131. Cascade Reactions

A Simple One-Pot Synthesis of the Mitomycin Skeleton

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(3.V.89)

Nitroso-arene dienophiles **1** react regiospecifically with the conjugated dienals **2** and **3a**/**3b**, and lead thereby to the unstable *Diels-Alder* cycloadducts **4** and **5**. These undergo two types of cascade reactions which give pyridinium betaines **6** and pyrrolo-indoles **8** as the major reaction products. The one-pot syntheses of pyrrolo-indoles **8** represent a new and easy access to the basic skeleton of mitomycins **10**. The scope and limitations of the cascade reactions were investigated.

***Diels-Alder* Cycloadditions of Nitroso-arene Dienophiles with Conjugated Dienals and their Cascade Reactions**[1]). – We shall describe herein some cascade-reaction sequences which we observed, when conjugated dienals were treated with nitrosoarene dienophiles **1**. To our knowledge, no cycloaddition reactions have been described so far between nitroso dienophiles and linear conjugated dienals. Nevertheless, some oxime- and dimethylacetal derivatives of these dienals are known to undergo *Diels-Alder* reactions with nitroso dienophiles [2–7].

The reaction of nitrosobenzene with pentadienal **2** or with the commercially available mixture of hexadienals **3a** (80%) and **3b** (20%) occurred rapidly leading, in each instance, to four heterocyclic products, none of which being the expected primary *Diels-Alder* adduct.

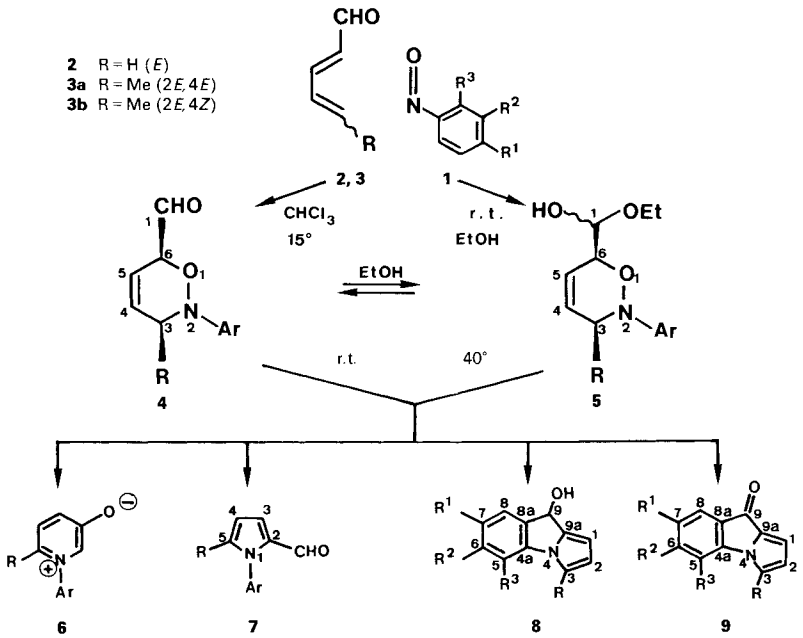
For example, the reaction of pentadienal **2** with PhNO gave the betaine **6a**, trace amounts of the pyrrole-2-carbaldehyde **7a**, the tricyclic alcohol **8a**, and the corresponding ketone **9a** *(Scheme 1)*. It should be noted that the preparation of the tricyclic products **8a** and **9a**, *via* a different multistep approach, had already been described as part of a synthetic plan for the mitomycins [8–10].

Mitomycins **10** represent a class of well-known natural products [11] which exhibit antibiotic and antitumor properties [12].

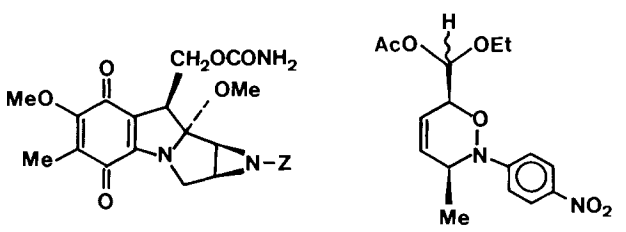
Since our procedure for the synthesis of pyrrolo-indoles **8a**/**8b** and **9a**/**9b** represents a new one-pot process, using easily available starting materials, we decided to investigate the scope and limitations as well as the mechanism of these obviously complex cascade reactions (see below), our ultimate goal being the synthesis of some mitomycin derivatives.

[1]) For a preliminary communication, see [1].

Scheme 1



	a	b	c	d	e	f	g	h	i	j
R	H	Me	Me	Me	Me	Me	Me	Me	Me	Me
R^1	H	H	NO_2	Cl	CO_2Me	MeO	Me_2N	H	Cl	MeO
R^2	H	H	H	H	H	H	H	H	Me	Me
R^3	H	H	H	H	H	H	H	Me	H	H



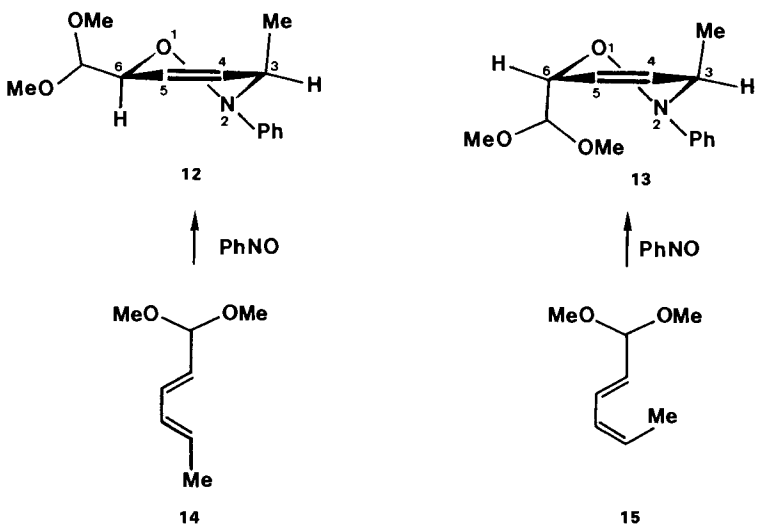
	X	Z
Mitomycin A	MeO	H
Mitomycin C	NH_2	H
Porphiromycin	NH_2	Me

The Primary *Diels-Alder* Cycloadducts. – *Experimental Results.* Since pentadienal **2** undergoes polymerization, we used the stable, commercially available mixture **3a**/**3b**. Reaction of PhNO (**1a**) with **3a**/**3b** at 30° directly led to the products **6b**–**9b** as shown by ^{1}H-NMR in $CDCl_3$. At 15°, however, the primary cycloadduct **4b** was detected by ^{1}H-NMR in 30% yield after 7 h, either in $CDCl_3$ or in C_6D_6. Reaction of **3a**/**3b** with the

more reactive *p*-nitronitrosobenzene (**1c**) in $CDCl_3$ led quantitatively, within 1 h at r.t., to the corresponding primary adduct **4c**. Due to its instability, this adduct could not be isolated; nevertheless, it was characterized in $CDCl_3$ solution by IR and ^{1}H-NMR and appeared to be a homogenous product, its relative configuration being as indicated in *Scheme 1* (see below, for the structural analysis). Interestingly, both **1a** and its *p*-nitro derivative **1c**, when treated with **3a**/**3b** in EtOH at r.t., led quantitatively to the corresponding cycloadducts **5b** and **5c**, respectively, in which the aldehyde function is in the hemiacetal form. The ^{1}H-NMR spectra of these adducts showed complex patterns, which is due to the fact that they occur as diastereoisomeric mixtures (*ca.* 1:1). Furthermore, hemiacetals **5b** and **5c** are in equilibrium with the corresponding aldehydes **4b** and **4c**, respectively, in $CDCl_3$ or in (D_6)benzene solution. Acetylation of **5c** with Ac_2O/pyridine led to the stable acetals **11** (6:4 mixture of two diastereoisomers) which could be isolated and characterized.

Structural Analysis of the Cycloadducts. The ^{1}H-NMR spectra of the cycloadducts could be interpreted unambiguously, in particular by comparison with cycloadducts **12** and **13** [13] which were obtained by regiospecific *Diels-Alder* cycloadditions of the dimethyl acetals **14** (80%) and **15** (20%) with **1a**. The dimethyl acetal **14** (*E*,*E*) gave the major adduct **12** (80%), while **15** (*E*,*Z*) gave the minor adduct **13** (20%; *Scheme 2*).

Scheme 2



Similar cycloadducts have been described previously, *e.g.* 3,6-dihydro-2*H*-oxazines [13] and 1,2,3,6-tetrahydropyridazines [14]. For all these adducts, the relative configuration and the conformation could be deduced from a set of ^3J, ^4J, and ^5J values between *H*–C(3), *H*–C(6), *H*–C(4), and *H*–C(5): a pseudo-equatorial H-atom leads to a ^3J of *ca.* 4–5 Hz with the vicinal olefinic H-atom and to a weak ^4J (*ca.* 1.5 Hz) with the allylic H-atom; a pseudo-axial H-atom leads to a weak ^3J (*ca.* 1.5 Hz) and to a ^4J of *ca.* 2 Hz with the vicinal and allylic H-atoms, respectively.

