VIh (*E*)-VIh

We should note that only those pyridylalkadienones and pyridyl-2H-pyrans synthesized in this work, which contain a 2-pyridyl ring, undergo conversion to ylidenic pyrans IX. This behavior is probably related to the stability of the five-membered chelates formed in these cases.

The condensation of pyridylacroleins IIIc-IIIe, IIIh, and IIIi with malonates Va and Vb gave dienic diesters VIIg-VII*l* (see scheme), which are formed only in the open form and lack the corresponding 2H-pyrans as indicated by ^{1}H and ^{13}C NMR spectroscopy.

The UV spectra of δ-pyridyl dienic diesters VIIg-VII*l* have only one absorption maximum at 313-325 nm, characteristic for dienic diesters containing a phenyl substituent in the δ-position [19]. We should note that there is only one maximum in the UV spectra of dienic diesters VIIa-VIIf, which have a furyl or thienyl substituent in the δ-position, but at longer wavelengths (345-360 nm).

Table 2 gives the isomer composition of products VIa-VIh and VIIIc (the content of the valence isomers is the same in $CDCl_3$ and CD_3OD). The data in this table show that the pyran form is not found in γ-unsubstituted dienones VIa, VIb, VIe, VIf, and VIh, which have a hetaryl substituent in the δ-position.

The introduction of a methyl group at the γ-position in δ-furyl- VIc and δ-thienyldienones VId leads to a ternary equilibrium mixture of the (*E*) and (*Z*) isomers and corresponding 2H-pyran VIIIa and VIIIb, while the equilibrium is completely shifted toward the 2H-pyran form VIIIc, VIIId, and VIIIe in γ-methyl-δ-pyridyldienones. We note that γ-methyl-δ-phenyldienones are found also only in the cyclic form, while, in contrast, their γ-unsubstituted analogs are found in the open form [21].

The results of a study of the valence photoisomerization of these dienones and 2H-pyrans will be presented in subsequent communications.

EXPERIMENTAL

The UV spectra of ethanolic solutions of these compounds were taken on a Specord UV-VIS spectrophotometer. The PMR spectra were taken on a Bruker WM-250 spectrometer at 250 MHz with $CDCl_3$ as the solvent and TMS as the internal standard. The ^{13}C NMR spectra were taken on a Bruker AM-300 spectrometer at 75.432 MHz.

TABLE 4. PMR Spectral Indices of Furyl and Thienyl Derivatives in $CDCl_3$, δ, ppm

Compound	Diene fragment/2H-pyran						2-furyl/2-thienyl (Het)			Coupling constant (J), Hz
	MeCO/6-Me (3H, s)	COOMe (s)	γ-Me/3-Me (3H, s)	β-H/4-H (1H)	γ-H/3-H (1H)	δ-H/2-H (1H)	3-H (1H)	4-H (1H)	5-H (1H)	
(*E*)-VIa	2,38	3,74 (3H)	—	7,31 (d)	7,11 (t)	6,75 (d)	6,52 (d)	6,38 (d.d)	7,40 (d)	$J\beta,\gamma = J\gamma,\delta = 12,0$; $J_{3,4} = 3,5$; $J_{4,5} = 1,75$
(*Z*)-VIa	2,31	3,83 (3H)	—	7,31 (d)	7,11 (t)	6,81 (d)	6,50 (d)	6,40 (d.d)	7,43 (d)	$J\beta,\gamma = J\gamma,\delta = 12,0$; $J_{3,4} = 3,5$; $J_{4,5} = 1,75$
(*E*)-VIb	2,44	3,81 (3H)	—	7,00...7,45 (6H, m)						—
(*Z*)-VIb	2,38	3,89 (3H)	—	7,00...7,45 (6H, m)						—
(*E*)-VIc	2,48	3,80 (3H)	2,07	7,27 (s)	—	6,61 (s)	6,28...6,55 (m)		7,48 (br.s)	—
(*Z*)-VIc	2,35	3,87 (3H)	2,14	7,22 (s)	—	6,72 (s)	6,58 (d)	6,50 (br.s)	7,53 (br.s)	$J_{3,4} = 3,5$
VIIIa	1,87	3,74 (3H)	1,68	6,28...6,55 (m)	—	5,56 (s)	6,28...6,55 (m)		7,46 (br.s)	—
(*E*)-VId	2,48	3,81 (3H)	2,06	6,9...7,5 (m)	—	6,9...7,5 (m)		6,9...7,5 (m)		—
(*Z*)-VId	2,36	3,88 (3H)	2,12	7,27 (s)	—	7,14 (s)	7,23 (d)	7,12 (d.d)	7,48 (d)	$J_{3,4} = 3,6$; $J_{4,5} = 4,8$
VIIIb	2,22	3,73 (3H)	1,75	6,34 (s)	—	5,76 (s)		6,9...7,5 (m)		
VIIa	—	3,88 (3H) 3,81 (3H)	—	7,49 (d)	7,10 (d.d)	6,80 (s)	6,57 (d)	6,45 (d.d)	7,46 (d)	$J\beta,\gamma = 11,5$; $J\gamma,\delta = 15,0$; $J_{3,4} = 3,5$; $J_{4,5} = 1,7$
VIIb	—	3,78 (3H) 3,84 (3H)	2,08	7,37 (s)	—	6,64 (s)	6,54 (d)	6,45 (d.d)	7,49 (d)	$J_{3,4} = 3,5$; $J_{4,5} = 1,7$
VIIc	—	3,76 (3H) 3,84 (3H)	—	7,45 (d)		6,95...7,15 (4H, m)			7,31 (d)	$J\beta,\gamma = 11,5$; $J_{4,5} = 4,8$
VIId*	—	—	—	7,48 (d)		7,00...7,20 (4H, m)			7,35 (d)	$J\beta,\gamma = 11,5$; $J_{4,5} = 4,8$
VIIe	— —	3,81 (3H) 3,87 (3H)	2,11	7,45 (s)	—	7,11 (s)	7,21 (d)	7,10 (d.d)	7,47 (d)	$J_{3,4} = 3,5$; $J_{4,5} = 4,8$
VIIf*2	—	—	2,14	7,40 (s)	—	7,10 (s)	7,21 (d)	7,10 (d.d)	7,45 (d)	$J_{3,4} = 3,6$; $J_{4,5} = 4,8$

