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Derivatives and Reactions of Glutaconaldehyde. XI. *N*-Substituted 5-Amino-2,4-pentadienenals, their Oximes, and 5-Amino-2,4-pentadienenitriles. Structural Analysis by ^{1}H and ^{13}C NMR Spectroscopy

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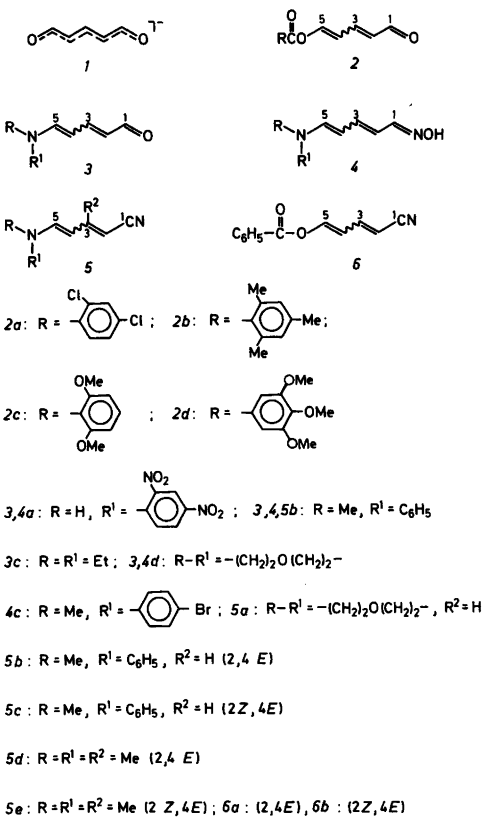
The structures of a series of thermal ring-opening products from pyridines, *i.e.*, glutaconaldehyde and some of its derivatives, are determined and compared to those of some photochemically generated ring-opening products from pyridine *N*-oxides by ^{1}H and ^{13}C NMR spectroscopy. It is inferred that the initially formed products from the pyridine *N*-oxide possess the *Z*-configuration at the double bond which originates from the 3,4-bond of the pyridine *N*-oxide ring.

Both in the thermal ring-opening of pyridine to products like glutaconaldehyde,[1] or 5-dialkylamino-2,4-pentadienal,[2] and in the photochemical ring-opening of pyridine *N*-oxides,[3,4] several geometrical isomers could be formed. Furthermore, these compounds are labile, and are more or less easily transferred to the thermally most stable all-*E* isomers. Consequently, the initially isolated products from either thermal or photochemical ring opening are, as a rule, not pure but consist of mixtures of stereoisomers, and, since several of the products may be promising synthons, it was found important not only to determine their gross structure, but also their geometrical configuration.

Previously it was shown that the all-*E* salt (*1*)[5] of glutaconaldehyde did not always lead to all-*E* enol esters upon acylation;[6] thus, upon treatment of *1* with ethyl isothiocyanatoformate (EtOCONCS) at low temperature, a mixture of *E* and *Z* ethoxycarbonate (*2*, R = EtO) was formed.[6] In a series of



Scheme 1.

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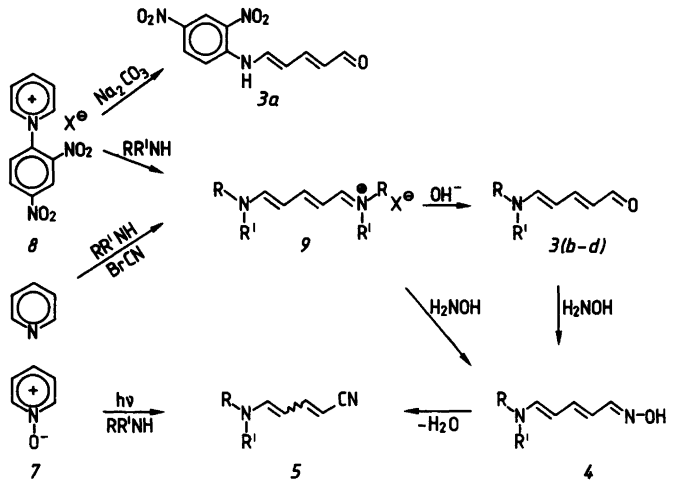
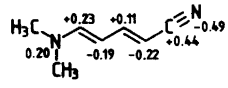


Scheme 2.

investigations, a number of the related 5-dialkylamino-2,4-dienals (*3*) were shown to be the all-*E*-isomers,[7] and in the ring-opening of *N*-alkoxycarbonylpyridinium salts with secondary amines, *Z* products were also observed.[8]

When it was observed that pyridine *N*-oxides upon photolysis in the presence of secondary amines generated 5-dialkylamino-2,4-pentadienenitriles (*5*),



Scheme 3. The electron density found by a CNDO/2 calculation for *N,N*-dimethyl-5-amino-*2E,4E*-pentadienonitrile. Molecular dimensions were taken from Refs. 19 and 20.