Table 1. *^{1}H-NMR Spectra of Dihydro-2*H*-oxazines* **4b**, **4c**, **11**, **12**, *and* **13** (80 MHz, 300 K; δ in ppm and J in Hz, internal standard TMS)

	Solvent	H–C(1′)	H–C(3)	H–C(4)	H–C(5)	H–C(6)	Me–C(3)	arom. H	Other signals
4b	$CDCl_3$	9.86	3.97	6.01	6.01	4.73	1.03	7.32	
4c	$CDCl_3$	9.73	4.35	6.15	5.95	5.05	1.24	7.12; 8.20	
11 (major)	(D_6)Benzene	5.98	3.66	5.64	5.87	4.65	0.91	6.61; 8.15	EtO: 3.65 (*m*, CH_2); 1.04 (*t*, J = 7, Me) AcO: 1.81 (*s*, Me)
11 (minor)		6.08	3.66	5.64	5.85	4.69	0.91	6.65; 8.00	EtO: 3.65 (*m*, CH_2); 0.95 (*t*, J = 7, Me) AcO: 1.74 (*s*, Me)
12	(D_6)Benzene	4.42	3.83	5.73	6.02	4.81	1.01	6.9–7.17	2 MeO: 3.17; 3.25
13	(D_6)Benzene	4.71	3.80	5.73	5.96	4.47	0.98	6.7–7.2	2 MeO: 3.13; 3.25

	Solvent	^3J(1′,6)	^3J(3,4)	^4J(3,5)	^5J(3,6)	^3J(4,5)	^4J(4,6)	^3J(5,6)	^3J(3, Me)
4c[a])	$CDCl_3$	0.5	4.7	–1.8	2.6	10.0	2.8	–1.8	6.5
11 (major)	(D_6)Benzene	6.0	4.4	1.3	2.4	10.1	2.0	1.3	6.5
11 (minor)		4.7	4.4	1.3	2.4	10.1	2.0	1.2	6.5
12[a])	(D_6)Benzene	6.6	4.5	–1.8	2.2	10.2	2.2	–1.5	6.6
13[a])	(D_6)Benzene	7.4	4.9	–1.6	0.7	10.0	–1.7	3.7	6.4

[a]) J values calculated using a PANIC program.

Table 1 clearly shows that H–C(3) is pseudo-equatorial in all instances; H–C(6) is pseudo-axial in adducts **4c**, **11**, and **12** (major adducts) and pseudo-equatorial in **13** (minor adduct). It follows that the conformation of these various adducts is as depicted in *Scheme 2*. The homoallylic ^5J between H–C(3) and H–C(6) is strongly dependent on the relative orientation of these two H-atoms: ^5J is small (*ca.* 0.8 Hz), when both H-atoms are pseudo-equatorial, and much larger (*ca.* 2.5 Hz), when one of these two H-atoms is pseudo-axial.

The exclusive formation of **12**/**13** in pseudo-chair conformations, as indicated in *Scheme 2*, is governed by the Me–C(3) group which is always pseudo-axial. This is due to a strong steric interaction between Me–C(3) and the N-substituent in the other pseudo-chair conformation, a fact which we have already reported in [13]. *Kresze* and *Firl* have already assigned to the type **13** minor adduct (*p*-chlorophenyl instead of Ph at the N-atom) the inverse regioisomeric structure with respect to the one depicted in *Scheme 2* [7]. As we have demonstrated above and in *Table 1*, **12** and **13** are diastereoisomers and not regioisomers. Their chemical shifts are very similar, and they differ only in their configuration at C(6).

Regiospecificity and FMO Theory. The regiospecific cycloadditions which we observed during the reaction of pentadienal **2a** and hexadienals **3a**/**3b** with nitrosoarene dienophiles are in accordance with the predictions of the FMO theory: the largest MO coefficients are at C(5) of the dienal HOMO; and at the N-atom of the nitroso dienophile LUMO, as indicated below [15].

The same type of regiospecificity was also observed, when the dimethyl acetals **14** and **15** were treated with nitroso dienophiles [13], leading, for example, to the adducts **12** and

HOMO LUMO

2, 3a, 3b 1

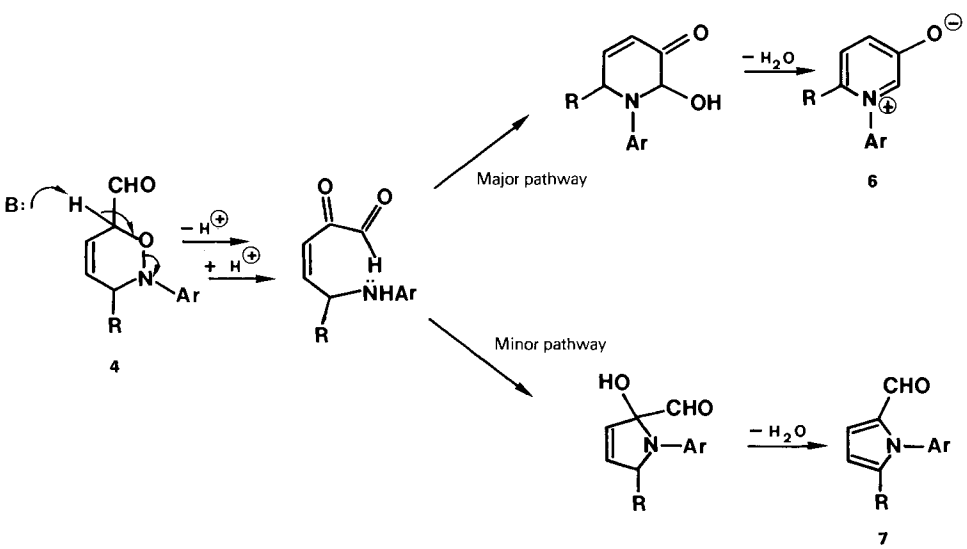
13, respectively. If we assume that the $\pi \rightarrow \sigma^*$ delocalization of the acetal function leads to MO coefficients similar to those depicted above for the dienals, it follows that the steric and orbital factors complement each other, so that the regiospecificity of these cycloadditions can be reasonably rationalised.

The concertedness of the *Diels-Alder* reactions with **3a** and **3b** is open to discussion, since both educts lead to the same and only *cis*-cycloadduct **4** which is the thermodynamically favoured one. Educt **3b** was expected to give the *trans*-adduct which is not observed during the reaction. Merely as a hypothesis, we surmise that this latter *trans*-adduct does indeed form but rapidly isomerises to the more stable *cis*-isomer **4**.

The Rearrangement Pathways of the Cycloadducts. – The primary cycloadducts **4** are instable species, and they represent the starting point for the ensuing rearrangement processes which lead to the final products **6–9**. It is worth noting that, in EtOH solution, the adducts **4** are in equilibrium with the somewhat more stable hemiacetal species **5** (see below).

Firl and *Kresze* have described some base-catalysed rearrangements of oxazine derivatives, which are similar to **4** and bear slightly acidic H-atoms in α-position to a

Scheme 3

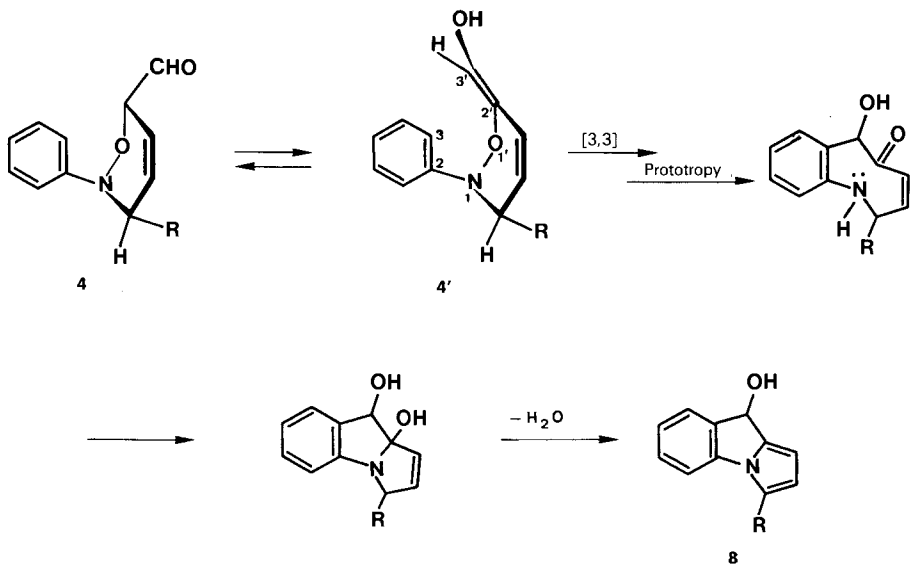


C=O function (ester or carboxylic-acid groups at C(6)), and which lead to pyrrole derivatives [16]. By analogy with *Kresze*'s work, the formation of the betaines **6** and of the pyrrole-carbaldehydes **7** can be explained according to some straightforward mechanisms as depicted in *Scheme 3:* base-catalysed deprotonation at C(6) leads, by cleavage of the weak N–O bond *via* a *β*-elimination, to acyclic keto-aldehydes; intramolecular nucleophilic addition of the aniline-N-atom to the aldehyde or to the ketone, followed by dehydration, gives the aromatic betaines **6** (major products) and the pyrrole-carbaldehydes **7** (minor products), respectively. As a consequence, the betaines **6** and the tricyclic alcohols **8** are the major reaction products. The yield of betaines could be increased by addition of Et_3N to the reaction medium.

The formation of the pyrrolo-indoles **8** obviously follows a more complex process, particularly in view of the fact that the pyrrole-carbaldehydes **7**, which could function as immediate precursors are known to be stable products [8] and do not cyclise to the isomeric tricyclic alcohols **8**, at least under the mild conditions applied. The pyrrolo-indole structure of **8** – and particularly the formation of a covalent bond between C(8a) and C(9) – is strongly reminiscent of the *Fischer* indole synthesis in which a hetero-*Cope* rearrangement is of paramount importance. The hypothetical multistep mechanism, which in our opinion accounts best for the transformation of **4** into **8**, is represented in *Scheme 4*; *i.e.*: equilibrium between **4** and its enol tautomer **4′**; 1-aza-1′-oxa-*Cope* rearrangement of **4′**, followed by rapid re-aromatisation, leading to an 8-membered amino-ketone; transannular nucleophilic addition of the secondary amine to the ketone, followed by dehydration, to give **8**.

The formation of the enol tautomer **4′** is favoured by resonance stabilization with the endocyclic double bond. A 1-aza-1′-oxa-*Cope* rearrangement, then, occurs to yield an 8-membered ring, provided that the C-atoms C(3) and C(3′) of **4′** are in close proximity.