*1.31 t and 1.38 t (6H, $C\underline{H}3CH_2O$), 4.26 q and 4.36 q (4H, $CH_3C\underline{H}_2O$).

*2 1.31 t and 1.36 t (6H, $C\underline{H}_3CH_2O$), 4.27 q and 4.38 q (4H, $CH_3C\underline{H}_2O$.

TABLE 5. ^{13}C NMR Spectral Data for Furyl and Thienyl Derivatives in $CDCl_3$, δ, ppm ($^3J_{13C,H}$) [$^4J_{CO,H\beta}$]

Compound	Diene fragment/2H-pyran									2-furyl/2-thienyl (Het)			
	$C_{(\alpha)}/C_{(5)}$	$C_{(\beta)}/C_{(4)}$	$C_{(\gamma)}/C_{(3)}$	$C_{(\delta)}/C_{(2)}$	Me (in R^1)/6-Me	CO (in R^1)/$C_{(6)}$	MeO (in R^2)	CO (in R^2)	γ-Me/3-Me	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$
(*E*)-VIa	131,05	144,72	121,70 (162)	131,54 (153)	31,09	200,16	52,02	165,76	—	151,97	113,93 (176)	112,45 (176)	144,53
(*Z*)-VIa	131,70	144,84	121,77 (160)	131,70 (151)	27,77	195,31	52,02	166,79	—	151,97	114,28 (176)	112,54 (176)	144,53
(*E*)-VIb	130,47	145,49 (155)	122,94 (161)	138,3 (159)	31,17	200,03	52,06	165,85	—	141,1	130,23	128,13 (161)	128,59 (185)
(*Z*)-VIb	131,18	145,04 (155)	123,04 (161)	138,2 (159)	28,03	195,41	52,06	166,68	—	141,1	130,06	128,22 (161)	128,59 (185)
(*Z*)-VIc	131,68	145,74 (154)	129,61	128,95 (154)	25,94	194,56 [5, 6]	51,92	166,35	14,36	151,64	114,65 (172)	112,02 (176)	143,91 (203)
(*E*)-VId	123,18	*	*	*	31,78	*2	52,05	166,40	16,60	*	*	*	*
(*Z*)-VId	126,4	146,23 (155)	131,11	135,31 (155)	26,13	194,63 [6, 5]	52,05	168,54 [13]	14,85	139,26	131,5 (167)	127,24 (167)	129,08
VIIIb	104,02	116,87 (166)	*	75,51 (153)	19,40	165,5	50,89	162,48	18,79	141,68	*	*	*
VIIa	123,55	145,48 (156)	121,29 (156)	130,86 (156)	—	—	52,20, 52,20	165,03, 165,60	—	151,76	113,98 (176)	112,39 (176)	144,64 (202,6)
VIIb	122,57	146,78 (157)	129,67	135,14 (155)	—	—	52,15, 52,15	167,28, 164,78	14,36	151,89	114,48 (176)	112,0 (176)	143,85 (203)
VIIc	123,22	145,62 (156)	122,57 (160)	137,26 (159)	—	—	52,16, 52,08	165,46, 165,02	—	140,91	129,93 (167)	128,07 (169)	128,31 (186)
VIIe	122,67	147,49 (155)	130,01	135,04 (155)	—	—	52,49, 52,49	167,60, 165,13	15,06	139,45	131,47	127,47 (169)	129,01

