Here H_Y appeared as a doublet at 5.75 ($J = 4.5$ Hz) and H_X as 6 lines at 4.72 derived by the superposition of 2 triplets centered at 281 and 285.5 Hz, respectively, belonging to the X part of an ABX system where $J_{AX} = J_{BX} = 6.5$ Hz. Double resonance experiments confirmed this interpretation since irradiation at 2.48 δ transformed H_X and H_Y into 2 doublets with $J_{XY} = J_{YX} = 4.5$ Hz; irradiation at 4.72 δ reduced H_Y to a singlet at 5.75 δ and irradiation at 5.75 δ transformed H_X into a triplet at 4.72 δ with $J_{AX} + J_{BX} = 13$ Hz.

Chromic oxidation of dihydrothermozymocin III in acetic acid followed by methylation with diazomethane in ethyl ether of the reaction mixture, allowed the isolation of the ketoester XI, ruling out the alternative formulation X for compound V.

The relative configuration of the asymmetric carbon atoms of thermozymocidin could not be resolved by NMR-methods as it has been demonstrated[5] that stereoisomeric γ-lactones do not show any significant differentiation in the coupling of their protons. The strong absorption at 965 cm^{-1} in the IR-spectrum of I, II, IV and V suggested a trans configuration of the double bond.

Riassunto. La termozimocidina è un antibiotico antifungino prodotto da una muffa termofila. Le sue caratteristiche IR, NMR e MS, insieme a quelle dei suoi derivati e dei suoi prodotti di ossidazione, indicano la struttura I.

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The Addition of Ethyl Azodicarboxylate to Pyrroles

Although the reactions of azodicarboxylic esters have been studied extensively[1–11] little is known of their addition to pyrroles[12] since only poorly characterised products were obtained in this study. In principle, the reaction of these esters with a pyrrole could proceed in three different ways: the azoester might attack the pyrrole nitrogen, a ring carbon atom or a side chain carbon atom. The present communication allows one to distinguish between these possible modes of attack.

It has been found that the free α- and β-positions in substituted pyrroles react with ethyl azodicarboxylate to give the corresponding dicarboethoxyhydrazino pyrrole. The conversion of these products into the corresponding benzene sulfonyl pyrrole hydrazines, in which the benzene sulfonyl hydrazine residue represent a blocking group of a free position which will not deactivate the ring, has not been realized.

The Table lists the various pyrroles used and the adducts formed[13]. In no case was a catalyst necessary. 2,4-Dimethyl (1) and 2,4-dimethyl-3-ethylpyrroles (2) react exothermally at room temperature in ether/*n*-pentane with ethyl azodicarboxylate at the α-position to give 1:1 adducts. 3-Methyl-4-ethylpyrrole (3) reacts at both α-positions to form a 2:1 adduct. 2,5-Dimethylpyrrole (4) reacts in one β position to give a 1:1 adduct. The above adducts are unstable and decompose on standing at room temperature. In contrast the adducts from the carbethoxypyrrole (5), and the acetylpyrrole (6) are stable at room temperature.

The structures assigned to the adducts are in all cases consistent with their NMR- and IR-spectra. Thus for example, the NMR-spectrum of (1) (Figure) in $CDCl_3$

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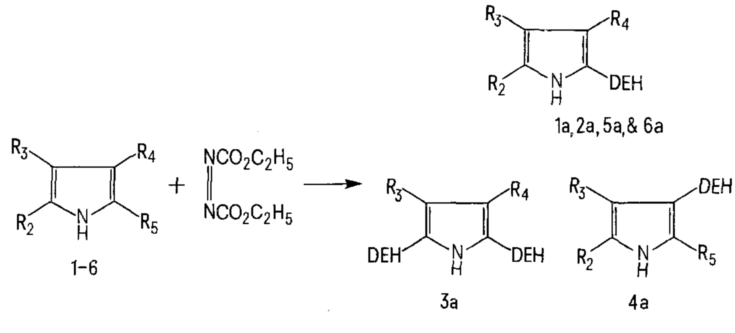

