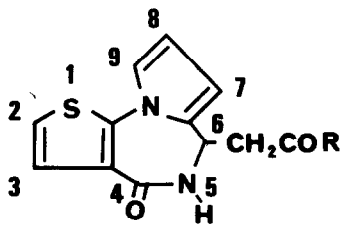
Tetrahedron Letters No. 7, pp 643 - 644. 0040-4039/79/0208-0643$02.00/0

PYRROLO [1,2-a] THIENO [3,2-f] 1,4-DIAZEPINES. NOVEL SYNTHESIS AND X-RAY ANALYSIS

S. Rault, M. Cugnon de Sévricourt et M. Robba
Laboratoire de Pharmacie Chimique.
Nguyen Huy Dung
Laboratoire de Chimie Minérale.
U.E.R. des Sciences Pharmaceutiques, Université de Caen, 1 rue Vaubénard 14000 CAEN, France.

Previously we reported the synthesis of pyrrolo [1,2-a] thieno [3,2-f] diazepines particularly using N-(aminomethyl-3-thienyl-2) pyrrole (1-3). In continuation of our studies, we now describe a novel synthesis of some other new 5,6-dihydro- 4 H-pyrrolo [1,2-a] thieno [3,2-f] 1,4-diazepines-4-ones Ia-c and the X-ray analysis of 6-(2-oxopropyl)-pyrrolo thienodiazepinone Ia. Thus a mixture of N-(3-cyano-2-thienyl)-2-formyl pyrrole and the appropriate ketone, in ethanol, was refluxed with alkaline hydrogen peroxide for 1 hr. The solvent was removed under vacuum and the reaction mixture was then left to cool, when a crystalline product deposited Ia-c in about 60% yield.

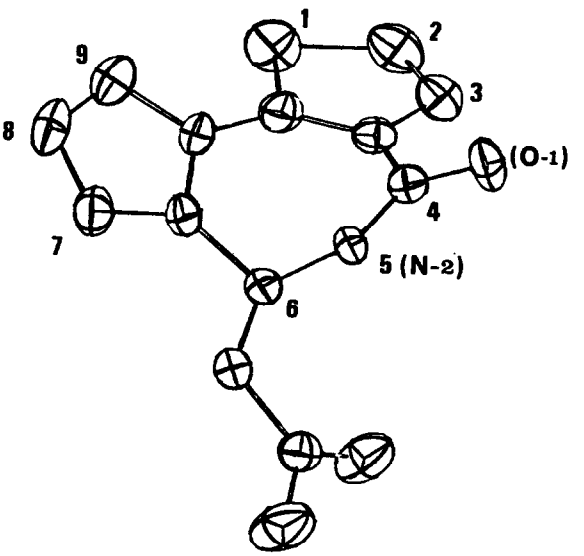


I*

a, R = CH_3

b, R = $CH(CH_3)_2$

c, R = C_6H_5



Molecular structure of Ia as found in the crystal

* Chemical Abstracts numbering system.

Elemental analysis, ir and nmr data are consistent with the structures proposed (cf table 1). A conclusive X-ray analysis is in support of the structural assignments.

The crystal of Ia belongs to the monoclinic system with space group P 21/b. The cell parameters are : a = 9,285; b = 9,330; c = 14,316 Å; $\alpha = \beta = 90°$; $\gamma = 94,05°$; z = 4. 1924 independent reflections were recorded on an automatic NONIUS CAD4 four circles diffractometer with MoK radiation using $\omega - 2\theta$ scan technique. The structure was determined by direct methods using the MULTAN program [4] and successive Fourier syntheses.

TABLE 1

Cpd	mp °c	ir (KBr, cm^{-1})	nmr δ $(CD_3)_2SO$ ppm							
			H2H3	H6	H7	H8	H9	CH_2	NH	other protons
Ia	240 (acetone)	C=O 1645 1700 NH 3180, 3270	7.35	4.71	6.18	6.33	7.20	3.23	8.26	CH_3 2.25
Ib	160 (ethanol)	C=O 1650 1710 NH 3175, 3280	7.31	4.70	6.16	6.30	7.15	3.23	8.26	CH 2.70 CH_3 1.06
Ic	205 (ethanol)	C=O 1640 1675 NH 3320	7.35	4.92	6.33	6.33	7.15	3.81	8.33	C_6H_5 7.6 8.1
J CH_2/H_6 = 6.7 Hz, J NH/H_6 = 5.2 Hz.										

Refinement was carried out by least-squares method with full matrix. Difference Fourier synthesis allowed the locations of the hydrogen atoms which were also refined. The final R and Rω are found to be 0,048 and 0,047 respectively. The Figure shows the computer generated drawing of the crystal structure. There is no intramolecular H bonding however intermolecular H bonding links N-2 to O-1 of the two different molecules contributing to the crystal cohesion. The chemical and pharmacological properties of I , and the application of this method in the synthesis of other 1,4-diazepines, in particular benzopyrrolodiazepines, are currently being investigated.

References and Footnotes

(1) S. Rault, M. Cugnon de Sévricourt et M. Robba, Compt. Rend. Acad. Sc., 284, Série C, 1977, p. 533.

(2) S. Rault, M. Cugnon de Sévricourt et M. Robba, ibid, 285, Série C, 1977 p. 381.

(3) S. Rault, M. Cugnon de Sévricourt et M. Robba, ibid, 1978, to be published.

(4) G. Germain, P. Main, M.M. Woolfson, Acta Cryst. B 26, 1970, 274-285.

(5) Atomic coordinates, thermal parameters and tables of bond lengths, bond angles and structure factors are available from one of the authors (NHD).

(Received in UK 29 September 1978)