Table 1. Chemical shifts of methine protons in δ (ppm from TMS). J in Hz.

Compound	H(5)	H(4)	H(3)	H(2)	H(1)	$J_{4,5}$	$J_{3,4}$	$J_{2,3}$	$J_{1,2}$
2a[a,c]	8.05	6.45	7.04	6.18	9.65	12	11	16	8
2b[a,c]	8.18	6.29	7.55	6.17	9.55	12.6	11.0	16.2	7.8
2c[a,c]	8.15	6.35–6.70	7.55	6.25	9.57	12	10	15	8
2d[a,c]	8.05	6.47	7.25	6.21	9.58	12	12	15	8
3a[b,c]	7.95	6.62	7.45	6.08	9.47	12.0	12.0	16.0	7.5
3b[a,c]	6.97–7.53	5.63	6.97–7.53	5.96	9.38	12	12	15	8
3c[a,c]	6.88	5.32	7.18	5.73	9.26	12.5	12.0	15.0	8.5
3d[a,c]	6.73	5.41	7.12	5.85	9.32	13.0	11.5	14.0	8.0
4a[b,c]	?	?	7.41	?	7.87	?	11	16	9
4b[a,c]	?	5.53	?	6.33	7.82	12.8	10.4	17.2	9.6
4c[a,c]	7.10	5.64	6.67	6.21	7.73	13	11	15	10
4d[a,c]	6.61	5.32	6.56	6.27	7.25	13.2	10.2	15.5	9.2
5a[a,d]	6.56	5.25	6.95	4.80	–	13.0	11.2	15.5	–
5b[a,d]	7.08	5.46	6.99	4.91	–	12.8	11.3	15.6	–
5c[a,d]	7.09	5.79	6.80	4.64	–	12.2	12.2	10.4	–
5d[a,d]	6.52	5.08	–	4.64	–	13.2	–	–	–
5e[a,d]	6.58	5.48	–	4.37	–	13.2	–	–	–
6a[a,d]	8.23	6.67	7.51	5.87	–	11.6	11.2	15.9	–
6b[a,d]	?	6.53	?	5.80	–	12.0	12.0	10.0	–

[a] In $CDCl_3$. [b] In DMSO-d_6. [c] 60 MHz. [d] 270 MHz.

the stereochemical details were not discussed.[3,4] More recently the preparative potential of this ring-opening has been examined,[9] and the present paper reports the stereochemistry of the products. Furthermore, we have prepared some new enol esters (*2*) and a CNDO/2 calculation of all-*E*-*5a* ($R^1=R^2=CH_3$, $R^3=H$) was carried out.

RESULTS

The preparation and isolation of the nitriles (*5*) are described elsewhere.[9] The preparation of the new enol esters (*2a–b*) was undertaken analogously to the method already described.[6] Some of the previously determined NMR spectra of the dialkylaminopentadienals (3) were not complete; consequently some of those compounds (*3a,b,d*) were prepared and their spectra recorded. The preparation of the oximes (*4a–d*) is well-known.[3] (See Scheme 2).

The ^1H NMR spectra are recorded in Table 1 and the ^{13}C spectra are recorded in Table 2. Furthermore, the $Pr(fod)_3$ dependence of the chemical shifts of *5d, e* are shown in Fig. 1. The results of a CNDO/2 calculation of *5a* are given in Scheme 3.

