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Beckmann and Cyclization Reactions of δ-Oxo-α,β-Unsaturated Ketoximes obtained from Pyrylium Salts and Hydroxylamine. Formation of 2-Aryl(or Alkyl)amino-4,6-disubstituted Pyrylium Salts

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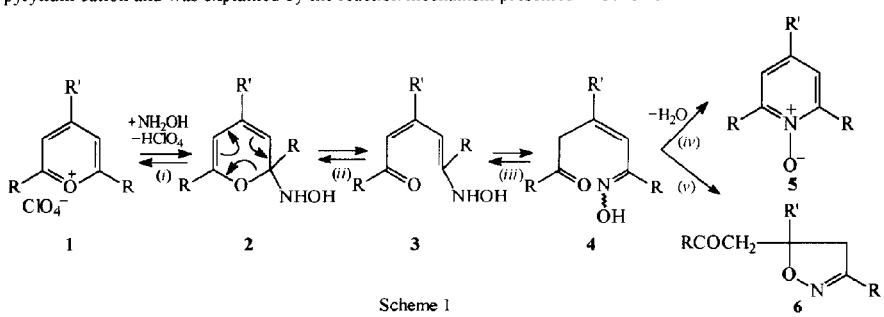
Abstract: The reaction of 2,4,6-trisubstituted pyrylium salts **1** with hydroxylamine gave regio- and stereo-selectively 1,3,5-trisubstituted 2-*cis*-pentene-1,5-dione 1-oximes **4**. On cyclization, 3,5,5-trisubstituted 2-isoxazolines **6** and 2,4,6-trisubstituted pyridine 1-oxides **5** were obtained, originating in the *anti*/*syn* stereoisomers of oxime **4**, respectively. Beckmann reaction of keto-ketoximes **4** with thionyl chloride unexpectedly gave 2-aryl (or alkyl)amino-4,6-disubstituted pyrylium salts **7**, the first example of rearrangement/cyclization involving carbonylic oxygen as terminator. Crystallographic data are provided for (*Z*)-*N*-*t*-butyl-3,6,6-trimethyl-2-heptenecarboxamide **13b**.

INTRODUCTION

The competing formation of pyridine 1-oxides **5** and 2-isoxazolines **6** from 2,4,6-trisubstituted pyrylium salts **1** and hydroxylamine[1] was substantiated with a systematic variation of the substitution pattern around the pyrylium cation and was explained by the reaction mechanism presented in Scheme 1.[2]



Scheme 1

Following the general pattern of ANRORC reactions,[3] Scheme 1 shows the keto-ketoxime **4** as common open-chain intermediate of the recyclization steps, assuming that the *syn* isomer (with reference to the hydroxyl and the group R) gave pyridine 1-oxide by nitrogen nucleophilic attack at the carbonyl group and dehydration (path *iv*) whereas the *anti* isomer gave 2-isoxazoline by internal Michael addition (path *v*). It accounts for the observed increase of the **6**/**5** ratio along with increasing size of the α-substituents R in **1**,[2] just as the *anti*/*syn* ratio in **4** is expected to do.

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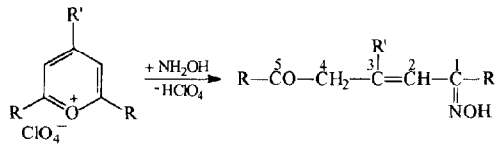
Still, the open-chain intermediate with alternative (3-C, 4-C in **4**) double bond position might equally well explain the reaction outcome. The intermediate is actually decided one step earlier in the prototropic process (*iii*), which may occur by 1,5-hydrogen shift leading to **4** as depicted, but just as well by 1,3-hydrogen shift leading to the isomer with 3-C, 4-C double bond (or both). Therefore, only the attempt for isolation and subsequent cyclization of the open-chain intermediate(s) would be a clear-cut proof for the *regioselective* formation of **4** advanced in Scheme 1. This attempt succeeded and this paper presents the structure and stereochemistry of several intermediates **4**, unambigously established by spectroscopic and/or chemical methods. The Beckmann reaction of compounds **4** with thionyl chloride gave unexpectedly 2-aryl (or alkyl)amino-4,6-disubstituted pyrylium salts by cyclization following the actual rearrangement. A minor fragmentation pathway of **4b** (R = *t*Bu, R' = Me) occurred with geometric isomerization of the carbon-carbon double bond. The cyclization of the keto-ketoximes **4** was performed under both acidic and basic catalysis, monitoring the ratio between **5** and **6**.

RESULTS

δ-Oxo-α,β-unsaturated ketoximes 4 from pyrylium salts and hydroxylamine. Isolation and spectroscopic characterization.

On brief treatment with hydroxylamine, the pyrylium perchlorates **1a**, **1b** gave crystalline 1,3,5-trisubstituted 2-pentene-1,5-dione 1-oximes **4a**, **4b** in almost quantitative yield.



1 **4**

	R	R'
a	Ph	Ph
b	*t*Bu	Me
c	Ph	Me
d	*i*Pr	Me

The ^{1}H-NMR spectra of the crude compounds indicated as side-products the 2-isoxazolines **6a** (R = R' = Ph), **6b** (R = *t*Bu, R' = Me) respectively, in amounts up to 4-6%. Chromatography on silica gel did not improve the purity, giving instead full conversion of **4a** into **6a**. Therefore, the spectroscopic characterization and the subsequent reactions were performed with samples of **4a**, **4b** with approx. 95% purity.