*Chemical shifts not determined due to signal overlapping.

*2Signal could not be accumulated.

TABLE 6. PMR Spectral Data for Pyridyl Derivatives in $CDCl_3$, δ, ppm

Compound	Diene fragment\2H-pyran(pyran)						Pyridyl/pyridylidene					NH (1H, s)	Coupling constant (J), Hz
	MeCO/6-Me (3H, s)	COOMe (s)	γ-Me/3-Me (3H, s)	β-H/4-H (1H)	γ-H/3-H (1H)	δ-H/2-H (1H)	2-H (1H)	3-H (1H)	4-H (1H)	5-H (1H)	6-H (1H)		
(*E*)-VIe	2,48	3,83 (3H)	—	7,00...7,70			—	7,00...7,70			8,60 (d)	—	—
(*Z*)-VIe	2,40	3,90 (3H)	—	7,00...7,70			—	7,00...7,70			8,60 (d)	—	—
(*E*)-VIf	2,48	3,82 (3H)	—	7,23...7,45		7,00 (d)	8,67 (s)	—	7,81 (d)	7,27 (d.d)	8,58 (d)	—	$J_{\gamma,\delta}$ = 14,0
(*Z*)-VIf	2,38	3,90 (3H)	—	7,23...7,45		7,05 (d)	8,70 (s)	—	7,81 (d)	7,27 (d.d)	8,54 (d)	—	$J_{\gamma,\delta}$ = 14,0
VIIIf	2,20	3,74 (3H)	1,65	6,42 (s)	—	5,60 (s)	8,62 (s)	—	7,70 (d)	7,30 (d.d)	8,59 (d)	—	—
(*Z*)-VIg	2,38	3,87 (3H)	2,02	7,40	—	6,92	8,51	—	7,25...7,55		8,51	—	—
(*E*)-VIh	2,44	3,82 (3H)	—	7,25...7,45		6,90...7,10	8,50...8,65	7,25...7,45	—	7,25...7,45	8,50...8,65	—	—
(*Z*)-VIh	2,39	3,90 (3H)	—	7,25...7,45		6,90...7,10	8,50...8,65	7,25...7,45	—	7,25...7,45	8,50...8,65	—	—
VIIg	—	3,84 (3H); 3,94 (3H)	—	7,55...7,70		7,10 (d)	—	7,42 (d)	7,71 (m)	7,22 (m)	8,61 (d)	—	$J_{\gamma,\delta}$ = 13,5
VIIh	—	3,82 (3H); 3,88 (3H)	2,30	7,48 (s)	—	6,90 (s)	—	7,30 (d)	7,70 (d.d)	7,18 (d.d)	8,67 (d)	—	—
VIIi*[3]	—	—	2,30	7,42 (s)	—	6,88 (s)	—	7,26 (d)	7,70 (d.d)	7,16 (d.d)	8,66 (d)	—	—
VIIj	—	3,83 (3H); 3,90 (3H)	—	7,55 (d)	7,27...7,38	7,03 (d)	8,70 (s)	—	7,83 (d)	7,27...7,38	8,57 (d)	—	$J_{\beta,\gamma}$ = 12,5, $J_{\gamma,\delta}$ = 15,0
VIIk	—	3,80 (3H); 3,84 (3H)	1,99	7,43 (s)	—	6,87 (s)	8,56 (s)	—	7,61 (d)	7,29 (d.d)	8,50 (d)	—	—
VIIl	—	3,85 (3H); 3,93 (3H)	—	7,53 (d)	7,39 (d.d)	6,95 (d)	8,63 (d)	7,30...7,40	—	7,30...7,50	8,63 (d)	—	$J_{\beta,\gamma}$ = 12,5, $J_{\gamma,\delta}$ = 15,0
VIIIc	2,28	3,75 (3H)	1,72	6,32 (s)	—	5,71 (s)	—	7,40 (d)	7,70 (m)	7,22 (m)	8,60 (d)	—	—
IXa	2,18	3,67 (3H)	1,78	6,35 (s)	—	—	—	7,30 (d)	6,65 (d.d)	6,46 (t)	7,51 (d)	13,42	$J_{3,4}$ = 8,75
IXa*[1]	2,15	3,64 (3H)	1,75	6,30 (s)	—	—	—	7,29 (d)	6,64 (d.d)	6,45 (t)	7,57 (d)	—	$J_{4,5}$ = 6,50
IXa*[2]	2,08	3,59 (3H)	1,70	6,29 (s)	—	—	—	7,32 (d)	6,66 (d.d)	6,46 (t)	7,68 (d)	13,36	$J_{5,6}$ = 7,00
IXb*[3]	2,19	—	1,79	6,35 (s)	—	—	—	7,31 (d)	6,64 (d.d)	6,45 (t)	7,52 (d)	13,54	—
IXc	1,85	3,67 (3H)	—	6,50...6,75		—	—	7,41 (d)	6,50...6,75		7,58 (d)	13,40	—