Scheme 4



As shown by a *Dreiding* model, such a topology can only be obtained when the N-atom of **4′** is pyramidal. Evidence for this has been obtained in a different context in which we have demonstrated by X-ray analysis that the N-atom of a O-NCOPh moiety is pyramidal, the sum of the three angles with the N-atom at the apex being 339° [17]. Albeit, 1-aza-1′-oxa-*Cope* rearrangements are of relatively recent vintage in organic synthesis[2]). The driving force for this [3,3]-sigmatropic rearrangement is the easy cleavage of the weak N–O bond of **4′**.

Tricyclic ketone by-products **9** are formed by oxidation of the corresponding alcohols **8**. The nitroso-aryl educts play the role of oxidizing agents, since azoxybenzene derivatives are formed (see *Exper. Part*).

Secondary alcohols **8** could easily be oxidized by MnO_2 to the crystalline ketones **9** which are deep-yellow compounds.

Formation of Pyrrolo-indoles 8/9: Scope and Limitations. – Pyrrolo-indoles **8/9** are the most interesting products of the above described cascade-reaction manifold. It seemed, therefore, desirable to optimize their yields by a proper choice of experimental conditions. It appeared that in aprotic solvents ($CHCl_3$, THF, acetone), the reaction of pentadienals with nitroso-arene dienophiles was incomplete, and the yields of **8/9** were rather modest (*ca.* 20%). Temperature had no noticeable effect on the course of the reaction.

In contrast, in EtOH solution, *Diels-Alder* cycloadditions proved to be complete, leading to the relatively stable (in solution only) hemiacetal derivatives **5**. The cascade reactions occurred, when these products were heated above 40°. Most interestingly, the yields of the tricyclic products **8/9** were improved to *ca.* 50% (see *Exper. Part*). We surmised that an acidic medium would enhance enol formation. Unfortunately, addition

Table 2. *Experimental Results of the Reaction of Nitrosodienophiles* **1** *with Pentadienal* **2** (line a) *and with Hexadienals* **3a/3b** (lines b–j) *in 70 mmol·l^{-1} EtOH Solutions.* The yields of **8** and **9** should be added up, since compounds **8** were partly oxidised *in situ* to **9**.

Exper. runs	Dienophile	Isolated product [%][a])						Reaction conditions: temp. [°C]; duration (days)
		6	**7**	**8**	**9**	Recovered aldehyde	Azoxy compound	
a	**1a**	48	1	28	9	–	[b])	40; 3
b	**1a**	10	1	35	11	–	[b])	45; 2
c	**1c**	37	6	*ca.* 2	25	–	4	45–50; 7
d	**1d**	44[c])	1	33	14	–	[b])	45–50; 4
e	**1e**	17	–	35	15	–	2	45; 4
f	**1f**	57[c])	1	11	15	10	10	45; 3
g	**1g**	59	–	–	–	–	–	45; 4
h	**1h**	36	1	–	10	18	15	50; 2
i	**1i**	60	1	21	4	–	9	45–50; 2
j	**1j**	45	1	4	7	–	5	45; 3

[a]) For the sake of clarity, the lettered indices were left out; in each line they are identical with those indicated in the first column.

[b]) Not determined.

[c]) Yield of the crude product.

[2]) For a recent review article on hetero-*Cope* rearrangements, see [18].

of *Lewis* acids ($ZnCl_2$) or protic acids (HCO_2H) lead to the formation of more complex mixtures, partly due to the fact that the alcohols **8** were also dehydrated. Addition of weaker acids (AcOH) had no effect upon the product distribution.

All cycloaddition ractions of nitroso-dienophiles **1** with the dienal mixture **3a**/**3b** were performed in EtOH solutions at temperatures which allowed rearrangement of the hemiacetalic cycloadducts *(Table 2)*. Pentadienal was used in one case to prepare a mitomycin reference compound.

The data collected in *Table 2* deserve some comment: *i)* *p*-Cl (d) and *p*-CH_3OCO (e) groups gave similar results, when compared to those obtained in the unsubstituted nitroso-benzene series. The other substituents led to smaller yields of the corresponding tricyclic products **8** and **9**. One notices, in particular, that a *p*-NH_2 group is sufficiently basic to orient the reaction towards the formation of betaine **6g** only. On the other hand, an *o*-Me group led to a decrease of the hetero-*Cope* rearrangement. *ii)* Introduction of a *m*-Me group may lead to two types of tricyclic products (Me–C(6) and/or Me–C(8)). Actually, only **8i**/**9i** and **8j**/**9j** were obtained, albeit in lower yields (obviously for statistical reasons). The other regioisomer was not formed, probably because of some steric interactions which would occur in the transition state of the hetero-*Cope* rearrangement. These results are of interest in view of the fact that mitomycins **10** bear a Me group at C(6).

Structural Analyses. – The unsubstituted products **6a–9a** are known compounds; their physical properties agree with those reported in the literature: [19–21] for **6a**, [22] for **7a**, [9], and [23] for **8a**, [8] for **9a**. Interestingly, the NMR data of **9a** proved to be strictly identical with those reported in [23]. The betain **6a** was synthesised independently according to [21] for identification purposes.

The other substituted products were all characterized by their NMR spectra; their substitution patterns could be easily established (see *Exper. Part: Tables 3, 4,* and *5*). As to the betaines **6**, their structure was established by analogy to the one of **6a**. Furthermore, $^1J(^{13}C,^{13}C)$ coupling constants, and $^{13}C,^{13}C$ isotope effects upon the chemical shifts of **9b** have already been measured [1], allowing the assignment of the exact sequence of the C-atoms.

Eventually, it should be noticed that the alcohols **8** are quite sensitive towards acids, due to their bis-benzylic nature. Therefore, their NMR spectra were recorded in C_6D_6.

Cascade Reactions. – Multistep reactions which occur in one-pot experiments are commonly encountered in organic synthesis. In some instances, though, the structure of the reaction products does not relate in a straightforward retrosynthetic manner to the educts, due to the occurrence of some rapid skeletal rearrangements along the non-stop reaction sequence.

We shall define *cascade reactions* as one-pot multistep processes in which at least one skeletal rearrangement is involved. In that respect, the *Fischer* indole synthesis is probably the oldest cascade reaction[3]): not even counting all the prototropies, the mechanism of the *Fischer* indole synthesis requires no less than five individual steps, the key-step being a hetero-*Cope* rearrangement [24]. A few reactions, similar to the *Fischer* indole synthesis, are already known [18]: they should also be called cascade reactions.

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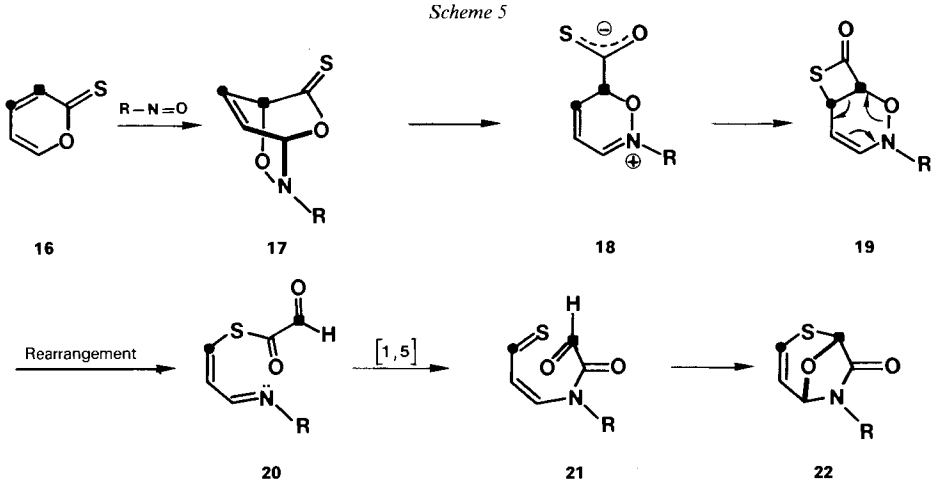
[3]) *Emil Fischer* discovered the indole synthesis in 1883 [24].

Scheme 5



In [25], we described the reaction of 2*H*-pyran-2-thione (**16**) and of some of its derivatives with nitroso-dienophiles which gave the 'adducts' **22** in good-to-excellent yields. Formation of these latter products led us to postulate and then to demonstrate, the essential features of the mechanism of this cascade reaction which consists of no less than six consecutive reaction steps *(Scheme 5)* [26]: *i)* a rate-determining regiospecific *Diels-Alder* cycloaddition leading to **17**; *ii)* formation of betaine **18** by a push-pull ring-opening mechanism; *iii)* ring-closure of **18** by an intramolecular nucleophilic 1,4-addition leading to the key intermediate **19**, which was isolated and characterised in a few cases, *e.g.* when R = CO_2Bn; *iv)* a *retro-Diels-Alder* reaction which is due *both* to the *specific positioning* of the double bond *and* to the *weak* N–O bond; *v)* a [1,5]-sigmatropic acyl migration from the S- to the N-atom, and *vi)* an intramolecular *hetero-Diels-Alder* cycloaddition[4]).

The above mentioned cascade reaction [25] was then subject of the 1983 'Reaction Mechanism Contest' organized at the Department of Chemistry of U.C.L.A. Among the proposed hypothetical mechanisms, the most plausible ones were published in 1988 [27]. In this contest, one of the proposed mechanisms came very close to the one we had described in 1985 (see *Scheme 1*) [26], compound **19** also being the key intermediate. Furthermore, this reaction sequence was used as a testing ground for some new software packages – for example *Ugi's* RAIN and PEMCD programs [27] [28], which have been developed to unravel complex reaction mechanisms.

Overall, these various non-stop cascading processes represent strongly exothermal reactions, as demonstrated, for example, in the above described reaction [26]. This is to say that an *energy cascade* is operating along the reaction sequence, the final reaction products being particularly stable. An energy cascade is also operating in the cascade reaction which is described herein. With respect to educts **4** or **5**, products **6**–**9** all bear an additional aromatic ring; therefore, they are much more stable than the primary *Diels-Alder* adducts from which they are derived.