The isolation of the open-chain intermediate failed with other pyrylium salts **1**, due to much higher recyclization rates and to further oximation giving open-chain dioximes. For instance, under similar treatment, the 2,4,6-trimethylpyrylium perchlorate gave 2,4,6-trimethylpyridine 1-oxide in over 60% yield. However, as will be shown later, an indirect chemical proof was obtained for the formation of open-chain intermediates with structure **4** from 4-methyl-2,6-diphenylpyrylium perchlorate **1c** and 2,6-diisopropyl-4-methylpyrylium perchlorate **1d**.

The cyclization rate of **4a**, **4b** in solution was low enough to enable recording of the IR, ^{1}H- and ^{13}C-NMR spectra immediately after preparation (Tables 1 and 2). According to the number of signals in the ^{1}H- and ^{13}C-NMR spectra (300 MHz and 75 MHz, respectively), compounds **4a**, **4b** emerged as single isomeric species, denoting that the reaction occurred both *regio-* and *stereo-selectively*. Based on the IR absorption maxima and particularly on the ^{13}C-NMR chemical shifts, the compounds **4a**, **4b** were assigned structures of δ-oxo-α,β-unsaturated ketoximes. In fact, an open-chain intermediate was previously isolated

from pyrylium salt **1a** and hydroxylamine but was assigned a different functional group distribution (namely, saturated oxime and unsaturated ketone).[4] However, since the IR and ^{1}H-NMR data of this intermediate (1675, 3360 cm^{-1} in KCl pellet and δ 6.80, 4.09 ppm in $CDCl_3$)[4] are in good agreement with those of **4a** (see Table 1), we are dealing with one and the same compound and therefore the original functional group assignment should be reversed.

In order to ascertain the stereochemistry of the carbon-nitrogen double bond, compounds **4a**, **4b** were subjected to Beckmann rearrangement. It was hoped that conversion of the highly reactive **4a**, **4b** into more stable amides would allow reliable configurational proof for the carbon-carbon double bond as well. For convenience, the geometry of the C=C double bond is designated as *cis/trans* (with respect to the main C_5 - chain), using *E/Z* nomenclature only for the systematic names of the compounds.

Table 1. Chemical Shifts (δ, ppm) and Coupling Constants (*J*, Hz) in the ^{1}H-NMR Spectra (300 MHz, solv. $CDCl_3$) and IR Maxima (cm^{-1}) of Compounds **4**.

4	1-R	2-H	3-R′	4-CH_2	5-R	IR
a	7.62 (2H, d, *J* = 8.0) 7.25 - 7.35 (3H, m)[c]	6.80 (1H, s)	7.50 (2H, d, *J* = 7.2) 7.25 - 7.35 (3H, m)[c]	4.10 (2H, s)	7.72 (2H, d, *J* = 7.2) 7.47 (1H, t, *J* = 7.6) 7.25 - 7.35 (2H, m)[c]	1685[a] 3300[broad] 3560[sharp]
b	1.10 (9H, s)	5.66 (1H, s)	1.90 (3H, s)	3.20 (2H, s)	1.14 (9H, s)	1705[b] 3300[broad] 3585[sharp]

[a] in $CHCl_3$; [b] in CCl_4; [c] inseparably overlapped signals.

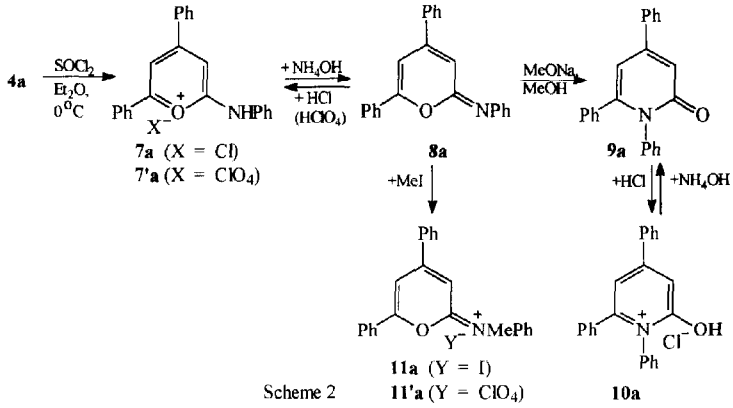
Table 2. Chemical Shifts (δ, ppm) in the ^{13}C-NMR Spectra (75 MHz, solv. $CDCl_3$) of Compounds **4**.

4	1-R	1-C(=NOH)	2-CH=	3-C(R′)	3-R′	4-CH_2	5-CO	5-R
a	135.1(Cq)	155.7	121.2	140.8	142.3(Cq)	42.4	196.3	136.6(Cq)
	129.5(*p*-CH)				128.4(*m*-CH)			133.0(*p*-CH)
	128.5(*m*-CH)				128.2(*p*-CH)			128.6(*m*-CH)
	127.3(*o*-CH)				126.4(*o*-CH)			127.9(*o*-CH)
b	29.7(CH_3)	162.7	117.4	139.5	23.5	42.0	212.6	26.3(CH_3)
	37.2(Cq)							44.2(Cq)

Beckmann rearrangement of compounds 4. Formation of 2-aryl(alkyl)amino-4,6-substituted pyrylium salts 7.

The Beckmann rearrangement of compounds **4** was performed with thionyl chloride or phosphorus pentachloride, taking into account their high tendency towards recyclization under catalysis by protic acids.

Treating the keto-ketoxime **4a** with an equimolar amount of thionyl chloride in anhydrous ethyl ether at 0°C, a yellow crystalline compound precipitated. According to elemental analysis and spectroscopic data, this compound was 2-anilino-4,6-diphenylpyrylium chloride **7a** (Scheme 2).



