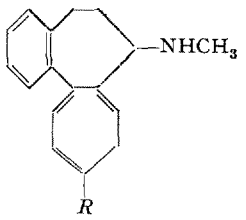
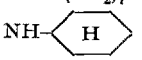
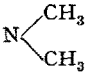
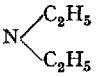
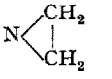
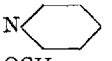
Tabelle II



Präparat	Chemische Bezeichnung	Bakteriostatische Wirkung		Bakterizide Wirkung	
		Staph. aureus	*E. coli*	*Staph. aureus*	*E. coli*
13153	$R = NHCH_3$	Spur	> 1,0	> 1,0	> 1,0
14697	NHC_2H_5	> 1,0	> 1,0	> 1,0	> 1,0
14080	$NHCH(CH_3)_2$	> 1,0	> 1,0	> 1,0	> 1,0
14081	$NHCH_2CH_2OH$	> 1,0	> 1,0	> 1,0	> 1,0
13485	$NHCH_2CH=CH_2$	1,0–(0,5)	> 1,0	> 1,0	> 1,0
13486	$NHCH_2CH_2CH_2CH_3$	1,0–(0,5)	> 1,0	1,0–(0,5)	> 1,0
13540	$NH(CH_2)_7CH_3$	0,01–0,005	0,5–0,1	0,1–0,05	> 1,0
14063		0,1	> 1,0	0,5	> 1,0
13286		> 1,0	> 1,0	> 1,0	> 1,0
14698		> 1,0	> 1,0	> 1,0	> 1,0
14844		> 1,0	> 1,0	> 1,0	> 1,0
14055		Spur	> 1,0	Spur	> 1,0
Demecolcin	OCH_3	> 1,0	> 1,0	> 1,0	> 1,0
Colchicin		> 1,0	> 1,0	> 1,0	> 1,0

hinsichtlich einer bestimmten Eigenschaft reziprok zu verhalten und eine gewisse Spezifität der hervorgebrachten Wirkungs- bzw. Konstitutionsänderung zu zeigen.

R. MEIER, B. SCHÄR und L. NEIPP

Aus den Biologischen Laboratorien der CIBA Aktiengesellschaft, Basel, den 22. Oktober 1953.

Summary

A series of demecolceinamids was examined *in vitro* on chicken fibroblasts, leucocytes, and different bacteria. It was found that with increasing length of the side chain on ring C the antimitotic activity is decreasing while the antibacterial effect is increasing.

Demecolceinamide

Aus den Knollen[1], Blüten[2], Blättern[3] und Samen[4] der Herbstzeitlose isolierte zuerst SANTAVY die Substanz F, deren Konstitution in den Arbeiten von ŠANTAVY, WINKLER und REICHSTEIN[1] sowie von UFFER, SCHINDLER, ŠANTAVY und REICHSTEIN[2] aufgeklärt wurde. Es handelt sich darnach um das Desacetyl-N-methylcolchicin, dem der Name Demecolcin gegeben wurde. Dem Verseifungsprodukt kommt daher in Analogie zum Colchicein die Bezeichnung Demecolcein zu. Wir setzten das Demecolcin mit Aminen um und erhielten dabei die Demecolceinamide[3], denen als Mitose-Inhibitoren einige Bedeutung zukommt. Wir geben hier die physikalischen Eigenschaften der von uns hergestellten und in unsern pharmakologischen Laboratorien geprüften Verbindungen bekannt.

A. UFFER

Forschungslaboratorien der CIBA Aktiengesellschaft, Pharmazeutische Abteilung, Basel, den 23. Oktober 1953.

Summary

The physical data of a number of Demecolceinamides are described.

[1] F. ŠANTAVY, Chem. Listy *42*, 177 (1948); Chem. Abstr. *44*, 9518 (1950); Pharm. Acta helv. *25*, 248 (1950); Zbl. Chem. *1952*, 3844.

[2] F. ŠANTAVY, Coll. Trav. Chim. Tchécoslov. *15*, 552 (1950); Chem. Abstr. *46*, 126 (1952).

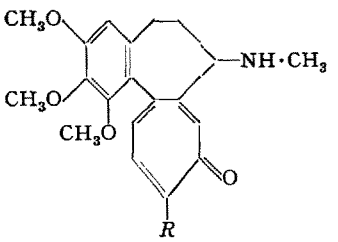
[3] F. ŠANTAVY, J. LIPOVA und E. COUFALIK, Čekoslovenska farmacie *1*, 239 (1952); Chem. Abstr. *46*, 10545 (1952).

[4] F. ŠANTAVY und M. TALAS, Chem. Listy *47*, 232 (1953).

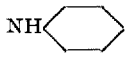
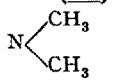
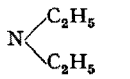
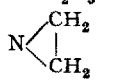
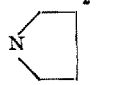
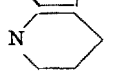
[1] F. ŠANTAVY, R. WINKLER und T. REICHSTEIN, Helv. chim. Acta *36*, 1319 (1953).

[2] A. UFFER, O. SCHINDLER, F. ŠANTAVY und T. REICHSTEIN, Helv. chim. Acta *37*, 18 (1954).