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[4]) This cascade-reaction sequence seems to be of relatively broad scope [26]. For the sake of clarity, various substitution patterns have been omitted and replaced by a didactic labelling (dots and squares) in *Scheme 5*.

The support of the *Centre National de la Recherche Scientifique* (URA-135), and of the *Ministère de la Recherche et de la Technologie* (PhD – grant to D.S.) is gratefully acknowledged. We wish to thank Prof. *T. Gilchrist,* University of Liverpool for having prepared compounds **6f**–**9f** during his sabbatical leave as the 1986 Emilio Noelting visiting professor in Mulhouse, and Prof. *H. Fritz, Ciba-Geigy,* Basle, for some high-field NMR measurements.

Experimental Part

General. Flash chromatography (FC) [29]: silica gel (*Merck 60;* 230–400 mesh). TLC: Al roll silica gel (*Merck 60 F_{254}*). M.p.: *Kofler* hot bench or *Büchi SMP 20* apparatus; corrected. IR spectra (cm^{-1}): *Perkin-Elmer 157-G.* ^1H- and ^{13}C-NMR spectra: *Varian T 60, Bruker WP-80-DS, WH-360,* and *WM-400* using double irradiation techniques; TMS (^1H-NMR) and $CDCl_3$ ($\delta(CDCl_3) = 77.00$ with respect to TMS; ^{13}C-NMR) as internal references; δ in ppm and J in Hz. High-resolution (HR) MS were measured on a *MAT-311* spectrometer at the University of Rennes. Microanalyses were carried out by the Service Central de Microanalyses of the CNRS, Vernaison, and by the Service de Microanalyses of the Institut de Chimie of the Louis Pasteur University, Strasbourg.

Starting Materials. Nitrosobenzene and 2-nitrosotoluene were purchased from *Aldrich;* 4-chloroaniline, 4-nitroaniline, methyl 4-aminobenzoate, and *o*-cresol from *Fluka;* hexadienal mixture **3a**/**3b** was purchased from *Aldrich* and from *Lancaster Synthesis.* (*E*)-penta-2,4-dienal (**1a**) was prepared according to [30]; acetotoluidine was prepared from *m*-toluidine according to [31]. Anh. EtOH was purified by distillation over Mg/I_2.

Arylnitroso Dienophiles. – *Preparation of a Soln. of AcOOH According to* [32]. To a stirred soln. of conc. H_2SO_4 (0.3 g) in AcOH (30 g), 85% H_2O_2 (30 g) was added dropwise at 25–30°. According to ^1H-NMR, the equilibrium between the two species was reached after 1 d (AcOOH 60%, AcOH 40%; the Me signal of AcOOH is deshielded by 0.02 ppm with respect to that of AcOH). H_2SO_4 contained in this soln. was then neutralized with $AcONa \cdot 3\,H_2O$ (1.5 g), and the resulting mixture was ready for the ensuing oxidation purposes.

1-Nitro-4-nitrosobenzene (**1c**; according to [33])[5]. To a stirred suspension of *S,S*-dimethyl-*N*-(*p*-nitrophenyl)sulfinimine (5 g, 25 mmol) [33] in MeOH (100 ml) at 0°, the oxidizing mixture (15.1 g, 76 mmol) was added. The sulfinimine rapidly dissolved, and the yellow-green nitroso derivative precipitated. After 1 h, it was filtered off and washed twice with MeOH leading to a crude product (**1c** 85%, sulfoximine 15%) which was recrystallised in MeOH (60 ml) to give pure **1c** (2.2 g, 57%). M.p. 128–130° ([33]: 118–120°). IR (KBr): 3100, 3090, 1615, 1525, 1350, 1260, 1110, 875, 865, 815, 750, 688. ^1H-NMR ($CDCl_3$, 60 MHz): 8.03 (*d*, $J = 9$, H–C(3), H–C(5)); 8.46 (*d*, $J = 9$, H–C(2), H–C(6)).

1-Chloro-4-nitrosobenzene (**1d**) was prepared according to [34]. To a stirred soln. of *p*-chloroaniline (5.0 g, 39 mmol) in MeOH (20 ml) at 0° were added successively aq. Na_2CO_3 (1M, 45 ml), aq. $NaHCO_3$ (1M, 53 ml) and thence the oxidising mixture (17.1 g, 86 mmol of AcOOH) whereby a colourless product precipitated which turned gradually green and then yellow-brown. After 2 h, it was filtered off, washed twice with H_2O, and twice with cold i-PrOH leading to crude yellow-brown crystals (4.8 g, 86%) which contained some (dichloroazoxy)benzene. Recrystallisation from EtOH (100 ml) gave **1d** as cream-coloured crystals (3.8 g, 68% containing some of the corresponding azoxy compound (*ca.* 5%)). M.p. 130–140° (dec.; [36]: 92–93°). IR (KBr): 1580, 1480, 1255, 1090, 855, 820, 810. ^1H-NMR ($CDCl_3$, 60 MHz): 7.56 (*d*, $J = 9$, H–C(3), H–C(5)); 7.82 (*d*, $J = 9$, H–C(2), H–C(6)).

Methyl 4-nitrosobenzoate (**1e**) was prepared according to [37] and purified, in 40% yield, by recrystallisation in AcOEt. M.p. 130° ([37]: 126–127°; [38]: 128–129.5°). IR (KBr): 3060, 2950, 1725, 1600, 1440, 1415, 1260, 1110, 870, 765, 690. ^1H-NMR ($CDCl_3$, 60 MHz): 4.00 (*s*, MeO); 7.93 (*d*, $J = 8$, H–C(2), H–C(6)); 8.33 (*d*, $J = 8$, H–C(3), H–C(5)).

4-Nitrosoanisole (**1f**). 4-Nitrosophenol was prepared according to [39] and purified, in 79% yield, according to [40]. M.p.: 157–160° ([39]: 135–137°). IR (KBr): 3180, 3060, 2860, 1625, 1555, 1445, 1360, 1155, 1030, 860, 795. ^1H-NMR ($CDCl_3/CD_3OD$ 9:1, 60 MHz): 4.75 (*s*, OH); 6.55 (*d*, $J = 10$, H–C(2), H–C(6)); 7.58 (*d*, $J = 10$, H–C(3), H–C(5)).

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[5]) 4-Nitroaniline, when oxidized according to *'d'Ans'* procedure led to a mixture of *p*-nitroso and *p*-nitro derivatives [34] [35].

Compound **1f** was prepared, in 75% yield, from 4-nitrosophenol according to [41] as emerald-green crystals[6]). M.p. *ca.* 22° (hexane) ([42] [43]: 22.5–23°). IR (CCl_4): 2960, 2840, 1600, 1585, 1505, 1455, 1415, 1265, 1110, 1030. ^{1}H-NMR (CCl_4, 60 MHz): 3.90 (*s*, MeO); 6.93 (*d*, J = 9, H–C(2), H–C(6)); 7.78 (*d*, J = 9, H–C(3), H–C(5)).

1-Chloro-2-methyl-4-nitrosobenzene (**1i**). 4-Chloro-3-methylaniline was prepared, in 60% yield, by chlorination of *m*-acetyltoluidine according to [44]. M.p. 84–85° (cyclohexane) ([44]: 83°). IR (KBr): 3410, 3320, 1630, 1470, 1450, 1310, 1260, 1180, 1045, 870, 820, 690, 635, 570. ^{1}H-NMR ($CDCl_3$, 60 MHz): 2.27 (*s*, Me); 6.50 (*m*, 2 arom. H); 7.05 (*d*, J = 8, H–C(5)); 3.5 (br. *s*, NH_2). Compound **1i** was prepared, in 70% yield, from 4-chloro-3-methylaniline in a similar way as **1d** in colourless crystals. M.p. 73–74° (EtOH). IR (KBr): 3090, 1580, 1475, 1290, 1245, 1135, 1050, 880, 825, 770. ^{1}H-NMR ($CDCl_3$, 60 MHz): 2.53 (*s*, Me); 7.61 (*s*, H–C(5), H–C(6)), 7.79 (*s*, H–C(2)). Anal. calc. for C_7H_6ClNO (155.58): C 54.04, H 3.88, N 9.00, Cl 22.78; found: C 53.8, H 3.7, N 8.9, Cl 22.3.

2-Methyl-4-nitrosoanisole (**1j**). 4-Nitroso-*o*-cresol (mono-oxime of 3-methyl-*p*-benzoquinone) was prepared, in 64% yield, from *o*-cresol according to [45] as brown crystals. M.p. 135° ([45]: 134°). IR (KBr): 3160, 3050, 1630, 1595, 1422, 1340, 1315, 1020, 980. ^{1}H-NMR ($CDCl_3/D_2O$, 80 MHz; (*Z*)- and (*E*)-oximes): 7.75 (*dd*, H–C(6), minor); 7.64 (*m*, H–C(2), major); 7.17 (*dd*, H–C(6), major); 7.05 (*m*, H–C(2), minor); 6.48 (*d*, H–C(5)); 2.07 (*d*, Me–C(3) major); 2.03 (*d*, Me–C(3), minor) (J(2,Me) = 1.4; J(2,6) = 2.6; J(5,6) = 10.0).

Compound **1j** was prepared using a method similar to that for **1f**. Compound **1j** formed as green crystals which were washed with chilled hexane and dried (35%). M.p. 52–53° ([42]: 53.5°). IR (CCl_4): 2960, 2940, 2840, 1605, 1490, 1440, 1400, 1260, 1250, 1200, 1085, 1030. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.27 (*s*, Me–C(2)); 3.98 (*s*, MeO); 7.01 (*d*, H–C(6)); 7.40 (*d*, H–C(3)); 8.17 (*dd*, H–C(5)) (J(3,Me) = 0.8; J(3,5) = 2.2; J(5,6) = 8.7).