Scheme 2

In the ethereal phase only the 2-isoxazoline **6a** was found, in amounts slightly exceeding those already existing in the starting **4a**, demonstrating thereby that the cyclization competed poorly with the rearrangement under these conditions. The perchlorate **7'a** precipitated with 70% perchloric acid from the hydrochloric solution of **7a**. The salts **7a**, **7'a** gave with aqueous ammonia the *N*,4,6-triphenyl-*2H*-pyran-2-imine **8a**. On heating with sodium methoxide in methanol, **8a** was isomerized to 1,4,6-triphenyl-2-pyridone **9a**. The 2-hydroxy-1,4,6-triphenylpyridinium chloride **10a** precipitated with dry hydrochloric acid in ethyl ether; it regenerated the pyridone with ammonia. On heating the imine **8a** with methyl iodide, the methiodide **11a** was obtained; the methoperchlorate **11'a** was also prepared.

The sequence of reactions from **7a** to **9a** in Scheme 2 is actually a structure proof for the rearrangement product, based on literature data.[5-7] 2-Arylamino-4,6-diarylpyrylium chlorides have been previously prepared from 4,6-diaryl-2-pyrone and aromatic (carbo- or hetero-cyclic) amines in phosphoryl chloride at reflux; on recrystallization from pyridine-methanol, the chlorides gave the free bases, *N*,4,6-triaryl-*2H*-pyran-2-imines.[5,6] Both the salts and the free bases were isomerized with sodium ethoxide to 1,4,6-triaryl-2-pyridones. Unambiguous support for discriminating the isomeric pyranimine/pyridone pair came from their mass spectra.[6,7]

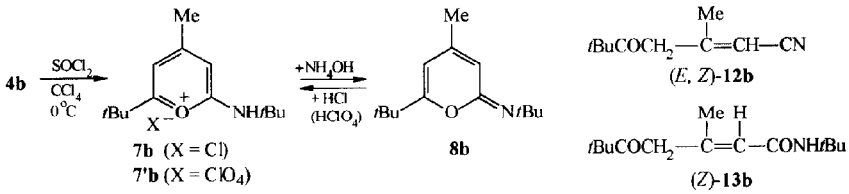
The mass spectra of the Beckmann rearrangement product **7a**, of its free base **8a** as well as of the isomeric pyridone **9a** are in full agreement with the above literature data. The salt **7a** and the imine **8a** gave identical EI mass spectra (direct inlet probe) with the highest ion corresponding to the molecular ion *m/z* 323 of the free base **8a** and characteristic 2,4-diphenylfuran (*m/z* 220) and $PhC{\equiv}O^+$ (*m/z* 105) fragment ions, whereas the pyridone **9a** with the same molecular ion *m/z* 323 gave 2,4-diphenylpyrrole (*m/z* 218) and $PhC{\equiv}N^{+\bullet}$ (*m/z* 103) as characteristic fragments.

The rearrangement of **4a** with phosphorus pentachloride gave the pyrylium chloride **7a** in only 30% yield but larger amounts of **6a** along with pyridine 1-oxide **5a** (R = R' = Ph) and small amounts of 2,4,6-triphenylpyridine as side-products. Traces of hydrochloric acid (from manipulating the catalyst) might be responsible for this result, accelerating the cyclization and promoting the isomerization of *anti*-**4a** to *syn*-**4a**, the precursor of the pyridine 1-oxide. The origin of the 2,4,6-triphenylpyridine is less obvious. Pyridines

were however mentioned among the products obtained from hydroxylamine and particularly 2,4,6-trisubstituted pyrylium salts with α-standing Ph or *i*-Pr groups.[1,2]

Treatment of the keto-ketoxime **4b** with an equimolar amount of thionyl chloride in carbon tetrachloride at 0°C gave the 2-*t*-butylamino-6-*t*-butyl-4-methylpyrylium chloride **7b** (Scheme 3) in 67% yield. The perchlorate **7'b** and the *N*,6-di-*t*-butyl-4-methyl-2*H*-pyran-2-imine **8b** were also obtained as described above. The salts **7b**, **7'b** and the imine **8b** had identical mass-spectra, the highest ion corresponding to the molecular ion *m/z* 221 of the free base **8b**. The ion at *m/z* 138, assigned to the 2-*t*-butyl-4-methylfuran fragment, identified the endocyclic heteroatom.

Examination of the side-products resulted in the separation and identification of the 2-isoxazoline **6b** (in amounts similar to those already existing in starting **4b**) and minor amounts (*ca.* 4%) of the 3,6,6-trimethyl-5-oxo-2-heptenenitrile **12b** (Scheme 3).



7b (X = Cl)
7'b (X = ClO_4)

Scheme 3

According to the GCMS and NMR data, the nitrile **12b** was formed as (*E*, *Z*) pair. Both stereoisomers presented the molecular ion *m/z* 165 of very low intensity and the common fragment ions $NCCH{=}C(Me)CH_2CO^+$ (*m/z* 108), Me_3CCO^+ (*m/z* 85) and Me_3C^+ (*m/z* 57). The configurational assignment is disscussed in the next paragraph.

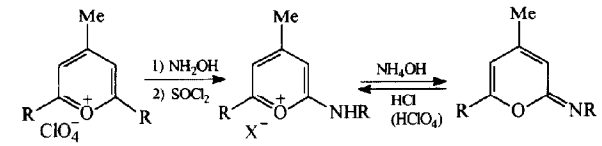
By performing the reaction of **4b** with thionyl chloride in ethyl ether at 0°C with subsequent aqueous work-up, a more complex reaction mixture was obtained. Column chromatography on silica gel of the products in the ethereal layer gave the pyridine 1-oxide **5b** (R = *t*Bu, R' = Me) in 1% yield, the 2-isoxazoline **6b** in 13% yield, the (*E,Z*)-**12b** in 6% yield (actually isolated as mixture with **6b**), and the (*Z*)-*N*-*t*-butyl-3,6,6-trimethyl-2-heptenecarboxamide **13b** (Scheme 3) in 41% yield. Extraction with methylene chloride of the aqueous phase gave the salt **7b** (32% yield), or alternatively the perchlorate **7'b** was precipitated with perchloric acid.