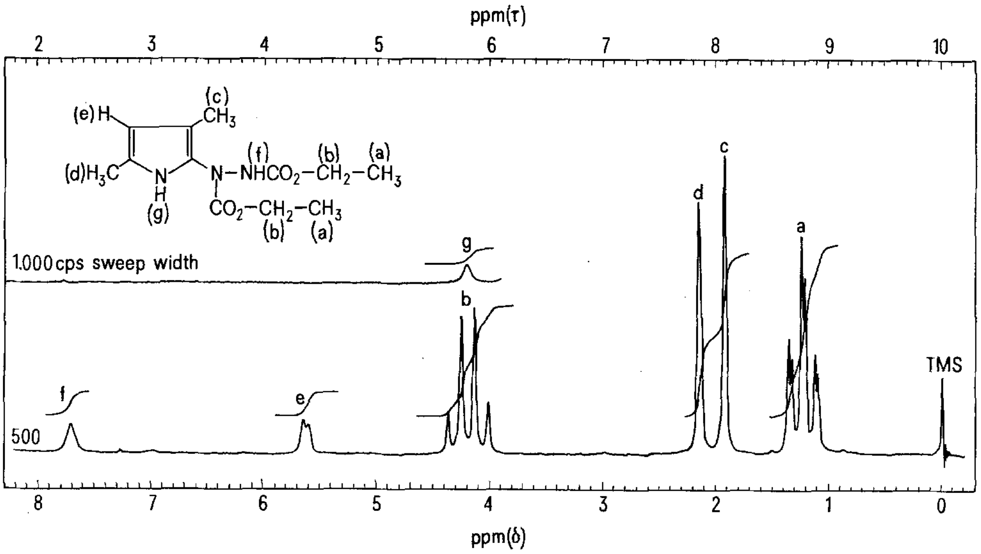

NMR-spectrum of 1 in $CDCl_3$

exhibits signals at 1.20 and 1.25 (triplets, 3H each, $-\underset{|}{N}-$ and $-N'H-CO_2CH_2\underline{CH_3}$) 1.9 and 2.15 (singlets, 3H each, β- and α-CH_3) 4.2 (quartet, 4H, $-\underset{|}{N}-$ and $N'H-CO_2\underline{CH_2}CH_3$) 5.65 (doublet, 1H, β-H) 7.7 (singlet, 1H, $-\underset{|}{N}-\underline{N'H}-CO_2C_2H_5$) and 8.4 ppm (singlet, 1H, N–H).

The IR-spectrum showed bands at 3340 cm^{-1} and 3236 cm^{-1} due to N–H and at 1754 cm^{-1} and 1715 cm^{-1} due to $C = O$.

Compound	R_2	R_3	R_4	R_5	Product	Yield (%)	m.p.
1	CH_3	H	CH_3	H	1a	87	129–130°
2	CH_3	C_2H_5	CH_3	H	2a	70	105–107°
3	H	CH_3	C_2H_5	H	3a	80	74– 76°
4	CH_3	H	H	CH_3	4a	86	136–138°
5	CH_3	$CO_2C_2H_5$	CH_3	H	5a	79	162–164°
6	CH_3	$COCH_3$	CH_3	H	6a	72	160–162°

DEH– $-\underset{\underset{CO_2C_2H_5}{|}}{N}-N'HCO_2C_2H_5$(N, N'-dicarboethoxyhydrazino)

Experimental. The purely alkyl pyrroles (1–4, 0.01 mol) in 20 ml of ether/n-pentane (1:1) were treated with the theoretical amount of the azoester. The solid which separated after a few minutes at room temperature was recrystallized from the same solvent. The remaining pyrroles 5 and 6 reacted similarly in ether and the products were re-crystallized from ethanol[14].

Zusammenfassung. Es reagieren die α- und β-Positionen von Pyrrol-Derivaten ohne weiteres mit Äthyl-Azodicarboxylat unter Bildung von Hydrazindicarboxyester-Derivaten, was durch die NMR- und IR-Spektren bestätigt wird.

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Inhibition of Nuclear and Mitochondrial Respiration by Arsenite

Nuclear oxidative phosphorylation has clearly been demonstrated in cell nuclei isolated from the thymus gland[1–4]. Endogenous fatty acids are the major energy source for this ATP generating process[5]. No external substrate capable of stimulating nuclear oxidative phosphorylation has been found as yet[4]. Experiments with inhibitors and uncouplers of the respiratory chain suggest a similarity if the molecular mechanism of the mitochondrial and the nuclear system. Arsenite has been reported[3] to have no effect on nuclear respiration, while this compound is a well known inhibitor of mitochondrial oxidative phosphorylation[6]. Because this observation could be of great importance in finding a significant difference in the molecular mechanism of energy production between these two cell organells, a further study on this subject seemed justified. In this report a comparison is made between the effect of different concentrations of sodium arsenite on the respiration of rat thymus nuclei and rat liver mitochondria.

Nuclei were isolated as published before[5]. Mitochondria were prepared by the method of Hogeboom[7]. Oxygen uptake was measured manometrically in 15 ml Warburg flasks. A piece of accordion-folded filter paper (Whatman-1) with 2 cm sides was inserted in the center well to which 0.1 ml 10% KOH had been added. The nuclei (15 mg protein) were incubated in 2.3 ml of a medium