*Spectrum taken in CD_3OD.

*[2]Spectrum taken in DMSO-d_6.

*[3]Chemical shifts for CO_2Et: 1.14 (3H, t, CH_3), 4.17 (2H, q, CH_2) for IXb, 1.2-1.4 (6H, m, CH_3), 4.1-4.3 (4H, m, CH_2) for VIIi.

TABLE 7. ^{13}C NMR Spectral Data for Pyridyl and Pyridylidene Derivatives in $CDCl_3$, δ, ppm ($^1J_{13C,H}$)

Compound	Diene fragment/2H-pyran									Pyridyl/pyridylidene				
	$C_{(\alpha)}/C_{(5)}$	$C_{(\beta)}/C_{(4)}$	$C_{(\gamma)}/C_{(3)}$	$C_{(\delta)}/C_{(2)}$	Me (in R^1)/6-Me	CO (in R^1)/$C_{(6)}$	MeO (in R^2)	CO_2 (in R^2)	γ-Me/3-Me	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$
(Z)-VIf	125,13	143,64 (157)	123,54 (165)	141,37 (157)	27,67 (128)	195,21	52,05 (148)	166,25	—	149,54 (178)	131,14	133,61 (161)	125,27 (157)	150,37 (182)
(E)-VIf	*	144,16	*	141,22	30,92 (128)	*2	52,05 (148)	165,8	—	149,40	*	133,46	*	*
VIIIf	103,53	117,32 (164)	121,60	78,55	19,16	166,10	50,82	162,53	18,71 (127)	148,92 (178)	133,47	135,40 (162)	123,40 (164)	149,83 (179)
(Z)-VIg	122,91	*	*	*	26,04	194,49	52,05	*	14,40	148,58	131,60	*	*	150,10
VIIg*3	126,5	144,30 (160)	123,50 (165)	143,20 (152)	—	—	52,20 (148)	164,70; 165,20	—	153,80	123,38 (165)	136,40 (165)	126,70 (162)	150,00 (178)
VIIh	124,86	147,40 (152)	136,50	139,53 (154)	—	—	52,55; 52,66	164,91; 167,33	14,58 (128)	155,28	122,35 (164)	136,21 (162)	125,88 (157)	149,55 (178)
VIIj	124,98	144,64 (160)	123,36 (163)	140,51 (150)	—	—	52,04 (148)	165,02; 164,47	—	149,27 (177)	130,91	133,38 (150)	124,66 (157)	150,14 (181)
VIIk	124,48	146,50 (157)	134,79	137,85 (153)	—	—	52,60; 52,65	164,80; 167,24	14,59 (125)	148,96 (179)	—	136,39 (161)	123,24	150,49 (179)
IXa	92,28	*4	115,25	132,51	12,09 (124)	178,90	51,99 (149)	173,30	19,34 (129)	124,61	*4	*4	*4	122,31 (178)
IXb	92,47	*5	115,39	132,35	11,98	178,62	*6	*6	19,16 (129)	124,58	*5	*5	*5	122,25 (179)

*Chemical signals not determined due to signal overlapping.