Traces of water in the solvent were most probably responsible for the formation of the amide **13b**, since a check experiment using carefully dried ethyl ether gave only **7b** as rearrangement product, while the cyclization products **6b**, **5b** and the nitrile **12b** were obtained in comparable amounts.

It is interesting to note that, although the fragmentation product **12b** appeared in similar amounts in the two solvents, the ratio between the *E/Z* stereoisomers was different: (*E*)-**12b** was the major isomer in carbon tetrachloride, while in ethyl ether (*Z*)-**12b** predominated. On the other hand, the rearrangement product **13b** was formed as a single *Z*-stereoisomer, as will be demonstrated in the next section.

As mentioned earlier, treatment of the pyrylium salts **1c**, **1d** with hydroxylamine gave mixtures containing significant amounts of recyclization products even at short reaction times (5-10 min.), preventing the actual isolation of the open-chain intermediate. However, by performing thereafter the Beckmann reaction, the chlorides **7c** and **7d** (Scheme 4) were obtained as rearrangement products. The corresponding perchlorates

7'c, **7'd** and the free bases **8c**, **8d** were also prepared. We may conclude therefore that pyrylium salts **1c**, **1d** shared the fate of giving open-chain intermediates with the general structure **4** by reacting with hydroxylamine, since they gave the same rearrangement products as when starting from **4a** or **4b**.



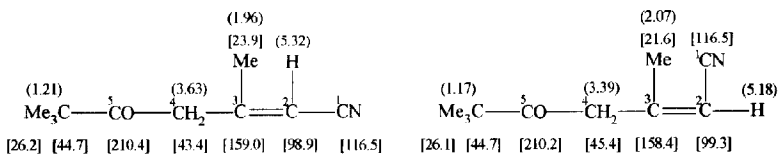
1c (R = Ph), **1d** (R = *i*Pr) **7c**, **7d** (X = Cl) **8c**, **8d**

7'c, **7'd** (X = ClO_4)

Scheme 4

The stereochemistry of the Beckmann reaction products.

The configurational assignment in the *Z/E* pair of the nitrile **12b** was based on the NMR data displayed in Figure 1.



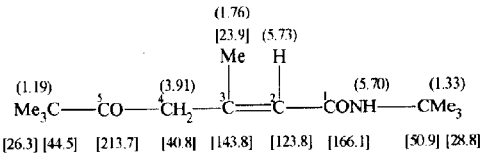
(*Z*) - **12b** (*E*) - **12b**

Figure 1. ^{1}H-NMR (in round brackets) and ^{13}C-NMR [in square brackets] δ values (ppm, in $CDCl_3$) of the (*Z,E*)-3,6,6-trimethyl-5-oxo-2-heptenenitrile **12b**.

The downfield 4-CH_2 signal (δ 45.4) was assigned to the methylene *cis* to the hydrogen atom at C-2, whereas the upfield signal (δ 43.4) belongs to the methylene subjected to the "γ-compression effect"[8] of the cyano group. Reasoning similarly for the 3-methyl group gave the same result.

The NOEDIF experiments performed for an additional independent configurational proof were in full agreement with the data shown above. In (*Z*)-**12b**, irradiation of the 3-Me group (δ 1.96) evidenced in the differential spectrum the signals for both 2-H (δ 5.32) and 4-CH_2 (δ 3.63), whereas irradiation of the 4-CH_2 gave only the signal for the 3-Me group. In (*E*)-**12b**, irradiation of the 4-CH_2 protons (δ 3.39) gave in the differential spectrum the signals of 2-H (δ 5.18) and 3-Me (δ 2.07), while irradiation of the vinylic proton gave only the signal belonging to the 4-CH_2 group.

Figure 2 presents the NMR data of the amide (*Z*)-**13b**, enabling the conformational assignment by NOEDIF: irradiating the 2-H atom at δ 5.73, only the signal of the 3-Me group at δ 1.76 appeared in the differential spectrum.



(*Z*) - **13b**

Figure 2. ^{1}H-NMR (in round brackets) and ^{13}C-NMR [in square brackets] δ values (in $CDCl_3$) of the (*Z*)-*N*-*t*-butyl-3,6,6-trimethyl-2-heptenecarboxamide **13b**.

The results of the single-crystal X-ray analysis of **13b** were in full agreement with the configurational assignment in solution. Figure 3 presents the ORTEP representation of the crystallographically determined structure of **13b**, including the numbering of the atoms (hydrogens are not numbered). Table 3 lists significant bond lengths, bond angles and torsion angles.

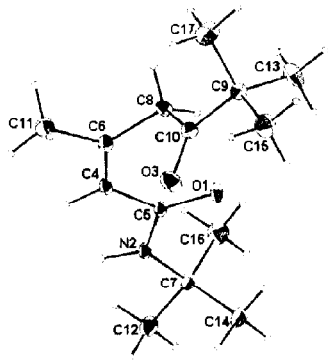


Figure 3. The ORTEP representation of the crystallographically determined structure of (*Z*)-**13b**.

Table 3. Bond Lengths (Å), Bond Angles and Torsion Angles (deg) in (*Z*)-**13b** .