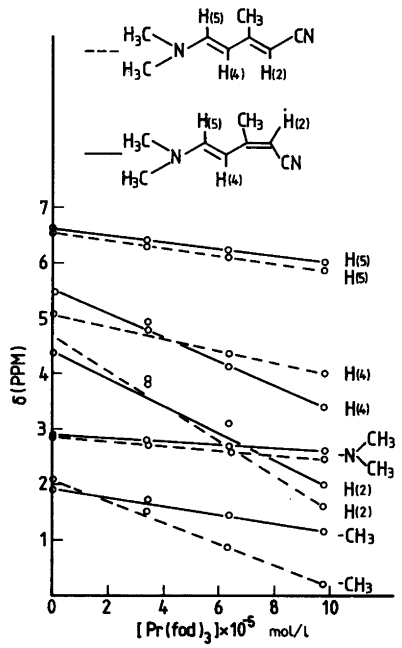
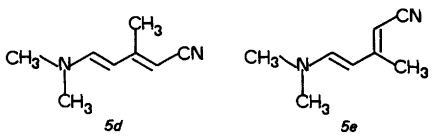


Fig. 1. Induced shift in the ^1H NMR spectrum of a mixture of *5d* and *5e* as a function of $Pr(fod)_3$ concentration.

DISCUSSION

The ^1H NMR spectra of the novel enol esters (*2a–d*, Table 1) are in excellent agreement with those previously described.[6] The 2′,6′-substituents were intended to render the esters less prone to hydrolysis, but this turned out not to be the case since they were as susceptible to moisture as the unsubstituted ones. In the ^1H NMR spectra it can be seen, by comparison with the spectra of those enol esters previously prepared,[2] that the chemical



Scheme 4.

shifts of H(2) and H (4) are found at higher fields than those of H(1), H(3) and H(5), and that H(2) and H(3) are observed at higher fields than those of H(4) and H(5), respectively. In each compound, $J_{2,3}=15-16$ Hz, whereas $J_{3,4}$ and $J_{4,5}$ are 11–12 Hz. It is noteworthy that $J_{2,3}$ is always larger than $J_{4,5}$.

The ^1H NMR spectra of the 5-dialkylamino-2,4-pentadienals (*3a–d*) are shown in Table 1, and it is seen that there is excellent agreement between these spectra and those of the enol esters (2). It is not surprising that the dinitrophenyl group in *3a* has a marked influence on the chemical shifts. It should be noted that less detailed ^1H NMR spectra of compounds *3a,b* were previously reported,[11] and that the spectrum of 5-dimethylamino-2,4-pentadienal, which was previously described, is in agreement with the present one. The ^1H NMR spectra of the oximes (*4*) and the nitriles (*5*) (Table 1) are in excellent agreement with those of *2* and *3*, and this agreement is regarded as good evidence for our assignments.

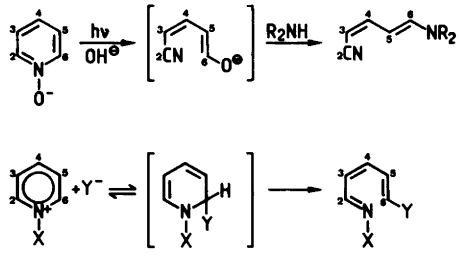
In order to further strengthen these assignments the shift reagent study (Fig. 1) was undertaken on the unseparated mixture of the stereoisomers, *5d* and *5e*, obtained from the irradiation of 4-methylpyridine *N*-oxide in the presence of dimethylamine.[9] From this it is seen that our analysis is based on complexation taking place at the cyano group. Although a non-conjugating secondary amino

Table 2. Chemical shifts of methine carbons in δ (ppm from TMS). *5b,c* in $CDCl_3$. *6a,b* in DMSO-d_6. *N*-CH_3 at 36.00 in both *5b* and *5c*. *C* = O at 162.16 in both *6a* and *6b*. The aromatic C-atoms were found as expected in the region 120–145 ppm.

Compound	C(5)	C(4)	C(3)	C(2)	C(1)
5b	144.80	100.63	150.69	85.54	120.58
5c	144.47	100.25	149.59	83.80	120.58
$\Delta\delta = \delta_{trans} - \delta_{cis}$	0.33	0.38	1.10	1.74	0.00
6a	145.34	112.87	145.77	98.11	127.38
6b	145.12	111.84	144.73	96.82	127.38
$\Delta\delta = \delta_{trans} - \delta_{cis}$	0.22	1.03	1.04	1.29	0.00

group will be a much better complexing site than a free nitrile group,[10-12] the "push-pull" effect[21] made possible by the conjugated double bond, change the relative electron densities. This phenomenon is in excellent agreement with our CNDO/2 study (Scheme 3).