*2Signal could not be accumulated.

*3Arbitrary assignment to C(β) and C(δ).

*4Signals at 99.52 (170), 109.45 (163), 116.51 (163), 116.23 (163) for $C_{(3)}$, $C_{(4)}$, $C_{(5)}$, and C(β) not assigned.

*5Signals at 99.47 (170), 109.13 (166), 116.33 (163) and 118.16 for $C_{(3)}$, $C_{(4)}$, $C_{(5)}$, and C(β) not assigned.

*614.14 ($\underline{C}H_3CH_2O$), 60.52 ($CH_3\underline{C}H_2$), 172.71 (CO).

β-(2-Pyridyl)acrolein (IIIc). A sample of 9.5 ml (0.1 mole) freshly prepared 2-pyridinaldehyde was added to a mixture of 0.87 ml (0.01 mole) morpholine and 0.6 ml (0.01 mole) acetic acid in 400 ml benzene. The reaction mass was warmed with the simultaneous dropwise addition of a solution of 9 ml (0.16 mole) acetaldehyde in 31 ml benzene. The mixture was brought to 75°C over 1 h and the acetaldehyde solution was added over 2.5 h. The reaction mass was then stirred for an additional 2.5 h at 75°C and maintained for 16 h at room temperature. The solvent was evaporated and the residue was distilled to give 2.4 g (18%) aldehyde IIIc, bp 76-78°C (0.47 mm Hg), which crystallizes upon cooling [bp 60-65°C (0.001 mm Hg), mp 46-49°C [14]].

α-Methyl-β-(3-pyridyl)acrolein (IIIi). A sample of 4.8 ml (0.05 mole) freshly distilled 3-pyridinaldehyde was added in one portion to a mixture of 0.5 g KOH and 65 ml DMF and, then, a solution of 4.4 ml (0.06 mole) propionaldehyde in 25 ml DMF was added dropwise over 1 h. The reaction mass was stirred for an additional 3 h. Water was added and the mixture was extracted with benzene. The organic layer was washed with water and dried over anhydrous $MgSO_4$. The solution was evaporated. The residue was filtered and washed with ether to give 2.1 g (29%) IIIi, mp 40-45°C.

α-Methyl-β-(4-pyridyl)acrolein (IIIj). A sample of 8 g (0.075 mole) freshly distilled 4-pyridinaldehyde was added in one portion to a mixture of 0.75 g KOH and 115 ml DMF. Then, a solution of 5.22 g (0.09 mole) propionaldehyde in 35 ml DMF was added dropwise over 1.5 h. The reaction mixture was stirred for an additional 3.5 h and treated as in the case of aldehyde IIIi to give 0.45 g (4%) aldehyde IIIj, bp 156-165°C (10 mm Hg), n_D^{20} 1.5730.

Methyl Ester of α-Acetyl-δ-(2-furyl)butadienecarboxylic Acid (VIa). A mixture of 0.04 mole ketoester IVa, 0.04 mole aldehyde IIIa, and 0.005 mole piperidine was maintained at room temperature for seven days. The reaction mass was then diluted by adding 15 ml ether and 10 ml ether and 3% aqueous sulfuric acid and, then, water. The organic layer was dried over anhydrous $MgSO_4$ and evaporated in vacuum. Found: C, 65.82; H, 5.71%. Calculated for $C_{12}H_{12}O_4$: C, 65.50; H, 5.45%.

Analogous procedures gave ketoester VIc and diester VIIa (Table 3). For VIIa: Found: C, 61.21; H, 5.12%. Calculated for $C_{12}H_{12}O_5$: C, 60.90; H, 5.07%.

Methyl Ester of α-Acetyl-δ-(2-thienyl)butadienecarboxylic Acid (VIb). A mixture of 0.02 mole ketoester VIa, 0.02 mole aldehyde IIIb, 0.003 piperidine, 0.0025 mole glacial acetic acid, and 1.5 ml benzene was maintained at room temperature for eight days and then treated as described above for VIa.

Analogous procedures gave VId, 2H-pyran VIIIf, diesters VIIb, VIIc, VIIe, VIIh, VIIk, and VIIf (Tables 2 and 3). After distillation, VIb, VIIb, VIId, and VIIf were recrystallized from ether, while diester VIIi was purified by chromatography on silica gel in a system of 2:3 acetone–petroleum ether. Ether was the eluent. Products VId, VIIc, VIIe, VIIh, and VIIk were isolated by crystallization of the treated but not distilled reaction mixture from ether.