Bond lengths (Å)		Bond angles (deg)		Torsion angles (deg)	
O(1)-C(5)	1.244	O(1)-C(5)-N(2)	122.4	C(7)-N(2)-C(5)-O(1)	-1.3
N(2)-C(5)	1.388	N(2)-C(5)-C(4)	113.9	C(7)-N(2)-C(5)-C(4)	179.7
N(2)-C(7)	1.473	O(1)-C(5)-C(4)	123.6	C(6)-C(4)-C(5)-N(2)	-179.1
O(3)-C(10)	1.208	C(5)-N(2)-C(7)	126.5	C(5)-C(4)-C(6)-C(11)	-178.1
C(4)-C(6)	1.324	C(5)-C(4)-C(6)	128.2	C(6)-C(4)-C(5)-O(1)	1.9
C(4)-C(5)	1.474	C(4)-C(6)-C(8)	124.4	C(11)-C(6)-C(8)-C(10)	75.3
C(6)-C(8)	1.508	C(6)-C(8)-C(10)	113.7	C(6)-C(8)-C(10)-O(3)	13.1

The molecular framework comprising the amide bond and the carbon-carbon double bond is almost planar, the geometry of both bonds being *Z*.

The relative orientation of the amide carbonyl and of the ketone group suggests an intramolecular donor-acceptor interaction. However, the O(1)-C(10) distance is 3.646 Å, much larger than the values of 2.8-3.0 Å characteristic for C=O...C close contacts in carbonyl compounds.[9] Analysis of the unit cell detected intermolecular hydrogen bonds with N...O 2.945 Å and H...O 2.07 Å distances, the angle at the hydrogen atom being 163°.

Cyclization reactions of the compounds 4.

The cyclization of the keto-ketoximes **4a**, **4b** was performed under the following conditions:

A: with an equimolar amount of sodium methoxide in methanol, at reflux

B: in glacial acetic acid, at reflux

The results obtained are presented in Table 4 as mole fractions of the cyclization products **5** and **6**, calculated from the ^{1}H-NMR spectra of the crude reaction mixture.

Table 4. Mole Fractions of the Products in Cyclization Reactions of the Compounds **4a**, **4b**.

Cyclization method	Reaction products			
	5a	**6a**	**5b**	**6b**
A	-	1.00	-	1.00
B	0.32	0.68	0.20	0.80

DISCUSSION

The 2,4,6-trisubstituted pyrylium salts **1** on reacting with hydroxylamine gave regio- and stereoselectively the highly reactive 1,3,5-trisubstituted 2-*cis*-pentene-1,5-dione 1-oximes **4**. Bulky α-substituents in **1**, such as *t*-butyl or phenyl, lower the recyclization rate allowing the isolation and chemical manipulation of compounds **4**, favoring also the *anti* geometry of the oxime moiety.

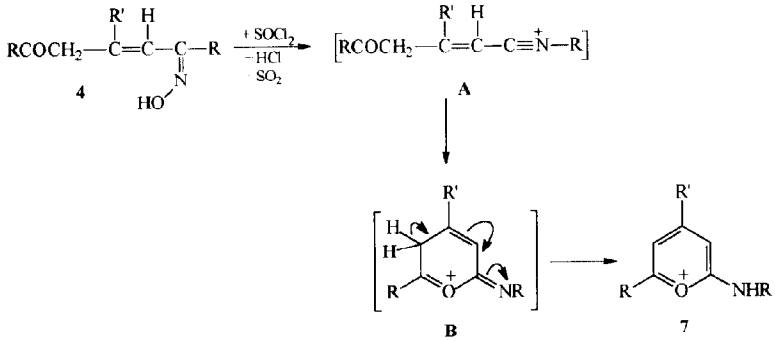
The data in Table 4 establish the keto-ketoxime **4** as being common precursor for both **5** and **6**. It is reasonable, therefore, to accept that the recyclization products originate in the geometrical isomers of the carbon-nitrogen double bond in **4**, the *anti*-isomer giving 2-isoxazoline **6** and the *syn*-isomer, pyridine 1-oxide **5**. Protonic acids promote the *anti*/*syn* isomerization by nitrogen protonation, lowering thereby the double-bond character of the carbon-nitrogen bond. This explains the formation of both **5a (b)** and **6a (b)** from *anti*-**4a (b)** under acidic conditions (B), whereas under basic conditions (A) only the Michael addition in *anti*-**4a (b)** occurred, giving **6a (b)**.

Under the terms of the mechanism in Scheme 1, the high reaction regioselectivity might suggest the disrotatory 2*H*-pyran ring-opening (step *ii*) occurring concerted with the prototropic step (*iii*), through a transition state favoring the suprafacial 1,5-hydrogen shift. The carbon-nitrogen double bond configuration apparently follows the usual thermodynamic trend with *anti* arrangement of the oxime hydroxyl and bulky groups R. Further attempts in isolation of such open-chain intermediates might allow a deeper insight into the

elemental steps of the mechanism. In this respect, the reaction of the pyrylium salts with alkoxyamines is under investigation.

The Beckmann reaction of the keto-ketoximes **4** with non-protic catalysts occurred with cyclization following the rearrangement, giving the pyrylium cation 7. The rearrangement stereospecifically involved the R group *anti* to the leaving group on nitrogen. On the other hand, the 2-C, 3-C double bond in **4** must be *cis* to allow the subsequent cyclization. Therefore the Beckmann reaction gave additional proof for the configuration of the carbon-nitrogen and carbon-carbon double bonds in **4**.