Cycloadducts. – *6r-(Dimethoxymethyl)-3c-methyl-2-phenyl-3,6-dihydro-2H-[1,2]oxazine* (**12**) *and its* trans-*Isomer* **13**. To a stirred soln. of the *6,6-Dimethoxyhexa-2,4-diens* (**14**/**15**) [13] (0.643 g, 4.55 mmol) in $CHCl_3$ (7 ml), nitrosobenzene (0.532 g, 4.97 mmol) was added at r.t. After 2 d, the solvent was evaporated and the crude residue purified by FC (AcOEt/cyclohexane 3:7): colourless oil (0.923 g, 82%). Separation of **12** and **13** required several FC.

Major oxazine **12**: colourless oil. IR (CCl_4): 2930, 2830, 1600, 1490, 1135, 1070. ^{1}H-NMR: *Table 1*. HR-MS: 249.1359 ($C_{14}H_{19}NO_3$, M^+; calc. 249.1365).

Minor oxazine **13**: colourless oil. IR ($CHCl_3$): 2930, 2835, 1595, 1490, 1185, 1125, 1070. ^{1}H-NMR: see *Table 1*.

(Ethoxy)[3c-methyl-2-(p-nitrophenyl)-3,6-dihydro-2H-[1,2]oxazin-6r-yl]methyl Acetate. To a stirred soln. of **1c** (0.943 g, 6.2 mmol) in $CHCl_3$ (12.5 ml) and EtOH (0.9 ml, 15.6 mmol), the hexa-2,4-dienal mixture **3a**/**3b** (0.55 ml, 5.2 mmol) was added at r.t. under Ar. The soln., which was initially green, turned to orange-brown. After 30 min, the hemiacetal **5c** had formed quantitatively (^{1}H-NMR). After 1 h, Ac_2O (2.95 ml, 31.2 mmol) and pyridine (2.5 ml, 31.2 mmol) were added at r.t. After one night, the reaction mixture was evaporated to dryness and the residue treated with EtOH and toluene. The black mixture (1.87 g) was separated by FC (CH_2Cl_2) which led successively to the dinitroazoxybenzene (54 mg, 6%) and to **11** (0.489 g, 28%) which, according to ^{1}H-NMR, is a 60:40 mixture of 2 diastereoisomers. IR (CCl_4): 2980, 1750, 1600, 1515, 1340, 1235. ^{1}H-NMR: *Table 1*. HR-MS: 336.1322 ($C_{16}H_{20}N_2O_6$, M^+; calc. 336.1321).

Cycloadditions of Dienals 2 and 3a/3b with Nitroso-arene Dienophiles 1 and their Cascade-Reaction Products. – *General Procedure*. To a stirred soln. of the dienals **2** or **3a**/**3b** (5 mmol) in abs. EtOH (75 ml), the nitrosodienophiles **1** (5 mmol) were added under Ar at 45 to 50°. The duration of the reaction varies between 2 and 4 d, the soln. becoming gradually colourless. The soln. was then evaporated to near dryness and filtered in AcOEt over silica gel. The very polar betaines **6**, being strongly adsorbed, were eluted with MeOH and recrystallised in toluene. The reaction products, which are contained in AcOEt, were separated by FC leading to the pyrrolo-indoles **8**/**9** and to the pyrrole-carbaldehydes 7. When the alcohols **8** could be crystallised, they were filtered off and their mother liquors oxidised with MnO_2 (100 mg) in acetone (5 ml), leading to the more stable ketones **9** which can easily be purified.

Reaction of Penta-1,3-dienal (**2**) *with* **1a**. General procedure using **2** (0.410 g, 5.00 mmol) and **1a** (0.535 g, 5.00 mmol), in EtOH (75 ml), 3 d at 35–40°. After filtration over silica gel, betaine **6a** (0.412 g, 48%) was obtained as a viscous oil which proved difficult to crystallise. The remaining reaction mixture was separated by FC (AcOEt/cyclohexane 2:8) leading successively to: **7a** (11 mg, 1%) as an oil which was purified by prep. TLC (CH_2Cl_2); **8a** (0.237 g, 28%) which was crystallised in toluene. The mother liquors were treated with MnO_2 in acetone for 2 d at r.t. leading to **9a** (78 mg, 9%) which was purified by sublimation (90°, 1 Torr).

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[6]) In our hands, *Hodgson*'s method [42] failed when applied for the synthesis by direct nitrosation of 2-methylanisole.

1-Phenylpyrrole-2-carbaldehyde (**7a**). Cream-coloured crystals. M.p. 25–28° ([22]: 27–30°). IR (CCl_4): 2800, 2730, 1680, 1600, 1530, 1500, 1470, 1455, 1420, 1370, 1335, 1095, 1040, 695. ^{1}H-NMR: *Table 3*.

Table 3. *^{1}H-NMR Spectral Data* (80 MHz, $CDCl_3$) *of Pyrrole-2-carbaldehydes* **7a**–**7f** *and* **7h**–**7j** (300 K, δ in ppm and J in Hz, internal standard TMS)

	H–C(3)	H–C(4)	R–C(5)	CHO	arom. H			*p*-MeO	*m*-Me	*J*(3,4)	*J*(4, *R*–C(5))
					ortho	*meta*	*para*				
7a[a])	7.06	6.40	7.15	9.57		7.40		–	–	3.9	2.6
7b	7.04	6.16	2.09	9.31	7.25	7.47	–	–	–	4.1	0.5
7c[b])	7.04	6.23	2.11	9.40	7.41	8.33	–	–	–	3.9	0.7
7d[c])	7.01	6.17	2.08	9.35	7.18	7.44	–	–	–	3.9	0.7
7f	7.04	6.15	2.08	9.31	7.18	6.97	–	3.87	–	4.4	0.6
7h	7.06	6.20	2.00	9.30		7.32		–	1.95[d])	4.0	0.4
7i[b])	7.02	6.15	2.08	9.33	*ca.* 7.1	7.43	–	–	2.42	3.9	0.7
7j	7.03	6.14	2.09	9.30		7.10	–	3.89	2.25	4.2	0.4

[a]) J(5,*CH*O) = 0.6; J(3,5) = 1.7.
[b]) J(3,*Me*–C(5)) = 0.4.
[c]) J(3,*Me*–C(4)) = 0.4.
[d]) *o*-Me.

9H-Pyrrolo[1,2-a]indol-9-ol (**8a**). Cream-coloured crystals. M.p. 120° (dec.; [9]: 116–118°). IR (KBr): 3360, 3110, 1615, 1600, 1490, 1470, 1450, 1305, 1260, 1175, 1160, 1070, 1015, 970, 835, 755,725, 705. ^{1}H-NMR: see *Table 4*.

Table 4. *^{1}H-NMR Spectral Data* (80 MHz, (D_6)Benzene) *of Pyrrolo-indolols* **8a**, **8b**, **8d**–**8f**, **8i**, *and* **8j** (300 K, δ in ppm and J in Hz, internal standard TMS)

	H–C(1)	H–C(2)	H–C(3)	H–C(5)	H–C(6)	H–C(7)	H–C(8)	H–C(9)	Me–C(3)	Me–C(6)	MeO–C(7)	MeOCO–C(7)	OH
8a	6.25	6.28	6.70	6.67	6.98	6.79	7.22	5.31	–	–	–	–	1.17
8b[a])	6.24	6.18	–		6.89		7.19	6.00	2.15	–	–	–	1.19
8c	6.23	5.92	–	6.63	7.94	–	8.27	5.38	2.06	–	–	–	[b])
8d	6.17	5.91	–	6.69	7.00	–	7.34	5.30	2.10	–	–	–	[b])
8e	6.19	5.93	–	6.80	8.05	–	8.22	5.34	2.06	–	–	3.55	[b])
8f	6.23	5.96	–	6.83	6.64	–	6.98	5.35	2.19	–	3.34	–	1.17
8i	6.17	5.96	–	7.18	–	–	7.28	5.24	2.13	2.18	–	–	[b])
8j	6.29	6.03	–	6.91	–	–	6.83	5.44	2.23	2.25	3.34	–	1.05

	J(1,2)	*J*(1,3)	*J*(1,9)	*J*(2,3)	*J*(5,6)	*J*(5,7)	*J*(5,8)	*J*(5,9)	*J*(6,7)	*J*(6,8)	*J*(6,9)	*J*(7,8)	*J*(8,9)	*J*(2,*Me*–C(3))
8a	3.4	1.2	1.1	3.4	7.4	1.6	0.9	0.4	7.3	1.7	0.4	6.9	0.8	–
8b[a])	3.4	–	1.2	–	[b])	[b])	[b])	[b])	[b])	[b])	[b])	[b])	[b])	0.9
8c[c])	3.3	–	1.4	–	8.6	–	0.4	0.4	–	2.3	0.5	–	0.9	1.0
8d[c])	3.3	–	1.3	–	8.3	–	0.5	0.3	–	2.1	0.5	–	0.8	1.0
8e	3.3	–	1.2	–	8.2	–	0.3	[b])	–	1.8	[b])	–	1.0	0.9
8f	3.3	–	1.0	–	8.6	–	0.5	[b])	–	2.6	[b])	–	0.5	0.8
8i[d])	3.3	–	1.2	–	–	–	0.4	0.5	–	–	–	–	0.6	1.0
8j[e])	3.4	–	1.4	–	–	–	[b])	[b])	–	–	–	–	[b])	1.0

[a]) Measured in $CDCl_3$.
[b]) Not determined.
[c]) J(1,*Me*–C(3)) = 0.4; J(9,*Me*–C(3)) = 0.8.
[d]) J(1,*Me*–C(3)) = 0.4; J(9,*Me*–C(3)) = 0.8; J(5,*Me*–C(6)) = 0.6; J(8,*Me*–C(6)) = 0.4.
[e]) J(1,*Me*–C(3)) = 0.4; J(5,*Me*–C(6)) = 0.6.

9H-Pyrrolo[1,2-a]indol-9-one (**9a**). Yellow crystals. M.p. 119–120° (by sublimation; [9]: 122–122.5° (EtOH)). IR (KBr): 1708, 1700, 1620, 1475, 1310, 1075, 870. ^{1}H-NMR: *Table 5*.

