JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
LENHERT, P. G. (1968). *Proc. Roy. Soc.* A**303**, 45–84.
LENHERT, P. G. & HODGKIN, D. C. (1961). *Nature, Lond.* **192**, 937–938.
PALENIK, G. J., SULLIVAN, D. A. & NAIK, D. V. (1976). *J. Amer. Chem. Soc.* **98**, 1177–1182.
RÉTEY, J. (1971). *Helv. Chim. Acta*, **54**, 2747–2752.
SCHRAUZER, G. N. (1968). *Acc. Chem. Res.* **1**, 97–103.
SCHRAUZER, G. N. (1971). *Advanc. Chem. Ser.* **100**, 1–20.
STEWART, J. M., KUNDELL, F. A. & BALDWIN, J. C. (1970). The XRAY 70 system. Computer Science Center, Univ. of Maryland, College Park, Maryland.

Acta Cryst. (1977). B**33**, 2388–2391

5-(*N*-Benzyl-*N*-methyliminioprop-2-enyl)-3,7,8,10-tetramethyl-1,5-dihydroisoalloxazine Perchlorate, a Model Compound of a Flavoprotein Inhibitor Complex

BY M. VON GLEHN AND B. STENSLAND

Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm, Sweden

AND B. GÄRTNER

Fachbereich Biologie, Universität Konstanz, D-775 Konstanz, Germany (BRD)

(*Received* 10 *December* 1976; *accepted* 23 *January* 1977)

5-(*N*-Benzyl-*N*-methyliminioprop-2-enyl)-3,7,8,10-tetramethyl-1,5-dihydroisoalloxazine perchlorate, $C_{25}H_{28}N_5O_2^+ClO_4^-.CH_3OH$, M_r = 562·03, is monoclinic, $P2_1/c$, with a = 7·742 (5), b = 17·890 (5), c = 18·830 (5) Å, β = 98·06 (1)°, D_c = 1·36 g cm^{-3}, Z = 4. Spectral and chemical evidence strongly suggests that this photochemically obtained flavin adduct is to be regarded as a relevant model compound of a monoamine oxidase inhibitor complex. The crystal structure confirms that the propargylamine-type inhibitor is covalently bonded to the N(5) position in the flavin nucleus, yielding a dihydroflavin-5-trimethinecyanine structure. The molecular packing is influenced by the presence of an intermolecular NH···O hydrogen bond which links the molecules in pairs across a centre of symmetry.

Introduction

The present investigation was undertaken to elucidate the structure of a photochemically obtained adduct from 3-methyllumiflavin and *N*-methyl-*N*-benzylpropargylamine (Gärtner, Hemmerich & Zeller, 1976). Propargylamine-type compounds are known to react irreversibly with, and to bond covalently to, the flavin component of mitochondrial monoamine oxidase, giving stable inhibitor complexes (Hellerman & Erwin, 1968). It has been shown (Chuang, Patek & Hellerman, 1974) that these very characteristic chromophores are identical with those of isolated synthetic photoadducts of 3-methyllumiflavin and related propargylamine compounds (Zeller, Gärtner & Hemmerich, 1972). By chemical analysis, dihydroflavin-5-trimethinecyanine structures were assigned to these products (Gärtner & Hemmerich, 1975; Maycock, 1975).

The pale-yellow crystals of the photoadduct were synthesized by Dr B. Gärtner, University of Konstanz, Germany (Gärtner *et al.*, 1976). The space group and preliminary cell parameters were determined by photographic methods. At room temperature the decomposition was too rapid to permit a collection of reliable data. Even at low temperature (−125 °C) decomposition was observed, especially along **a**. A single crystal, 0·33 × 0·12 × 0·12 mm, was mounted on an automatic Siemens diffractometer (AED), and the X-ray intensity data ($\theta \leq 57°$) were collected at −125 ± 5 °C with graphite-monochromatized Cu $K\alpha$ radiation (λ = 1·54184 Å). The θ–2θ scan technique was used.

2385 reflexions with $\sigma(I_{\rm net})/I_{\rm net} \leq 0·25$ were used in the subsequent calculations. The net intensities were corrected for Lorentz, polarization and absorption (μ = 17·44 cm^{-1}) effects.