The rationalization of the rearrangement results is presented in Scheme 5. The cyclization occurs by internal nucleophilic addition of the carbonyl oxygen in the nitrilium ion **A**, followed by hydrogen shift in **B** giving the pyrylium cation 7, the aromatization providing the driving force.



Scheme 5

In the rearrangement of **4b**, the addition of water as external nucleophile gave the normal rearrangement product, the amide **13b**. The minor fragmentation reaction giving the nitrile **12b** can be explained by the adjacency of the quaternary carbon of the *t*-butyl radical to the oxime carbon.[10,11] Surprisingly, the fragmentation occurred with isomerization of the carbon-carbon double bond, since **12b** was obtained as (*E,Z*)-pair, while the normal rearrangement product **13b** was definitely formed as the single (*Z*)-stereoisomer. This result provides evidence against the fragmentation and rearrangement products originating both in the nitrilium ion **A**, as generally known to be the case with α-alkylated or arylated ketoximes,[12] suggesting instead that the fragmentation occurred by an independent pathway.

CONCLUSION

The Beckmann reaction of compounds **4** resulted in the discovery of a new rearrangement/cyclization giving the six-membered aromatic pyrylium ring. To our knowledge, this is the first example of cyclization with carbonyl oxygen atom as terminator in the literature on Beckmann reactions.[10,11]

The sequence of reactions **1**→ (**4**) → **7** → **8** is a new route to 2*H*-pyran-2-imines. It should be recalled that 2-pyrones give usually, with ammonia or with primary amines, 2-pyridones[13] rather than 2*H*-pyran-2-imines,[5-7] severely limiting access to the latter. Less common routes to pyran-2-imines are also worth mentioning, involving unusual C-nitrosation of peralkylated 3,5-hexadienoic secondary amides followed by loss of a ketoxime molecule[14] or Hofmann degradation of the pyran-substituted phosphoranes obtained by

[4+2] cycloaddition of α,β-unsaturated carbonyl compounds and *N*-aryl (triphenylphosphoranylidene) ethenimines.[15] The procedure described in the present paper has its own limitations, starting only from pyrylium salts **1** with bulky α-substituents (such as *i*Pr, *t*Bu or Ph), which favor the *anti* oxime geometry in **4**. Still, it seems an attractive synthetic alternative for 2*H*-pyran-2-imines, involving accessible reagents and simple chemical manipulations.

EXPERIMENTAL

Instrumentation

Melting points were determined on Boetius hot plate and are uncorrected. The IR spectra were recorded on a Carl Zeiss UR20 instrument. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. The mass spectra were recorded with a Carlo Erba QMD 100 instrument, with direct inlet probe unless otherwise stated. The crystallographic X-ray data were obtained on a Kappa CCD diffractometer at 25°C. No absorption correction was made. All diagrams and calculations were performed using maXus (Mac Science, Japan).

Reaction of pyrylium perchlorates 1 with hydroxylamine; isolation of keto-ketoximes 4a, 4b.

(2-E)-1,3,5-Triphenyl-2-pentene-1,5-dione (1-E)-oxime **4a**: to 75 mL aqueous 0.2 M sodium hydroxide solution was added 1.04 g (15 mmol) hydroxylamine hydrochloride, 40-50 mL ethyl ether, 2.00 g (4.9 mmol) solid 2,4,6-triphenylpyrylium perchlorate **1a** and the mixture was vigorously shaken in a separatory funnel for 10-15 min. The unreacted pyrylium was filtered off, the ethereal layer of the filtrate was evaporated under reduced pressure leaving 0.75 g **4a** (90% yield based on reacted pyrylium) as colourless crystals, m.p. 114-7 °C (lit.[4] m.p.125°C).

(4-Z)-2,2,5,8,8-Pentamethyl-4-nonene-3,7-dione (3-E)-oxime **4b**: working as above, from 1.50 g (4.9 mmol) 2,6-di-*t*-butyl-4-methylpyrylium perchlorate **1b** resulted 1.17 g **4b** (quantitative yield) as colourless crystals, m.p. 80-83°C. The IR, ^{1}H- and ^{13}C-NMR spectroscopic data of **4a**, **4b** are given in Tables 1, 2.

Under similar treatment, the 2,6-diphenyl-4-methylpyrylium perchlorate **1c** and the 2,6-diisopropyl-4-methylpyrylium perchlorate **1d** gave oily products, subjected afterwards to Beckmann reaction (see below).

Beckmann reaction of the keto-ketoximes 4.

***4a** with thionyl chloride*: an ethereal solution of **4a** (0.75 g, 2.2 mmol) was treated dropwise over 15-20 min with thionyl chloride (0.16 mL, 2.2 mmol) in ethyl ether, with magnetic stirring and cooling in an ice-water bath. Pyrylium chloride **7a** precipitated as yellow crystals (0.58 g, 73% yield), giving satisfactory elemental analysis without further purification. Working-up of the filtrate gave 2-isoxazoline **6a** (0.14 g, 19% yield) as colourless crystals, m.p. 118-9°C (lit.[4] m.p. 124°C), identical in its spectroscopic properties with an authentic sample. On dissolving **7a** in hot dilute hydrochloric acid and adding 70% perchloric acid, perchlorate **7'a** precipitated as yellow crystals.

Solid salt **7a** suspended in ethyl ether was shaken briefly with conc. ammonia, then the aqueous phase was discharged. Evaporation of the solvent and chromatography on silica gel with 4/1 (v/v) petroleum ether/ethyl ether gave the analytical sample of the imine **8a** as orange crystals.

