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NOVEL HETEROCYCLIC SYSTEMS. PART 3.[1,2] THE FIRST DIPYRIDO-OXATHIIN, AND NEW ROUTES TO A DIPYRIDODIOXIN AND A DIPYRIDODITHIIN

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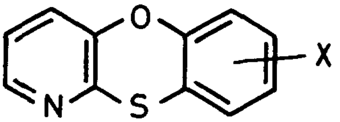
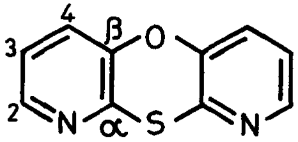
SUMMARY The first example of a dipyrido-oxathiin has been prepared, and a dipyridodithiin and a dipyridodioxin have been obtained by improved methods. Their spectroscopic properties are compared.

During some recent investigations in the pyridine series, we encountered small amounts of two isomeric compounds whose mass spectra suggested that they might be dipyrido-oxathiins. Unfortunately, we could find no examples of dipyrido-oxathiins in the literature; the closest analogues for comparison of spectroscopic properties were the monoazaphenoxathiins of type (I). We therefore decided to synthesize compound (II), [1,8-diaza-10-oxa-9-thia-9,10-dihydroanthracene], (1,9-diazaphenoxathiin). Such compounds are also of interest for their potential biological activity, since compounds of type (I) show central nervous system activity.[3]



(I)

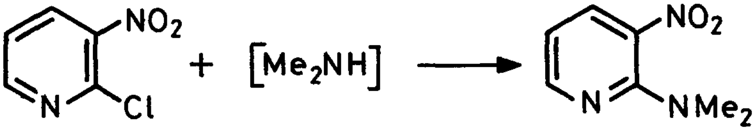


(II)

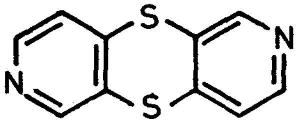
Compound (II) was synthesized as shown in equation (1), by a route similar to that developed for the monoaza analogues.[3] It was obtained in 31% yield as an off-white solid, mp 137 - 8°C (uncorrected). Its spectroscopic properties, particularly its ^{13}C n.m.r., confirmed the structure as (II). The pyridine ring of compounds of type (I) was used as a means to gauge the expected resonance positions of (II). The possibility that the isolated product was that derived by a Smiles rearrangement was ruled out by the ^{1}H n.m.r. data. The product showed only three separate proton signals, whereas the Smiles rearrangement product would show six.

(1)

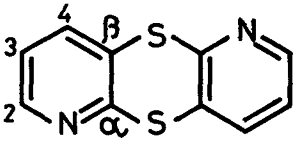
DMSO was used in reaction (1) after it had been found that using DMF, the Me_2NH produced by decomposition of the solvent gave rise to the yellow 2-(N-dimethylamino)-3-nitropyridine[4] (20% yield) as a by-product as follows:-



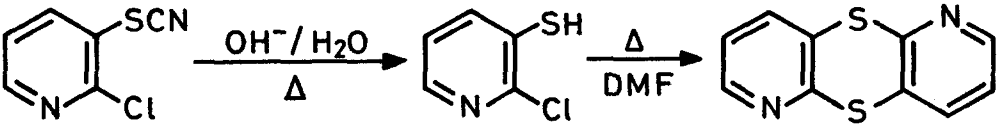
In order to be able to make reasonable extrapolations about the physical and spectroscopic properties of related heterocycles, we wished to have examples of a dipyridodithiin and a dipyridodioxin. The dipyridodithiin (III) was recently reported,[5] but it had the nitrogen atoms in positions other than adjacent to the ring fusions. 1,5-Diaza-9,10-dithia-9,10-dihydroanthracene (1,6-diazathianthrene] (IV), was therefore synthesized by the route shown in equation (2). (Compound IV has also been previously reported,[6] though obtained by an inconvenient route and in unstated yield. However, our spectral data for IV throw some doubt on the accuracy of the previous report of this compound - see below). In the present case, the product (IV) was obtained in 50% yield as a white, crystalline solid, mp 186 - 188°C (lit.[6] 183 - 185°C).