The crystal structure was solved by direct methods (Karle & Karle, 1966), with a program package based on a linear, weighted, phase-sum formula for phase determination (Norrestam, 1972). The E map based on the set of phases for the best solution revealed the position of the Cl atom together with 11 non-hydrogen atoms. The position of the Cl atom agreed with that found from a three-dimensional Patterson function. After a full-matrix least-squares refinement with isotropic thermal parameters, the remaining non-hydrogen atoms were located from a difference synthesis. The H atoms

Table 1. *Fractional atomic coordinates* (×10^4) *for non-hydrogen atoms with estimated standard deviations in parentheses*

	x	*y*	*z*
N(1)	6293 (7)	9160 (2)	10428 (3)
C(2)	5586 (8)	9520 (3)	10960 (4)
N(3)	5535 (7)	9154 (3)	11580 (3)
C(4)	6258 (8)	8451 (3)	11728 (4)
C(4a)	7111 (9)	8140 (3)	11180 (4)
N(5)	7976 (7)	7417 (2)	11283 (3)
C(5a)	7710 (8)	6964 (3)	10651 (4)
C(6)	7639 (8)	6178 (3)	10704 (4)
C(7)	7562 (8)	5743 (3)	10091 (4)
C(8)	7493 (8)	6071 (3)	9429 (4)
C(9)	7451 (8)	6876 (3)	9377 (4)
C(9a)	7574 (8)	7304 (3)	9988 (4)
N(10)	7505 (6)	8107 (2)	9955 (3)
C(10a)	7019 (7)	8458 (3)	10533 (4)
O(12)	4942 (6)	10159 (2)	10842 (3)
C(13)	4645 (10)	9539 (4)	12121 (4)
O(14)	6105 (6)	8152 (2)	12306 (3)
C(17)	7540 (10)	4899 (3)	10171 (4)
C(18)	7367 (11)	5624 (3)	8758 (4)
C(20)	7665 (9)	8471 (3)	9279 (4)
C(51)	9133 (9)	7226 (3)	11839 (4)
C(52)	9735 (8)	7634 (3)	12436 (4)
C(53)	11006 (8)	7294 (3)	12916 (4)
N(54)	11876 (7)	7589 (3)	13489 (3)
C(54)	11682 (10)	8365 (3)	13700 (4)
C(55)	13187 (9)	7138 (4)	13942 (4)
C(56)	12674 (9)	6935 (4)	14661 (4)
C(57)	12939 (10)	7450 (4)	15228 (4)
C(58)	12424 (11)	7253 (5)	15880 (5)
C(59)	11679 (12)	6565 (5)	15976 (5)
C(60)	11463 (10)	6079 (4)	15432 (5)
C(61)	11955 (10)	6255 (4)	14760 (4)
Cl	10004 (2)	10167 (1)	12310 (1)
O(1)	11377 (10)	10064 (4)	12934 (3)
O(2)	8600 (9)	10558 (3)	12549 (5)
O(3)	9470 (10)	9413 (3)	12103 (4)
O(4)	10689 (11)	10569 (4)	11788 (4)
C(*M*)	5083 (24)	6380 (7)	12115 (13)
O(*M*)	4566 (15)	6887 (5)	12536 (5)

were included in the subsequent calculations at ideal locations with fixed H distances of C–H = 1·10 Å and N–H = 1·02 Å. In a final refinement the non-hydrogen atoms were allowed to vibrate anisotropically, while the H atoms were given isotropic temperature factors fixed at 4·6 Å^2. The final *R* value obtained was 0·096 for 2342 reflexions accepted within the limit $0{\cdot}50 \leq |F_o|/|F_c| \leq 2{\cdot}00$.

The atomic scattering factors used were taken from *International Tables for X-ray Crystallography* (1974), and the weights were calculated according to Hughes (1941), with $|F_o|_{\min} = 4{\cdot}0$. Final fractional atomic coordinates with associated e.s.d.'s are given in Table 1.*

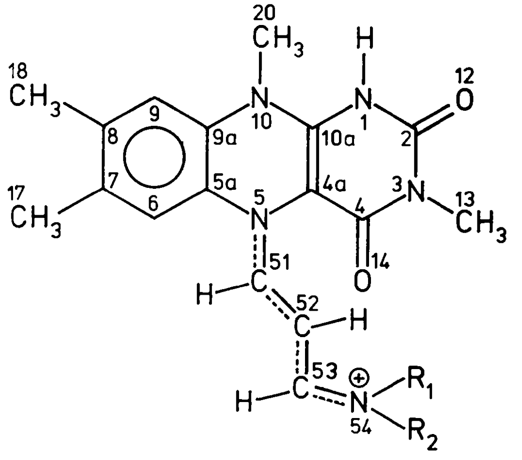

Fig. 1. Schematic drawing of the dihydroflavin-5-trimethinecyanine compounds, where R_1 and R_2 are alkyl and/or aromatic hydrocarbon groups.