Table 5. *^{1}H-NMR Spectral Data* (80 MHz, $CDCl_3$) *of Pyrrolo-indolones* **9** (300 K, δ in ppm and J in Hz, internal standard TMS)

	H–C(1)	H–C(2)	H–C(3)	H–C(5)	H–C(6)	H–C(7)	H–C(8)	Me–C(3)	Me–C(6)	MeO–C(7)	Other groups
9a[a])	6.78	6.31	7.06	7.11	7.42	7.13	7.58	–	–	–	–
[b])	6.74	6.27	7.03	7.03	7.38	7.09	7.54	–	–	–	–
9b[a])	6.69	5.98	–	7.17	7.38	7.12	7.57	2.51	–	–	–
9c[a])	6.80	6.10	–	7.28	8.34	–	8.39	2.57	–	–	–
9d	6.69	6.00	–	7.07	7.33	–	7.49	2.48	–	–	–
9e	6.75	6.05	–	7.22	8.15	–	8.24	2.54	–	–	3.92 (MeOCO–C(7))
9f	6.67	5.93	–	7.06	6.86	–	7.14	2.47	–	3.81	–
9h	6.73	5.99	–	–	7.20	7.04	7.43	2.58	–	–	2.58 (Me–C(5))
9i	6.64	5.95	–	6.97	–	–	7.46	2.47	2.39	–	–
9j	6.64	5.89	–	6.94	–	–	7.07	2.26	2.47	3.84	–

	J(1,2)	J(1,3)	J(2,3)	J(5,6)	J(5,7)	J(5,8)	J(6,7)	J(6,8)	J(7,8)	J(1,*Me*–C(3))	J(2,*Me*–C(3))	Other data
9a[a])	3.7	0.8	2.6	7.8	0.8	0.7	7.7	1.3	7.4	–	–	–
[b])	3.8	[c])	2.6	7.9	[c])	[c])	7.7	[c])	7.5	–	–	–
9b	3.7	–	–	7.9	0.9	0.7	7.7	1.4	7.4	0.4	0.8	–
9c	3.7	–	–	8.7	–	0.5	–	2.3	–	0.6	0.9	–
9d	3.7	–	–	8.2	–	0.6	–	2.2	–	0.6	0.8	–
9e	3.8	–	–	8.2	–	0.8	–	1.8	–	0.4	0.9	–
9f	3.8	–	–	8.7	–	0.8	–	2.6	–	0.5	0.8	–
9h	3.8	–	–	–	–	–	7.3	2.0	7.0	–	0.4	–
9i	3.7	–	–	–	–	0.4	–	–	–	0.5	0.8	J(5,*Me*–C(6)) = 0.6 J(8,*Me*–C(6)) = 0.4
9j	3.7	–	–	–	–	–	–	–	–	0.6	1.0	J(5,*Me*–C(6)) = 0.6

[a]) Calculated values using the *Bruker*-PANIC program.
[b]) Literature data for **9a**, see [27].
[c]) Data not published.

N-Phenylpyridinio-3-olate (**6a**). Brownish crystals. M.p. 120–125° (dec.; [21]: 160° (dec.)). IR and NMR data were identical with those of an identical sample prepared according to [21]. IR ($CHCl_3$): 2960, 1580, 1560, 1505, 1490, 1415, 1385, 1005. ^{1}H-NMR (DMSO, 80 MHz): 7.10 (*ddd*, J = 8.6, 2.6, 1.4, 1 arom. H); 7.3–7.8 (*m*, 8 arom. H). HR-MS: 171.0674 ($C_{11}H_9NO$, $M^{+\cdot}$; calc. 171.0684).

Reaction of **3a**/**3b** *with* **1a**. General procedure using **3a**/**3b** (0.538 g, 5.60 mmol) and **1a** (0.601 g, 5.61 mmol) in EtOH (85 ml), 2 d at 45–50°. After filtration over silica gel, **6b** (0.103 g, 10%) was obtained as a viscous oil which crystallised slowly; its brownish crystals were washed with AcOEt. The other reaction products were separated by FC (AcOEt/cyclohexane 1/9) in the following order: **7b** (10 mg, 1%) as a viscous oil which was purified by prep. TLC (CH_2Cl_2); **8b** and **9b** as a mixture from which **8b** (0.365 g, 35%) crystallised in toluene. The mother liquors were treated with MnO_2 in acetone for 2 d at r.t. and **9b** (0.111 g, 11%) was obtained as yellow crystals after sublimation (90°, 1 Torr).

5-Methyl-1-phenylpyrrole-2-carbaldehyde (**7b**). Cream-coloured crystals. M.p. 93–94° (cyclohexane). IR ($CHCl_3$): 1655, 1600, 1495, 1480, 1040. ^{1}H-NMR: *Table 3*. HR-MS: 185.0837 ($C_{12}H_{11}NO$, $M^{+\cdot}$; calc. 185.0839).

3-Methyl-9H-pyrrolo[1,2-a]indol-9-ol (**8b**). Cream-coloured crystals. M.p. 158–160° (toluene). IR (KBr): 3360, 1615, 1600, 1485, 1410, 1310, 1070, 765, 750, 730. ^{1}H-NMR: *Table 4*. HR-MS: 185.0836 ($C_{12}H_{11}NO$, $M^{+\cdot}$; calc. 185.0840).

3-Methyl-9H-pyrrolo[1,2-a]indol-9-one (**9b**). Yellow crystals. M.p. 123.5–124° (i-PrOH or AcOEt/cyclohexane). IR (KBr): 1690, 1615, 1500, 1465, 1450, 1405, 1355, 1310, 775, 750, 700. UV (EtOH): 405 (1170), 336 (10700), 290 (6800), 285 (6700), 280 (7500), 250 (22000), 245 (20000), 215 (9500). ^{1}H-NMR: *Table 5*. ^{13}C-NMR: see [1]. Anal. calc. for $C_{12}H_9NO$ (183.20): C 78.67, H 4.95, N 7.65; found: C 78.9, H 5.0, N 7.7.

*6-Methyl-*N*-phenylpyridinio-3-olate* (**6b**). Brownish crystals. M.p. 180° (dec., AcOEt). IR ($CHCl_3$). 2960, 1595, 1540, 1515, 1380. ^{1}H-NMR (C_6D_6/CD_3OD 9:1, 80 MHz): 1.34 (*s*, Me–C(6)); 6.48 (*m*, 3 arom. H); 6.92 (*m*, 3 arom. H); 7.51 (*m*, 2 arom. H). HR-MS: 185.0837 ($C_{12}H_{11}NO$, $M^{+\cdot}$; calc. 185.0841).

Reaction of **3a**/**3b** *with* **1c**. General procedure using **3a**/**3b** (0.673 g, 7 mmol) and **1c** (1.281 g, 8.42 mmol) in EtOH (120 ml) 7 d at 45–50°. After filtration over silica gel, **6c** (0.595 g, 37%) was obtained as a brown oil. The remaining mixture was treated with MnO_2 (1.483 g) in acetone (50 ml) for 7 d at r.t. After filtration and evaporation of the solvent, **9c** was crystallised and washed with cold acetone/Et_2O: 0.382 g (24%). The mother liquors were separated by prep. TLC (CH_2Cl_2) leading successively to 4,4′-dinitroazoxybenzene (44 mg, 4%); remaining **9c** (17 mg, 1%), **7c** (0.114 g, 6%), and remaining **8c** (37 mg, 2%).

*5-Methyl-1-(*p*-nitrophenyl)pyrrole-2-carbaldehyde* (**7c**). Deep-yellow crystals. M.p. 118° (iPr_2O). IR ($CHCl_3$): 1660, 1605, 1525, 1490, 1425, 1355, 1120, 1045, 865. ^{1}H-NMR: *Table 3*. HR-MS: 230.0712 ($C_{12}H_{10}N_2O_3$, $M^{+\cdot}$; calc. 230.0691).

*3-Methyl-7-nitro-9*H*-pyrrolo[1,2-a]indol-9-ol* (**8c**). Not purified (too small amounts; see the corresponding ketone **9c**). IR ($CHCl_3$): 3580, 3010, 2980, 1625, 1610, 1520, 1485, 1415, 1340, 1295, 1090, 835. ^{1}H-NMR: *Table 4*.

*3-Methyl-7-nitro-9*H*-pyrrolo[1,2-a]indol-9-one* (**9c**). Yellow crystals. M.p. 228–230° (acetone/iPr_2O). IR (KBr): 3110, 1695, 1620, 1605, 1515, 1505, 1335, 1290, 1070, 845, 775. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{12}H_8N_2O_3$ (228.21): C 63.16, H 3.53, N 12.28; found: C 63.30, H 3.5, N 11.9.

*6-Methyl-*N*-(*p*-nitrophenyl)pyridinio-3-olate* (**6c**). Ochre crystals. M.p. 196–198° (i-PrOH/(i-Pr)$_2$O). IR (KBr): 3400, 1590, 1515, 1340. ^{1}H-NMR ($CDCl_3$, 60 MHz): 2.18 (*s*, Me–C(6)); 7.0–7.4 (*m*, 3 arom. H); 7.61 (*d*, $J = 9$, H–C(2), H–C(6) of Ph); 8.51 (*d*, $J = 9$, H–C(3), H–C(5) of Ph). MS and HR-MS: without any significance due to strong decomposition.

Reaction of **3a**/**3b** *with* **1d**. General procedure using **3a**/**3b** (0.673 g, 7 mmol) and **1d** (1.250 g, 8.8 mmol) in EtOH (130 ml), 4 d at 45–50°. After filtration over silica gel, **6d** was obtained as a black resinous compound which proved difficult to crystallise (0.67 g, 44%). The remaining reaction mixture was separated by FC (AcOEt/cyclohexane 3:7) leading to 4,4′-dichloroazoxybenzene (0.234 g, impure), **8d** (0.502 g, 33%) which crystallised (benzene/cyclohexane), and a mixture of products, containing **9d**, which was treated with MnO_2 (0.425 g) in acetone (15 ml) for 6 d at r.t. After filtration and evaporation of the solvent, **9d** was isolated and recrystallised (0.192 g, 13%). The mother liquors were separated by prep. TLC (CH_2Cl_2) leading to some additional **9d** (18 mg, 1%) and **7d** (17 mg, 1%).