The induced chemical shifts in the spectra of the two stereoisomers are different. In the all-*E* isomer (*5d*) the C–CH_3 shift is larger and the *H*(4) shift is smaller compared to those of the *Z*-isomer (*5e*). The greater up-field shift for *H*(2) in the all-*E*-



Scheme 5.

isomer (*5d*) than that for *H*(2) in *5c* is assumed to be due to better delocalization in *5d*. On comparison of these results with the full spectrum of the mixture of *5d* and *5e*, as well as that of the mixture of *5c* and *5b* (not shown) it is seen that the signals from the individual stereoisomers can be picked out. Furthermore, the ^{13}C NMR spectra of *5b* and *5c* (Table 2) show that the differences in chemical shifts are the largest for C(2) and C(3), thus further strengthening our assignment. Consequently, the previous assignment of the *Z*-configuration to the C(4)–C(5) bond in isolated *5b* and *5c* is incorrect.[4]

We can furthermore conclude on the basis of the ^1H NMR spectra that the π-bond order is higher for the C(2)–C(3) bond than for the C(4)–C(5). This is in agreement with the π-bond orders calculated for all-*E*-5 dimethylamino-2,4-pentadienal,[7] and with the bond length measured[20] for *3d*.

The results indicate that the photochemical as well as the thermal pyridine ring openings take place with retention of the configuration (see Scheme 5).

A survey of the literature[13] shows that this result is in agreement with other results in which the primary products from pyridinium ring openings generally are obtained with the *Z*-configuration for the double bond originating from the C(3)–C(4) bond of the former pyridine ring. However, as *Z*–*E* isomerizations occur readily in these polyenes, it is noteworthy that a mixture of *E* and *Z* isomers (*5b–5c*) was observed also in the thermal preparation of these compounds (Scheme 2) from the corresponding all-*E* oxime.

EXPERIMENTAL

The previously known compounds were all prepared as described in the literature; thus *3a*, *3b*, *3c* and *4a* were prepared according to Refs. 14, 15, 16 and 14, respectively; for compounds *5a–5e* and *6a–6b*, see Refs. 3 and 9.

5-(2,6-Dichlorobenzoyloxy)-2E,4E-pentadienal (2a). Prepared by the procedure of Becher.[6] Yield: 28 %. M.p. 74–77 °C. IR (KBr): 2855, 2770 (CHO), 1675, 1285, 980 cm^{-1}. Anal. $C_{12}H_8Cl_2O_3$: C, H, Cl.

5-(2,4,6-Trimethylbenzoyloxy)-2E,4E-pentadienal (2b). The glutaconaldehyde potassium salt (1.02 g, 0.0075 mol) and 1.37 g (0.0075 mol) of 2,4,6-trimethylbenzoyl chloride were stirred in 13 ml dry dimethylformaldehyde at 0 °C for 3 h, after which the mixture was poured onto ice and extracted with chloroform (2 × 100 ml). After drying ($MgSO_4$) and evaporation of the solvent, crude *2b* was obtained as an oil which crystallized after one week. Recrystallization from ethanol – water gave 0.94 g (52 %) of *2b*. M.p. 62–63 °C. IR (KBr): 2869, 2770, 2740(CHO), 1688, 1290, 980 cm^{-1}. Anal $C_{15}H_{16}O_3$: C, H.

5-(2,6-Dimethoxybenzoyloxy)-2E,4E-pentadienal (2c). Prepared as described for *2a*, yield 87 %. M.p. 141 – 143 °C. IR(KBr) 2845, 2765, 2715 (CHO). Anal. $C_{14}H_{14}O_5$: C, H.

5-(3,4,5-Trimethoxybenzoyloxy)-2E,4E-pentadienal (2d). Prepared as described for *2a*, yield 48 %. M.p. 185 – 186 °C. IR (KBr) 2840, 2815, 2745 (CHO). Anal. $C_{15}H_{16}O_6$: C, H.

5-(4-Morpholinyl)-2E,4E-pentadienal (3d). *N*-(2,4-Dinitrophenyl)-pyridinium chloride (*8*) (73 g, 0.26 mol) and 44.0 ml (0.52 mol) of morpholine were refluxed for 1 h in abs. ethanol, after which the mixture was cooled and poured on 300 ml of water. Subseguent to removal of the precipitated 2,4-dinitroaniline, 250 ml of saturated sodium carbonate was added, and the mixture left for 2 days, After this 250 ml saturated sodium chloride was added, and *3d* was exctracted from the water phase with methylene chloride (4 × 250 ml). The organic phase was washed with water, dried ($MgSO_4$) and filtered, after which evaporation gave 31 g of dark crystals. Recrystallization from toluene – pentane gave 22 g (55 %) of pure material. M.p. 120 – 123 °C. UV (abs. EtOH): λ_{max} nm (log ε): 370.0 (4.71). IR (KBr): 2850, 2720 (CHO), 1635, 1290, 875 cm^{-1}. Anal. $C_9H_{13}NO_2$: C, H, N.