Table 2. *Interatomic distances* (Å) *less than* 3·5 Å, *with calculated e.s.d.'s*

Intramolecular distances

C(2)–O(3)	3·449 (10)	C(54)–O(1)	3·357 (9)
N(3)–O(3)	3·102 (9)	N(5)–C(*M*)	3·449 (20)
C(4)–O(3)	3·025 (9)	O(14)–O(*M*)	2·620 (10)
C(4a)–O(3)	3·263 (9)	O(14)–C(*M*)	3·273 (14)
C(52)–O(3)	3·242 (8)		

Intermolecular distances

N(1)–O(12$^{\mathrm{i}}$)	2·734 (7)	C(51)–C(58$^{\mathrm{iv}}$)	3·451 (11)
N(1)–C(61$^{\mathrm{ii}}$)	3·496 (9)	C(51)–C(59$^{\mathrm{iv}}$)	3·478 (11)
C(2)–O(12$^{\mathrm{i}}$)	3·411 (9)	C(6)–O(1$^{\mathrm{iii}}$)	3·252 (9)
C(2)–C(60$^{\mathrm{ii}}$)	3·382 (10)	C(13)–O(1$^{\mathrm{vi}}$)	3·274 (11)
N(3)–C(59$^{\mathrm{ii}}$)	3·303 (10)	C(18)–O(2$^{\mathrm{iv}}$)	3·343 (10)
C(4)–C(58$^{\mathrm{ii}}$)	3·408 (11)	C(53)–O(2$^{\mathrm{iii}}$)	3·252 (8)
N(10)–C(60$^{\mathrm{iv}}$)	3·398 (9)	C(59)–O(3$^{\mathrm{v}}$)	3·392 (12)
O(12)–O(12$^{\mathrm{i}}$)	3·237 (10)	C(20)–O(4$^{\mathrm{vii}}$)	3·053 (10)
O(12)–C(60$^{\mathrm{ii}}$)	3·489 (9)	C(53)–O(4$^{\mathrm{iii}}$)	3·428 (9)
O(12)–C(61$^{\mathrm{iii}}$)	3·415 (9)	C(53)–O(M^{viii})	3·033 (13)
C(13)–C(18$^{\mathrm{v}}$)	3·495 (11)	N(54)–O(M^{viii})	3·191 (12)
C(20)–C(60$^{\mathrm{iv}}$)	3·496 (11)	C(55)–O(M^{viii})	3·025 (12)
C(20)–C(61$^{\mathrm{iv}}$)	3·354 (10)		

Symmetry code superscript

None	x,y,z	(v)	$x, \frac{3}{2}-y, \frac{1}{2}+z$
(i)	$1-x, 2-y, z$	(vi)	$x-1, y, z$
(ii)	$x-1, \frac{3}{2}-y, z-\frac{1}{2}$	(vii)	$-x, -y, -z$
(iii)	$2-x, y-\frac{1}{2}, \frac{1}{2}-z$	(viii)	$x+1, y, z$
(iv)	$x, \frac{3}{2}-y, z-\frac{1}{2}$		

Discussion

Structural studies on isoalloxazine derivatives in different states of oxidation and protonation have indicated a connexion between the planarity of the flavin molecule and the oxidation state (Dudley, Ehrenberg, Hemmerich & Müller, 1964). Photochemical reactions between flavoquinones (oxidized flavins) and

---

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32456 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

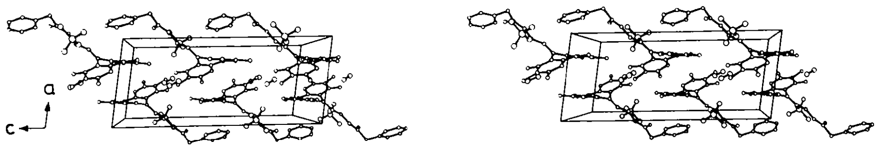

Fig. 2. A stereoscopic view of the molecular packing in the unit cell, shown with **b** directed from the viewer.