4,4′-Dichloroazoxybenzene. Cream-coloured needles. M.p. 144° ([46]: 158°), which were identified with an authentic sample. IR (KBr): 2930, 2860, 1585, 1480, 1465, 1090, 1010, 830, 665, 520. ^{1}H-NMR ($CDCl_3$, 60 MHz): 7.43 (*d*, 2 *o*-H); 7.47 (*d*, 2 *o*-H); 8.15 (*d*, 2 *m*-H); 8.25 (*d*, 2 *m*-H) ($J(o\text{-H}, m\text{-H}) = 9$).

*1-(*p*-Chlorophenyl)-5-methylpyrrole-2-carbaldehyde* (**7d**). Resin. IR (CCl_4): 1670, 1495, 1100. ^{1}H-NMR: see *Table 3*. MS: 219 (62), 218 (28), 208 (10), 190 (11), 183 (13), 154 (18), 129 (18), 127 (36), 112 (13), 110 (21), 107 (100), 99 (12), 97 (33), 78 (21), 75 (30). HR-MS: 219.0433 ($C_{12}H_{10}{}^{35}ClNO$, $M^{+\cdot}$; calc. 219.0451).

*7-Chloro-3-methyl-9*H*-pyrrolo[1,2-a]indol-9-ol* (**8d**). Cream-coloured crystals. M.p. 100–101° (benzene/cyclohexane 1:2). IR (KBr): 3290, 2900, 1605, 1475, 1440, 1400, 1165, 1070, 1050, 1000, 980, 965, 795, 755. ^{1}H-NMR: *Table 4*. HR-MS: 219.0426 ($C_{12}H_{10}{}^{35}ClNO$, $M^{+\cdot}$; calc. 219.0451). Anal. calc. for $C_{12}H_{10}ClNO$ (219,67): C 65.61, H 4.58, N 6.37, Cl 16.14; found: C 65.1, H 4.4, N 6.2, Cl 16.0.

*7-Chloro-3-methyl-9*H*-pyrrolo[1,2-a]indol-9-one* (**9d**). Yellow crystals. M.p. 148° (iPr_2O). IR (KBr): 1690, 1605, 1500, 1450, 1400, 1275, 835, 765, 750. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{12}H_8ClNO$ (217.66): C 66.22, H 3.70, N 6.44, Cl 16.29; found: C 65.9, H 3.8, N 6.5, Cl 16.4.

N-(*p*-*Chlorophenyl*)-*6-methylpyridinio-3-olate* (**6d**). Ochre crystals. M.p. 187° (i-PrOH/(i-Pr)$_2$O). IR (KBr): 3410, 1590, 1510, 1485, 1380, 1355, 1090. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.10 (*s*, Me); 7.0–7.6 (*m*, 7 arom. H). HR-MS: 219.0482 ($C_{12}H_{10}{}^{35}ClNO$, $M^{+\cdot}$; calc. 219.04508).

Reaction of **3a**/**3b** *with* **1e**. General procedure using **3a**/**3b** (0.538 g, 5.60 mmol) and **1e** (0.928 g, 5.62 mmol) in EtOH (85 ml), 4 d at 45°. After filtration over silica gel, **6e** crystallised (0.230 g, 17%) and was washed with AcOEt. The remaining products were taken up in Et_2O. From the resulting soln., **8e** crystallised (0.385 g, 29%). The mother liquors were separated by FC (AcOEt/cyclohexane 3:7) leading successively to dimethyl 4,4′-azoxydibenzoate (40 mg, 2%), **8e**, part of which crystallised in Et_2O (85 mg, 6%). The mother liquors were evapored and then treated with MnO_2 in acetone for 2 d at r.t. leading to **9e** (0.205 g, 15%).

Dimethyl 4,4′-Azoxydibenzoate. Cream-coloured crystals. M.p. 203–205° ([47]: 207°). IR (KBr): 2960, 1730, 1600, 1460, 1440, 1410, 1280, 1110, 1010, 770, 690. ^{1}H-NMR ($CDCl_3$, 60 MHz): 8.37 (*d*, $J = 9$, arom. H); 8.15 (*d*, $J = 9$, arom. H); 8.15 (*s*, 4 arom. H); 3.97 (*s*, CO_2Me); 3.95 (*s*, CO_2Me).

*Methyl 9-Hydroxy-3-methyl-9*H*-pyrrolo[1,2-a]indol-7-carboxylate* (**8e**). Cream-coloured crystals. M.p. 142–143° (CH_2Cl_2/cyclohexane). IR (KBr): 3430, 1685, 1620, 1490, 1445, 1410, 1290, 1070, 765. ^{1}H-NMR: *Table 4*. Anal. calc. for $C_{14}H_{13}NO_3$ (243.25): C 69.12, H 5.39, N 5.76; found: C 69.0, H 5.2, N 5.7.

*Methyl 3-Methyl-9-oxo-9*H*-pyrrolo[1,2-a]indole-7-carboxylate* (**9e**). Yellow crystals. M.p. 171–172° (Et_2O/cyclohexane). IR (KBr): 3100, 2950, 1720, 1680, 1618, 1495, 1400, 1275, 1240, 1210, 1135, 980, 775, 705. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{14}H_{11}NO_3$ (241.24): C 69.70, H. 4.59, N 5.80; found: C 69.9, H 4.4, N 5.8.

N*[4-(Methoxycarbonyl)phenyl]-6-methylpyridinium-3-olate* (**6e**). Brown crystals. M.p. 190–193° (dec., AcOEt). IR (KBr): 3300, 1715, 1600, 1590, 1535, 1510, 1435, 1375, 1290. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.15 (*s*, Me–C(6)); 3.99 (*s*, CO_2Me); 7.35 (*m*, 5 arom. H); 8.27 (*d*, J = 8.8, *m*-H). HR-MS: 243.0900 ($C_{14}H_{13}NO_3$, M^+; calc. 243.0895).

Reaction of **3a**/**3b** *with* **1f**. General procedure using **3a**/**3b** (0.536 g, 5.57 mmol) and **1f** (0.779 g, 5.68 mmol) in EtOH (83 ml), 3 d at 45°. After filtration over silica gel, **6f** was obtained as a brown oil (0.680 g, 57%) which crystallised while standing in AcOEt. The remaining mixture was separated by FC (AcOEt/cyclohexane 3/7) leading successively to 4,4′-dimethoxyazoxybenzene (75 mg, 10%); **7f** which was purified by prep. TLC (CH_2Cl_2; 10 mg, 1%); **8f** which was crystallised in $(i\text{-}Pr)_2O$ (0.137 g, 11%). The mother liquors were evaporated and treated with MnO_2 in acetone for 2 d at r.t. leading to **9f** (0.173 g, 15%).

4,4′-Dimethoxyazoxybenzene. Cream-coloured crystals. M.p. 118° (toluene) ([48]: 118.6°). IR (KBr): 2940, 2830, 1590, 1495, 1250, 1150, 1020, 830. ^{1}H-NMR ($CDCl_3$; 60 MHz): 8.27 (*d*, J = 9, 2 *m*-H); 8.23 (*d*, J = 9, 2 *m*-H); 6.95 (*d*, J = 9, 2 *o*-H); 6.92 (*d*, J = 9, 2 *o*-H); 3.87 (*s*, 2 MeO).

N*-(4-Methoxyphenyl)-5-methylpyrrole-2-carbaldehyde* (**7f**). Colourless resin. IR (CCl_4): 3000, 2940, 2840, 2780, 1670, 1515, 1480, 1250, 1045, 835. ^{1}H-NMR: *Table 3*. HR-MS: 215.0946 ($C_{13}H_{13}NO_2$, M^+; calc. 215.0946).

*7-Methoxy-3-methyl-9*H*-pyrrolo[1,2-a]indol-9-ol* (**8f**). Cream-coloured crystals. M.p. 135° (toluene). IR (KBr): 3330, 3000, 2930, 2900, 2830, 1605, 1510, 1490, 1465, 1460, 1435, 1410, 1290, 1240, 1140, 1065. ^{1}H-NMR: *Table 4*. No elemental analysis (see anal. of **9f**).

*7-Methoxy-3-methyl-9*H*-pyrrolo[1,2-a]indol-9-one* (**9f**). Yellow crystals. M.p. 114° (AcOEt). IR (KBr): 3100, 2840, 1680, 1625, 1605, 1500, 1475, 1410, 1355, 1290, 1225, 1205, 1030, 1020, 1000, 810, 785, 760. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{13}H_{11}NO_2$ (213.23): C 73.22, H 5.20, N 6.57; found: C 73.3, H 5.0, N 6.5.

N*-(4-Methoxyphenyl)-6-methylpyridinio-3-olate* (**6f**). Ochre crystals. M.p. 169–172° (AcOEt). IR ($CHCl_3$): 2960, 2840, 1590, 1535, 1510, 1380, 1255, 835. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.14 (*s*, Me–C(6)); 3.89 (*s*, MeO); 7.0–7.4 (*m*, 7 arom. H). HR-MS: 215.0954 ($C_{13}H_{13}NO_2$, M^+; calc. 215.0946).

Reaction of **3a**/**3b** *with* **1g**. General procedure using **3a**/**3b** (86 mg, 0.9 mmol) and **1g** (135 mg, 0.9 mmol) in EtOH (13.5 ml) for 4 d at 50°. After filtration over silica gel, only **6g** was obtained as a brown oil which crystallised in AcOEt (0.120 g, 59%).

N*-[4-(Dimethylamino)phenyl]-6-methylpyridinio-3-olate* (**6g**). Ochre crystals. M.p. 245–250° (AcOEt). IR ($CHCl_3$): 2940, 2810, 1610, 1590, 1505, 1445, 1360, 1185, 1125, 840, 815. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.16 (*s*, Me–C(6)); 3.05 (*s*, Me_2N); 6.73 (*d*, J = 9.0, 2 *m*-H); 7.06 (*d*, J = 9.0, 2 *o*-H); 7.06 (*d*, J = 7.4, H–C(5)); 7.39 (*dd*, J = 7.4, 2.9, H–C(4)); 7.44 (*d*, J = 2.9, H–C(2)). HR-MS: 228.1255 ($C_{14}H_{16}N_2O$, M^+; calc. 228.1263).