N-(4,6-Diphenyl-2H-pyran-2-ylidene)benzenamine **8a**: m.p. 162-163.5°C (lit.[6] m.p. 160°C). Anal. Calcd. For $C_{23}H_{17}NO$: C, 85.42; H, 5.30; N, 4.33. Found: C, 85.62; H, 5.48; N, 4.13. MS (rel. int.): 323(8)[M^+], 220(42), 191(28), 115(34), 105(13), 77(100).

Hydrochloride **7a**: m.p. 208-214°C (decomp.) (lit.[6] m.p. 210-220°C, decomp.). Anal. Calcd. For $C_{23}H_{18}ClNO$: C, 76.77; H, 5.04; N, 3.89; Cl, 9.85. Found: C, 76.57; H, 5.33; N, 4.17; Cl, 10.33. MS (rel. int.): 323(11)[M^+-HCl], 220(53), 191(32), 115(40), 105(13), 77(100).

Hydroperchlorate **7'a**: m.p. 246-7°C (acetic acid). Anal. Calcd. For $C_{23}H_{18}ClNO_5$: N, 3.30. Found: N, 3.54.

The imine **8a** (0.13 g, 0.4 mmol) in 3mL methanol was refluxed for 24 hrs. with 1 M sodium methoxide in methanol (2 mL, 2 mmol), giving after usual work-up pyridone **9a** (0,10 g, 77% yield). The analytical sample was obtained by chromatography on silica gel with 1/1 (v/v) petroleum ether/ethyl ether. Treatment of **9a** with dry hydrochloric acid in ethyl ether gave instant precipitation of hydrochloride **10a** as colourless crystals.

1,4,6-Triphenyl-2(1H)-pyridinone **9a**: m.p. 163-7°C (lit.[6] m.p. 164-6°C). MS (rel. int.): 323(22)[M^+], 218(3), 191(17), 115(21), 103(4), 77(100)

Hydrochloride **10a**: m.p. 167-9°C. Anal. Calcd. For $C_{23}H_{18}ClNO$: C, 76.77; H, 5.04; N, 3.89; Cl, 9.85. Found: C, 76.91; H, 5.32; N, 4.02; Cl, 10.13. MS (rel. int.): 323(24)[M^+-HCl], 218(3), 191(18), 115(23), 103(4), 77(100).

On heating gently **8a** with excess of methyl iodide, methiodide **11a** precipitated in a short time (orange crystals on recrystallization from ethanol, 60% yield). The perchlorate **11'a** precipitated as yellow crystals with 70% perchloric acid in hot dilute hydrochloric solution of **11a**.

N-(4,6-Diphenyl-2H-pyran-2-ylidene)-N-methylbenzenaminium iodide **11a**: m.p. 240-1°C. Anal. Calcd. For $C_{24}H_{20}INO$: C, 61.95; H, 4.33; N, 3.01; I, 27.27. Found: C, 61.76; H, 4.33; N, 2.84; I, 27.27

Perchlorate **11'a**: m.p. 223-5°C. Anal. Calcd. For $C_{24}H_{20}ClNO_5$: C, 65.83; H, 4.60; N, 3.20. Found: C, 65.81; H, 4.73; N, 3.41.

***4a** with phosphorus pentachloride*: working as above, but using an equimolar amount of phosphorus pentachloride as catalyst, the following cyclization products were isolated after aqueous work-up and separation by column chromatography: 2,4,6-triphenylpyridine, m.p. 126°C (lit.[16] m.p. 138°C), identified by comparison with an authentic sample; 2-isoxazoline **6a** (29% yield) and pyridine 1-oxide **5a**, m.p. 182-6°C (lit.[17] m.p. 186-9°C). The yield of the rearrangement product **7a** was 30%.

***4b** with thionyl chloride in carbon tetrachloride*: **4b** (0.50 g, 2.09 mmol) in 15 mL carbon tetrachloride was treated with thionyl chloride (0.16 mL, 2.2 mmol) as previously described. Removal of the solvent and trituration with ethyl ether gave 0.36 g (67% yield) colourless crystals of pyrylium chloride **7b**, with satisfactory elemental analysis. The ethereal washings was chromatographed on silica gel with mixtures of petroleum ether/ethyl ether giving 0.03 g (6% yield) 2-isoxazoline **6b** and 0.015 g (4% yield) nitrile **12b** (with cross-contamination). Perchlorate **7'b** precipitated as colourless needles from hot aqueous solution of **7b** and perchloric acid. The imine **8b** was obtained from either **7b** or **7'b** as described before.

2-Methyl-N-[6-(1,1-dimethylethyl)-4-methyl-2H-pyran-2-ylidene]-2-propanamine **8b**: oil; MS (rel. int.): 221(4)[M^+], 138(37), 109(7), 108(100), 95(3), 57(64), 53(15).

Hydrochloride **7b**: m.p. 200-1°C. (decomp.); Anal. Calcd. For $C_{14}H_{24}ClNO$: C, 65.23; H, 9.38; N, 5.43; Cl, 13.75. Found: C, 65.08; H, 9.23; N, 5.68; Cl, 13.48. MS (rel. int.): 221(2)[M^+-HCl], 138(16), 109(5), 108(64), 95(2), 57(100), 53(36).

Hydroperchlorate **7'b**: m.p. 200-2°C (acetic acid/ethyl ether). Anal. Calcd. For $C_{14}H_{24}ClNO_5$: C, 52.25; H, 7.52; Cl, 11.02. Found: C, 51.98; H, 7.39; Cl, 10.92.

(E,Z)-3,6,6-Trimethyl-5-oxo-2-heptenenitrile **12b**: oil; IR(CCl_4) 2223 cm^{-1}. The GC-MS analysis was performed on CP-Sil 5 CB fused capillary column (25 m/0.32 mm), the first eluting isomer being *Z*-**12b**.