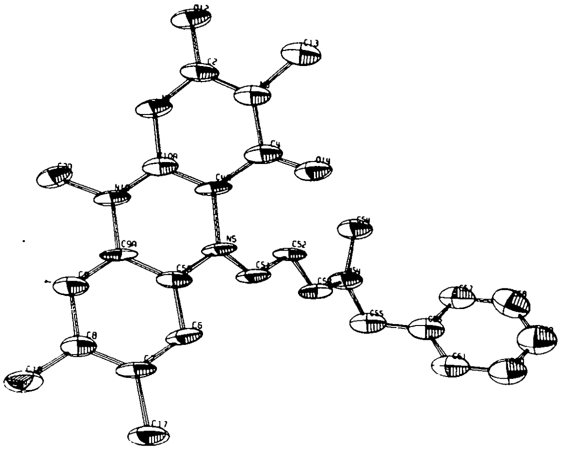

Fig. 3. The structure of the 5-(*N*-benzyl-*N*-methyliminioprop-2-enyl)-3,7,8,10-tetramethyl-1,5-dihydroisoalloxazine cation. The atoms are represented by 50% probability ellipsoids.

propargylamine-type compounds result in the formation of covalently linked adducts with dihydroflavin character.

A schematic drawing of the flavocyanine molecule so obtained, with atomic numbering, is seen in Fig. 1. For the present study $R_1 = CH_3$ and $R_2 = C_6H_5CH_2$. The molecular arrangement in the unit cell viewed along **b** is shown in Fig. 2. The isoalloxazine molecules are folded along the N(5)–N(10) line: they are almost perpendicular to **a** and thus form a *bc* plane from which the N(5)-substituted fixed cyanine chains extend. The molecules are held together in pairs across a centre of symmetry by a hydrogen bond (2·76 Å) which involves O(12) in one molecule and N(1) in another. Interatomic distances less than 3·5 Å are listed in Table 2. The shortest hydrogen bond (2·62 Å) found in the structure involves the O atom of the methanol solvent. The same atom also forms fairly short contacts to a cyanine chain in another molecule; this is the link which joins the molecules in the **a** direction.

The perchlorate ions are not involved in any particular bonds to the cations or to the solvent molecules. However, there are short contacts to the flavin nucleus, especially to the pyrimidinoid ring. Semi-empirical calculations on the lumiflavin molecule in different states of oxidation have been performed by both the restricted and unrestricted semi-empirical Hartree–Fock SCF–MO–LCAO–CI method in the PPP approximation;

Table 3. *Deviations in* Å *from best least-squares planes*

Atoms indicated with asterisks were omitted from the calculations of the planes.

Plane 1: The benzene ring of the flavine molecule
$0{\cdot}9976x - 0{\cdot}0109y - 0{\cdot}0684z = 4{\cdot}4208$

C(5a)	0·026	*N(5)	0·147
C(6)	−0·020	*N(10)	−0·066
C(7)	−0·004	*C(17)	−0·008
C(8)	0·021	*C(18)	0·022
C(9)	−0·014	*C(20)	0·140
C(9a)	−0·009		

Plane 2: The pyrimidine ring of the flavine molecule
$0{\cdot}8745x + 0{\cdot}4295y + 0{\cdot}0225z = 15{\cdot}5364$

N(1)	−0·012	*N(5)	0·106
C(2)	0·037	*N(10)	−0·235
N(3)	−0·016	*O(12)	0·056
C(4)	−0·029	*C(13)	−0·072
C(4a)	0·055	*O(14)	−0·112
C(10a)	−0·034	*C(20)	−0·137

Plane 3: The trimethinated carbons in the 5-substituted tail
$-0{\cdot}7071x - 0{\cdot}3959y + 0{\cdot}5859z = 2{\cdot}4243$