Reaction of **3a**/**3b** *with* **1h**. General procedure using **3a**/**3b** (0.269 g, 2.81 mmol) and **1h** (0.340 g, 2.81 mmol) in EtOH (42 ml) for 2 d at 50°. After filtration over silica gel, **6h** was isolated as a brown oil and crystallised from AcOEt (0.198 g, 36%). The remaining mixture, which, according to ^{1}H-NMR, contained **3a**/**3b** (15%), was separated by FC (CH_2Cl_2) leading successively to 2,2′-dimethylazoxybenzene which was crystallised in pentane (90 mg, 15%); mixture of **3a**/**3b** and **7h** which was purified by prep. TLC (CH_2Cl_2; 10 mg, 1%); and **9h** which was crystallised in i-PrOH (52 mg, 10%).

2,2′-Dimethylazoxybenzene. Cream-coloured crystals. M.p. 58–59° (pentane) ([49]: 59–60°). IR (CCl_4): 3070, 2980, 2930, 1485, 1455, 1330, 910, 710. ^{1}H-NMR (CCl_4, 60 MHz): 2.35 (*s*, Me); 2.50 (*s*, Me); 7.15 (*m*, 6 arom. H); 7.57 (*m*, 1 arom. H); 8.10 (*m*, 1 arom. H).

*5-Methyl-*N*-(2-methylphenyl)pyrrole-2-carbaldehyde* (**7h**). Resin. IR (CCl_4): 1670, 1500, 1485, 1420, 1345, 1035. ^{1}H-NMR: *Table 3*. HR-MS: 199.0996 ($C_{13}H_{13}NO$, M^+; calc. 199.0997).

*3,5-Dimethyl-9*H*-pyrrolo[1,2-a]indol-9-one* (**9h**). Yellow crystals. M.p. 176–177° (EtOH). IR (KBr): 3060, 2980, 1675, 1600, 1550, 1485, 1405, 1380, 1330, 1285, 1020, 755. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{13}H_{11}NO$ (197.23): C 79.16, H 5.62, N 7.10; found: C 79.1, H 5.7, N 7.1.

*6-Methyl-*N*-(2-methylphenyl)pyridinio-3-olate* (**6h**). Ochre crystals (AcOEt). M.p. 80–86° (dec.). IR ($CHCl_3$): 2950, 1595, 1545, 1515, 1380. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.04 (*s*, Me); 2.07 (*s*, Me); 7.2–7.6 (*m*, 7 arom. H). HR-MS: 199.0995 ($C_{13}H_{13}NO$, M^+; calc. 199.0997).

Reaction of **3a**/**3b** *with* **1i**. General procedure using **3a**/**3b** (0.479 g, 5 mmol) and **1i** (0.926 g, 6 mmol) in EtOH (100 ml) for 2 d at 45–50°. After filtration over silica gel, **6i** was isolated as a black resin (0.694 g, 60%). From the remaining mixture, **8i** was crystallised (benzene; 0.230 g, 21%), and the other products were separated by prep. TLC (CH_2Cl_2) leading successively to 3,3′-dimethylazoxybenzene (93 mg, 9%), **9i** (42 mg, 4%), and **7i** (10 mg, 1%) which was purified by sublimation (100°, 1 Torr).

4,4'-Dichloro-3,3'-dimethylazoxybenzene. Ochre crystals. M.p. 130–131° (EtOH). IR (KBr): 2960, 2930, 1575, 1545, 1475, 1385, 1320, 1295, 1050, 885, 815. ^{1}H-NMR ($CDCl_3$, 60 MHz): 2.45 (*s*, Me); 2.48 (*s*, Me); 7.40 (*d*, J = 9, 2 arom. H); 8.05 (*m*, 4 arom. H). Anal. calc. for $C_{14}H_{12}Cl_2N_2O$ (295.17): C 56.97, H 4.10, N 9.49, Cl 24.02; found: C 56.7, H 4.1, N 9.3, Cl 23.9.

N-*(4-Chloro-3-methylphenyl)-5-methylpyrrole-2-carbaldehyde* (**7i**). Yellow crystals which contain 20% **9i**. IR ($CDCl_3$): 1655, 1480, 1425, 1345, 1045. ^{1}H-NMR: *Table 3*. HR-MS = 233.0607 ($C_{13}H_{12}NO^{35}Cl$, M^+; calc. 233.0607).

*7-Chloro-3,6-dimethyl-9*H*-pyrrolo[1,2-*a*]indol-9-ol* (**8i**). Cream-coloured crystalline needles. M.p. 146–147° (benzene). IR (KBr): 3460, 2860, 1620, 1480, 1420, 1315, 1255, 1065, 755. ^{1}H-NMR: *Table 4*. Anal. calc. for $C_{13}H_{12}ClNO$ (233.70): C 66.81, H 5.17, N 5.99, Cl 15.17; found: C 66.5, H 5.2, N 5.3, Cl 15.3.

*7-Chloro-3,6-dimethyl-9*H*-pyrrolo[1,2-*a*]indol-9-one* (**9i**). Yellow crystals. M.p. 203° (AcOEt/MeOH). IR (KBr): 1685, 1620, 1500, 1455, 1275, 1145, 760. ^{1}H-NMR: *Table 5*. HR-MS: 231.0452 ($C_{13}H_{10}NO^{35}Cl$, M^+; calc. 231.0451).

N-*(4-Chloro-3-methylphenyl)-6-methylpyridinio-3-olate* (**6i**). Resin. IR ($CHCl_3$): 2950, 1590, 1540, 1515, 1480, 1390, 1065. ^{1}H-NMR ($CDCl_3$, 80 MHz) = 7.50 (*d*, J = 8.2, 2 arom. H); 7.0–7.4 (*m*, 4 arom. H); 2.46 (*s*, Me–C(3')); 2.13 (*s*, Me–C(6)). HR-MS: 233.0610 ($C_{13}H_{12}NO^{35}Cl$, M^+; calc. 233.0607).

Reaction of **3a**/**3b** *with* **1j**. General procedure using **3a**/**3b** (0.546 g, 5.68 mmol) and **1j** (0.860 g, 5.69 mmol) in EtOH (85 ml) for 3 d at 45°. After filtration over silica gel, **6j** was isolated and washed with AcOEt (0.591 g, 45%). The remaining mixture was separated by FC (AcOEt/cyclohexane 2:8) leading successively to 4,4'-dimethoxy-3,3'-dimethylazoxybenzene (42 mg, 5%) which was separated from **1j** (0.1 g, 11%) by washing it out with cyclohexane; **9j** (42 mg, 3%) which was separated from **7j** by washing with iPr_2O; **7j** which was purified by prep. TLC (CH_2Cl_2) and crystallised in (i-Pr)$_2$O (10 mg, 1%); and **8j** (50 mg, 4%) which was washed with (i-Pr)$_2$O. After evaporation of the solvents, the mother liquors were treated with MnO_2 in acetone, leading to some additional **9j** (50 mg, 4%).

4,4'-Dimethoxy-3,3'-dimethylazoxybenzene. Yellow crystals. M.p. 134° (toluene/cyclohexane). IR (KBr): 2920, 1590, 1495, 1435, 1250, 1115, 1020, 885, 805. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.27 (*s*, 2 Me); 3.87 (*s*, 2 MeO); 6.85 (*d*, J = 9, 2 arom. H); 6.88 (*d*, J = 9, 2 arom. H); 8.0–8.3 (*m*, 4 arom. H). Anal. calc. for $C_{16}H_{18}N_2O_3$ (286.32): C 67.11, H 6.34, N 9.78; found: C 67.3, H 6.4, N 9.8.

N-*(4-Methoxy-3-methylphenyl)-5-methylpyrrole-2-carbaldehyde* (**7j**). Colourless crystals. M.p. 92–93° ((i-Pr)$_2$O). IR (KBr): 3100, 3000, 2960, 2930, 2840, 1675, 1640, 1610, 1500, 1480, 1460, 1420, 1315, 1255, 1135, 1030, 815, 770. ^{1}H-NMR: *Table 3*. HR-MS: 229.1104 ($C_{14}H_{15}NO_2$, M^+; calc. 229.1103).

*3,6-Dimethyl-7-methoxy-9*H*-pyrrolo[1,2-*a*]indol-9-ol* (**8j**). Colourless crystals. M.p. 147° ((i-Pr)$_2$O). IR (KBr): 3280, 2910, 2830, 1620, 1600, 1490, 1465, 1430, 1315, 1240, 1210, 1120, 1060, 1040, 985, 750, 740. ^{1}H-NMR: *Table 4*. No microanalysis.

*3,6-Dimethyl-7-methoxy-9*H*-pyrrolo[1,2-*a*]indol-9-one* (**9j**). Yellow crystals. M.p. 177–178° (AcOEt). IR (KBr): 3090, 3010, 2960, 2825, 1675, 1610, 1495, 1465, 1420, 1265, 1205, 1035, 1015, 770, 760. ^{1}H-NMR: *Table 5*. Anal. calc. for $C_{14}H_{13}NO_2$ (227.25): C 73.99, H 5.77, N 6.16; found: C 74.0, H 5.7, N 6.3.

N-*(4-Methoxy-3-methylphenyl)-6-methylpyridinio-3-olate* (**6j**). Ochre crystals. M.p. 86–90° (AcOEt). IR ($CHCl_3$): 2950, 1590, 1530, 1510, 1500, 1260. ^{1}H-NMR ($CDCl_3$, 80 MHz): 2.16 (*s*, Me); 2.27 (*s*, Me); 3.91 (*s*, MeO); 6.9–7.5 (*m*, 6 arom. H). HR-MS: 229.1104 ($C_{14}H_{15}NO_2$, M^+; calc. 229.1103).

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