(*Z*)-**12b**: MS (rel. int.): 108(0.8), 85(7.5), 81(18.2), 69(5.8), 57(100).

(*E*)-**12b**: MS (rel. int.): 108(4.3), 85(8.7), 81(11.0), 69(1.3), 57(100).

4b with thionyl chloride in ethyl ether: **4b** (1.13 g, 4.73 mmol) was treated with thionyl chloride (0.4 mL, 5.5 mmol) as above but with ethyl ether as solvent. After completing the reaction, 20 mL water was added and the aqueous phase was repeatedly extracted with ethyl ether. Elution chromatography of the products in the ethereal extracts (on silica gel, with increasing amounts of ethyl ether in petroleum ether) gave: pyridine 1-oxide **5b** (0.01 g, 1% yield), a mixture of nitrile (*Z,E*)-**12b** and isoxazoline **6b** in 1:2 molar ratio (0.19 g, corresponding to 6% yield in **12b** and 13% in **6b**) and amide (*Z*)-**13b** (0.46 g, 41% yield). Extraction of the aqueous phase with methylene chloride gave pyrylium chloride **7b** (0.39 g, 32% yield).

(Z)-N-(1,1-Dimethylethyl)-3,6,6-trimethyl-2-heptenecarboxamide **13b**: colourless crystals, m.p. (aq. ethanol): 101-3°C; IR(CCl_4): 1647(C=C), 1672(C=O stretching amide I), 1707(C=O ketonic), 3370(NH stretching, assoc.), 3440 cm^{-1}(NH stretching, free); Anal. Calcd. For $C_{14}H_{25}NO_2$: C, 70.25; H, 10.53; N, 5.85. Found: C, 70.60; H, 10.62; N, 6.09. The crystallographic data for (*Z*)-**13b** are given in Figure 3 and Table 3.

Pyrylium salts ***7c, 7'c, imine 8c***: on treating the crude oily product obtained from 4-methyl-2,6-diphenylpyrylium perchlorate **1c** and hydroxylamine (see before) with thionyl chloride in ethyl ether at 0°C, a gummy solid deposited. Recrystallization from diluted hydrochloric acid (with charcoal) gave bright-yellow needles of pyrylium chloride **7c** (27% yield based on **1c**). The perchlorate **7'c** precipitated as yellow crystals on adding perchloric acid in the hot hydrochloric solution of **7c**. The imine **8c** was prepared from either **7c** or **7'c** with diluted aqueous ammonia, as described. Working-up of the ethereal phase gave 2-isoxazoline **6c** (32% yield based on **1c**), identical in its spectroscopic properties with an authentic sample.

N-(4-Methyl-6-phenyl-2H-pyran-2-ylidene)benzenamine, **8c**: m.p. 80-3°C. Anal. Calcd. For $C_{18}H_{15}NO$: C, 82.73; H, 5.84; N, 5.36. Found: C, 82.97; H, 6.08; N, 5.14. MS (rel. int.): 261(13)[M^+], 158(76), 129(23), 115(17), 105(7), 77(100), 53(41).

Hydrochloride **7c**: m.p. 168-170°C (decomp.) Anal. Calcd. For $C_{18}H_{16}ClNO$: C, 72.60; H, 5.42; N, 4.70; Cl, 11.91. Found: C, 72.43; H, 5.69; N, 4.59; Cl, 11.78. MS (rel. int.): 261(25)[M^+-HCl], 158(100), 129(22), 115(14), 105(7), 77(69), 53(29).

Hydroperchlorate **7'c**: m.p. 205-8°C (acetic acid) Anal. Calcd. For $C_{18}H_{16}ClNO_5$: C, 59.76; H, 4.46; N, 3.87; Cl, 9.80. Found: C, 60.04; H, 4.72; N, 3.71; Cl, 9.93. MS (rel. int.): 261(25)[M^+-$HClO_4$], 158(100), 129(23), 115(15), 105(8), 77(75), 53(31).

Pyrylium salts ***7d, 7'd, imine 8d***: the rearrangement was performed in carbon tetrachloride, followed by aqueous work-up. The perchlorate **7'd** was precipitated from the aqueous phase (55% yield) and converted

into the imine **8d** as described. The analytical sample of chloride **7d** was prepared by treating **8d** with ethereal dry hydrochloric acid. The cyclization products **5d** and **6d**, accounting for 35% yield, were identified by comparison with authentic samples.

N-[6-(1-Methylethyl)-4-methyl-2H-pyran-2-ylidene]-2-propanamine **8d**: oil. MS (rel. int.): 193(**12**)[M^+], 124(35), 108(100), 95(2), 81(6), 71(1), 53(53).

Hydrochloride **7d**: Anal. Calcd. For $C_{12}H_{20}ClNO$: N, 6.10. Found: N, 6.49.

Hydroperchlorate **7d**: m.p. 151°C (acetic acid/ethyl ether). Anal. Calcd. For $C_{12}H_{20}ClNO_5$: C, 49.07; H, 6.86; N, 4.77; Cl, 12.07. Found: C, 49.37; H, 6.58 N, 5.01; Cl, 11.87. MS (rel. int.): 193(9)[M^+-$HClO_4$], 124(29), 108(100), 95(2), 81(7), 71(1), 53(91).

Cyclization of compounds ***4a, 4b***: the reactions were performed by method A, B (see text); work-up consisted in aqueous treatment (prior evaporation of methanol in method A) and repeated extractions with chloroform until > 90% of the cyclization product(s) was recovered. The composition was calculated from the ^{1}H-NMR spectrum of the crude cyclization mixture.

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