4-(N-Methylphenylamino)-2,4-pentadienal oxime (4b). The oxime, *4b*, was prepared by either of two methods (Scheme 2). Method a: Preparation from the corresponding aldehyde *3b*, or Method b: Preparation directly from the salt *9*.

Method a. Hydroxylammonium chloride (2.10 g, 0.03 mol) in 5 ml water and 10 ml saturated sodium carbonate was added to 2.80 g (0.015 mol) of aldehyde *3b* in 18 ml of methanol, whereupon a yellow precipitate was formed instantaneously. The mixture was subsequently refluxed until this disappeared (*ca.* 10 – 20 min). After cooling of the reaction mixture, the precipitated oxime was filtered off and washed with water. Recrystallization from 50 % ethanol gave 2.17 g *4b* (72 %). M.p. 118.5 – 119.5 °C. UV (cyclohexane): λ_{max} nm (log ε): 347.0(4.63), 340.3(4.70), 234.1(3.75). IR (KBr): 3300 cm^{-1} (OH). Anal. $C_{12}H_{14}N_2O$: C, H, N.

Method b. Hydroxylammonium chloride (2.50 g, 0.036 mol) dissolved in 10 ml water and 10 ml saturated sodium carbonate was added to 6.78 g (0.018 mol) of the salt *9** in 60 ml methanol. Refluxed 1 h. After addition of 25 ml water (0 °C) the crude oxime was isolated by filtration. Yield: 73 %. The purified product was identical to the product from Method a. The overall yield of the oxime is highest when it is prepared directly from the salt *9*.

5-(N-Methyl-4-bromophenylamino)-2,4-pentadienal oxime (4c). Prepared by Method b as described for *4b*. From 1.00 g (0.014 mol) hydroxylammonium chloride in 5 ml water and 5 ml saturated sodium carbonate added to 3.29 g (0.07 mol) of the corresponding salt *9*[17] in 30 ml methanol was obtained 1.69 g (86 %) of the oxime *4c*. M.p. 149 – 150 °C(d). UV (abs. EtOH): λ_{max} nm (log ε): 348(4.70), 250(3.99). IR (KBr): 3300 cm^{-1} (OH). Anal. $C_{12}H_{13}BrN_2O$: C, H, Br, N.

5-(4-Morpholinyl)-2,4-pentadienal oxime (4d). A solution of *N*-(2,4-dinitrophenyl)pyridinium chloride (*8*) (28.2 g, 0.1 mol) in 100 ml abs. ethanol and 18 ml (0.2 mol) of morpholine was refluxed for 1 h. After this the reaction mixture was poured on 200 ml water(0 °C), the precipitated 2,4-dinitroaniline was removed by filtering and 14 g (0.2 mol) hydroxylammonium chloride in 100 ml saturated sodium carbonate followed by 40 ml water was added to the water – ethanol solution. Precipitation of the oxime started slowly and was completed after 30 min. The crystals were isolated by filtration and recrystallized from 96 % ethanol. Yield: 17.03 g (94 %). M.p. 169 – 172 °C. UV (abs. EtOH): λ_{max} nm log ε): 332.2(3.59), 215.4(3.64). IR (KBr): 3340 cm^{-1} (OH). Anal. $C_9H_{14}N_2O_2$: C, H, N.

The CNDO/2 calculation was carried out with the molecular dimensions taken from related compounds.[19,20] The lanthanide shift experiment was carried out by dissolving 4×10^{-4} mol of the mixture of isomers in deuteriochloroform and gradually adding Pr(fod)$_3$ = tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-octan-4,6-dionato)praseodymium.

Instrumentation. Microanalyses were carried out in the Microanalytical Department of the University of Copenhagen by Mr. Preben Hansen. IR: Perkin Elmer 580. UV: Varian Cary 219. ^{1}H NMR (60 MHz): JEOL JNM-PMX 60 and ^{1}H NMR (270 MHz): Bruker HX-270. ^{13}C NMR: JEOL JNM-FX 60 Q.

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* Prepared by the procedure of Zincke and Würker,[17] or by the procedure of König.[18]

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