Ester VIb: Found: C, 61.37; H, 5.29; S, 13.32%. Calculated for $C_{12}H_{12}O_3S$: C, 61.02; H, 5.08; S, 13.60%.

Ester VId: Found: C, 62.10; H, 5.56; S, 12.39%. Calculated for $C_{13}H_{14}O_3S$: C, 62.40; H, 5.60; S, 12.80%.

Product VIIc: Found: C, 57.10; H, 4.87; S, 12.54%. Calculated for $C_{12}H_{12}O_4S$: C, 57.14; H, 4.76; S, 12.70%.

Product VIIe: Found: C, 59.11; H, 5.31; S, 12.00%. Calculated for $C_{13}H_{14}O_4S$: C, 58.65; H, 5.26; S, 12.04%.

Methyl Ester of α-Acetyl-δ-(3-pyridyl)butadienecarboxylic Acid (VIf). A mixture of 0.003 mole piperidine, 0.0025 mole glacial acetic acid, and 1.5 ml benzene was added to a mixture of 0.02 mole ketoester IVc and 0.02 mole aldehyde IIId cooled to 0°C. The reaction mass was maintained for 72 h at 4°C and then diluted by adding 15 ml ether and 10 ml benzene. The mixture was washed with water. The organic layer was dried over anhydrous $MgSO_4$ and evaporated. The product was isolated by crystallization from ether. Analogous procedures gave VIh, VIIg, VIIj, and VII*l* (see Tables 2 and 3).

Product VIIg: Found: C, 63.20; H, 5.37: N, 5.75%. Calculated for $C_{13}H_{13}NO_4$: C, 63.20; H, 5.27; N, 5.67%.

3,6-Dimethyl-5-carbomethoxy-2-(2-pyridyl)pyran (VIIIc) and 3,6-Dimethyl-5-carbomethoxy-2-(pyrilidene)pyran (IXa). A mixture of 0.003 mole piperidine, 0.0025 mole glacial acetic acid, and 1.5 ml benzene was added to a mixture of 0.02 mole ketoester IVa and 0.02 mole aldehyde IIIh. The reaction mixture was maintained for eight days at room temperature and then treated as described above for VIf. After evaporation, one-fifth of the residue was subjected to chromatography on a Silufol UV-254 plate in a 15:7 chloroform-ethyl acetate system. Ether was the eluent. Pyran VIIIa was isolated as a thick oil. UV spectrum, λ_{max} nm (ε): 210 (14,000), 250 (5700), 318 (3300). The major portion of the residue after solvent removal was distilled in vacuum to give IXa in 39% yield, bp 110-120°C (0.03 mm Hg), mp 102-103°C (from ether). UV spectrum, λ_{max}, nm (ε): 243 (32,000). Mass spectrum: M^+ 245. Found: C, 68.25; H, 6.12; N, 5.94%. Calculated for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.13; N, 5.71%.

Analogously, 3,6-dimethyl-5-carboethoxy-2-(pyrilidene)pyran IXb was obtained from aldehyde IIIh and ketoester IVb in 31% yield, bp 115-120°C (0.3 mm Hg), n_D^{20} 1.5776. UV spectrum, λ_{max}, nm (ε): 245 (38,200). Mass spectrum: M^+ 259.

Methyl Ester of α-Acetyl-δ-(2-pyridyl)butadienecarboxylic Acid (VIe) and 6-Methyl-5-carbomethoxy-2-(pyrilidene)pyran (IXc). A mixture of 0.0015 mole piperidine, 0.0013 mole glacial acetic acid, and 1.5 ml benzene was added to a mixture of 0.02 mole ketoester IVa and 0.02 mole aldehyde IIIc cooled to 0°C. The reaction mixture was maintained for 120 h at 4°C and treated as in the previous experiment to give VIe as a thick oil with UV spectrum, λ_{max}, nm (ε): 330 (20,800) and IXc in 12% yield, bp 140-145°C (0.47 mm Hg), n_D^{20} 1.601, mp 47-51°C. UV spectrum, λ_{max}, nm (ε): 238 (33,300). Mass spectrum: M^+ 231. Found: C, 67.20; H, 5.67; N, 6.05%. Calculated for $C_{13}H_{13}NO_3$: C, 67.53; H, 5.63; N, 6.06%.

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