[3] Über Colchiceinamide siehe: S. ZEISEL, Mh. Chem. *9*, 1 (1888). – H. LETTRÉ, Angew. Chem. *55*, 265 (1942). – H. LETTRÉ und F. FERNHOLZ, Z. physiol. Chem. *278*, 175 (1943). – H. LETTRÉ, Angew. Chem. *63*, 421 (1952). – F. SANTAVY, Chem. Listy *46*, 280 (1952). – A. UFFER, Helv. chim. Acta *35*, 2135 (1952). – P. BELLET und P. REGNIER, Soc. Chem. *20*, 756 (1953). – J. L. HARTWELL, M. V. NADKARNI und J. LEITER, Amer. chem. Soc. *74*, 3180 (1952). – R. M. HOROWITZ und G. E. ULLYOT, Amer. chem. Soc. *74*, 587 (1952).



Demecolcin
$R = OCH_3$

R	Formel	Smp.	$[\alpha]_D$	in Chlf. c	t
NH_2	$C_{20}H_{24}O_4N_2$	120–122°	−126°	1,072	25°
$NH \cdot CH_3$	$C_{21}H_{26}O_4N_2$	213–214°	− 80°	0,688	24°
$NH \cdot C_2H_5$	$C_{22}H_{28}O_4N_2$	125–126°	− 70°	1,05	27°
$NH \cdot CH(CH_3)_2$	$C_{23}H_{30}O_4N_2$	159–160°	− 80°	0,975	24°
$NH \cdot C_4H_9$	$C_{24}H_{32}O_4N_2$	128–129°	− 58°	0,571	30°
$NH \cdot CH_2 \cdot CH=CH_2$	$C_{23}H_{28}O_4N_2$	141–142°	− 70°	0,854	30°
$NH \cdot CH_2 \cdot CH_2 \cdot OH$	$C_{22}H_{28}O_5N_2$	94– 96°/147–149°	− 88°	1,025	24°
	$C_{26}H_{34}O_4N_2$	166–168°	− 76°	0,985	24°
	$C_{22}H_{28}O_4N_2$	130–131°	+325°	0,915	31°
	$C_{24}H_{32}O_4N_2$	137–138°	+450°	0,535	26°
	$C_{22}H_{26}O_4N_2$	146–147°	− 90°	0,815	27°
	$C_{24}H_{30}O_4N_2$	172–174°	+534°	1,045	22°
	$C_{25}H_{32}O_4N_2$	151–152°	+ 76°	0,99	24°

Mittlerer Fehler der Drehungsbestimmung = ± 3°.

Studies on Organic Fluorine Compounds II[1]

Esters of Oxalofluoroacetic Acid

The biochemical mechanism of fluoroacetate poisoning which has been extensively studied during these last years[2] has been described by MARTIUS[3] and PETERS *et al.*[4] as follows:–Fluoroacetate is enzymatically converted into a fluorotricarboxylic acid, and the latter blocks the KREBS cycle at the stage of citric acid conversion, thus causing accumulation of this acid in the poisoned tissue.

In the light of this theory, it appeared that a study of the biological behaviour of monofluoro-derivatives of other intermediates of the KREBS cycle not only might contribute to a better understanding of the mode of action of fluoro-acetic acid, but also enhance our knowledge of the steps involved in the tricarboxylic acid cycle. To our knowledge, no such fluorine compounds have been prepared so far.

The present note reports on the preparation of esters of oxalofluoroacetic acid and some of their biological properties.

Diethyl sodio-oxalofluoroacetate was prepared by CLAISEN condensation of diethyl oxalate and ethyl fluoroacetate in the presence of alcohol-free sodium ethoxide as condensing agent in yields of 80–85%. The free ester was obtained from the enolate by acidification to pH = 2 and extraction with ether. B.p. 120–122/9 mm. d_4^{20} 1·261; n_D^{20} 1·42; MR, calc. 42·16; MR, found 42·38. Anal. Calc. for $C_8H_{11}O_5F$: C, 46·6; H, 5·3. Found: C, 46·7; H, 5·8.

With alcoholic ferric chloride solution, the ester gave the characteristic deep red color reaction. Its infra-red spectrum showed the C–F band at 1094 cm^{-1}. For further identification, the dinitrophenylhydrazone of the ester was prepared; it melted at 124°. Anal. Calc. for $C_{14}H_{15}N_4O_6F$: C, 43·7; H, 3·9; N, 14·5. Found: C, 44·2; H, 4·0; N, 13·9.

Attempts to prepare oxalofluoroacetic acid by saponification of the ester with cold concentrated hydrochloric acid, were unsuccesful. Therefore, the corresponding di-*t*-butyl ester was prepared by condensation of

[1] Part I: E. BERGMANN and I. BLANK, J. chem. Soc., in press (1953).

[2] G. R. BARTLETT and E. S. G. BARRON, J. Biol. Chem. *70*, 67 (1947). – M. B. CHENOWETH, Pharmacol. Rev. *1*, 383 (1949).

[3] C. MARTIUS, Ann. Chem. *561*, 227 (1949).

[4] R. A. PETERS, Proc. roy. Soc. [B] *139*, 143 (1952). – R. A. PETERS, R. W. WAKELIN, and P. BUFFA, Biochem. J. *50*, 13 (1952). – R. A. PETERS, Proc. roy. Soc. [B] *140*, 497 (1953).