(III)

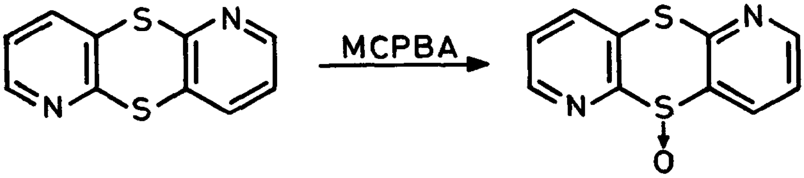


(IV)



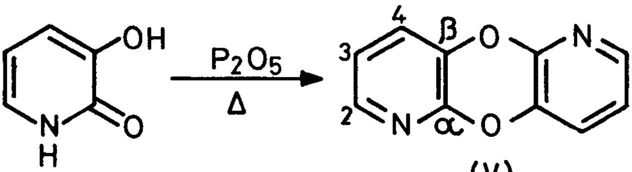
(2)

In order to confirm that the product was indeed (IV) and not the 1,9-diaza analogue which could conceivably result from rearrangement, a monosulphoxide was prepared (equation 3) by oxidation of (IV) with meta-chloroperbenzoic acid (MCPBA). The purified monosulphoxide showed the expected six proton signals in the ^1H n.m.r. spectrum, not the three signals expected for the 1,9-diaza isomer.



(3)

Finally, 1,5-diaza-9,10-dioxa-9,10-dihydroanthracene (1,6-diazaphenodioxin) (V) is a known compound, previously prepared by multistep procedures.[7,8] We were able to prepare it in 20% yield in a single step by treatment of commercially available 3-hydroxy-2-pyridone with phosphorus pentoxide (equation 4). The compound was identical in all respects with a sample of authentic material obtained from Dr. Weis.[7]



(V)

(4)

The spectral properties of the compounds (II), (IV) and (V) are recorded in Tables 1 and 2.

Table 1.

N.M.R. Properties of Diaza-9,10-dihetero-9,10-dihydroanthracenes

Compound[a]	^{13}C resonances (ppm)[b]					^{1}H resonances (ppm)[b]			^{1}H coupling constants (Hz)		
	C_2	C_3	C_4	C_α	C_β	H_2	H_3	H_4	$J_{2,3}$	$J_{3,4}$	$J_{2,4}$
(II)	145.2	123.7[c]	124.0[c]	146.6	142.9	8.10	7.01	7.13	4.5	8	2
(IV)	148.1	122.9	136.4	153.5	128.4	8.43	7.18	7.74	5	8	2
(V)	142.3	121.2	125.0	148.6	137.9	7.84	6.98	7.28	5	8	1.5

[a] Satisfactory analyses were obtained for all new compounds. [b] Relative to $Me_4Si=0(CDCl_3)$

[c] Resonances assigned arbitrarily, since two signals very close.

Table 2.

	u.v. spectra [λ_{max} nm (log ε)] in MeOH		
(II)	311 (3.97),	229 (4.23),	213 (4.30)
(IV)	300 (3.74),	255 (4.10),	225 (shoulder)
(V)	298 (4.13),	220 (shoulder),	209 (4.17)

The u.v. spectra of all three compounds show a similar, almost symmetrical band near 300 nm, but differ more markedly in the shorter wavelength region. On the basis of a comparison of the cmr spectra of (II), (IV) and (V) we favour the C_α and C_β assignments given in Table 1, which are in contrast to previously predicted values.[3] Finally, the mass spectra of the three compounds show significant similarities. All three show a substantial molecular ion, and a fragment ion corresponding to loss of CO (from II and V), or CS (from IV) supported by metastables. Compound (IV) also shows an ion corresponding to loss of a sulphur atom from the molecular ion. Other fragment ions are relatively small.

Although the melting point of the compound reported in the literature[6] to be (IV) corresponds reasonably well with that of our compound (IV), the u.v. and mass spectra differ significantly. Thus, the band at 300 nm in our compound (IV) was not reported for the literature compound. Neither was the loss of CS under electron impact mentioned, whereas the loss of two sulphur atoms appeared to be a significant mass spectral process,[6] although it was not for our compound. We can only assume that the literature compound either has a different structure, or is highly impure.

For the first time, examples of parent dipyrido-dithiins, -oxathiins, and -dioxins are available by simple synthetic procedures. We are currently attempting to extend the syntheses to substituted examples, and to other isomers of the systems reported herein.

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