C(51)	0·000	*N(5)	−0·065
C(52)	0·000	*N(54)	0·102
C(53)	0·000	*C(54)(CH_3)	−0·305
		*C(55)	−0·069
		*C(56)(C_6H_5)	1·162

Table 4. *Intramolecular distances* (Å) *with e.s.d.'s*

N(1)–C(2)	1·369 (9)	C(10a)–N(1)	1·379 (7)
C(2)–O(12)	1·255 (7)	N(5)–C(51)	1·323 (9)
C(2)–N(3)	1·343 (9)	C(51)–C(52)	1·366 (9)
N(3)–C(13)	1·477 (9)	C(52)–C(53)	1·381 (9)
N(3)–C(4)	1·390 (8)	C(53)–N(54)	1·300 (9)
C(4)–O(14)	1·233 (9)	N(54)–C(54)	1·458 (8)
C(4)–C(4a)	1·415 (10)	N(54)–C(55)	1·472 (9)
C(4a)–C(10a)	1·338 (10)	C(55)–C(56)	1·508 (11)
C(4a)–N(5)	1·456 (7)	C(56)–C(57)	1·403 (10)
N(5)–C(5a)	1·430 (8)	C(57)–C(58)	1·388 (12)
C(5a)–C(9a)	1·379 (9)	C(58)–C(59)	1·382 (13)
C(5a)–C(6)	1·412 (8)	C(59)–C(60)	1·337 (13)
C(6)–C(7)	1·387 (9)	C(60)–C(61)	1·406 (12)
C(7)–C(17)	1·518 (8)	C(61)–C(56)	1·362 (9)
C(7)–C(8)	1·370 (10)		
C(8)–C(18)	1·487 (10)	Cl–O(1)	1·481 (7)
C(8)–C(9)	1·443 (8)	Cl–O(2)	1·418 (7)
C(9)–C(9a)	1·375 (9)	Cl–O(3)	1·449 (6)
C(9a)–N(10)	1·439 (7)	Cl–O(4)	1·383 (8)
N(10)–C(20)	1·451 (8)	C(*M*)–O(*M*)	1·303 (21)
N(10)–C(10a)	1·354 (8)		

Table 5. *Intramolecular bond angles* (°) *with calculated e.s.d.'s*

C(10a)–N(1)–C(2)	121·4 (6)	C(5a)–C(6)–C(7)	119·8 (6)	C(52)–C(53)–N(54)	127·1 (5)
N(1)–C(2)–N(3)	118·1 (5)	C(6)–C(7)–C(8)	120·6 (5)	C(53)–N(54)–C(54)	123·4 (6)
N(1)–C(2)–O(12)	119·3 (6)	C(6)–C(7)–C(17)	118·3 (6)	C(53)–N(54)–C(55)	119·6 (5)
O(12)–C(2)–N(3)	122·6 (6)	C(17)–C(7)–C(8)	121·1 (6)	C(54)–N(54)–C(55)	116·9 (5)
C(2)–N(3)–C(4)	123·8 (6)	C(7)–C(8)–C(9)	119·1 (6)	N(54)–C(55)–C(56)	113·9 (6)
C(2)–N(3)–C(13)	116·5 (5)	C(7)–C(8)–C(18)	122·1 (5)	C(55)–C(56)–C(57)	119·8 (6)
C(13)–N(3)–C(4)	119·8 (6)	C(18)–C(8)–C(9)	118·7 (6)	C(55)–C(56)–C(61)	120·2 (6)
N(3)–C(4)–C(4a)	115·2 (6)	C(8)–C(9)–C(9a)	119·9 (6)	C(57)–C(56)–C(61)	120·0 (7)
N(3)–C(4)–O(14)	119·0 (6)	C(9)–C(9a)–C(5a)	120·1 (5)	C(56)–C(57)–C(58)	118·6 (7)
O(14)–C(4)–C(4a)	125·9 (6)	C(9)–C(9a)–N(10)	121·4 (6)	C(57)–C(58)–C(59)	121·2 (8)
C(4)–C(4a)–C(10a)	121·8 (6)	C(5a)–C(9a)–N(10)	118·4 (6)	C(58)–C(59)–C(60)	119·3 (9)
C(4)–C(4a)–N(5)	120·4 (6)	C(9a)–N(10)–C(10a)	116·2 (5)	C(59)–C(60)–C(61)	121·5 (8)
C(10a)–C(4a)–N(5)	117·6 (6)	C(9a)–N(10)–C(20)	118·6 (5)	C(60)–C(61)–C(56)	119·4 (7)
C(4a)–N(5)–C(5a)	112·5 (5)	C(20)–N(10)–C(10a)	124·4 (5)	O(1)–Cl–O(2)	107·9 (5)
C(4a)–N(5)–C(51)	125·5 (5)	N(10)–C(10a)–C(4a)	123·4 (5)	O(1)–Cl–O(3)	104·1 (4)
C(5a)–N(5)–C(51)	121·0 (5)	N(10)–C(10a)–N(1)	117·4 (6)	O(1)–Cl–O(4)	109·0 (4)
N(5)–C(5a)–C(6)	120·5 (6)	C(4a)–C(10a)–N(1)	119·1 (6)	O(2)–Cl–O(3)	110·0 (4)
N(5)–C(5a)–C(9a)	119·2 (5)	N(5)–C(51)–C(52)	128·9 (6)	O(2)–Cl–O(4)	110·9 (4)
C(9a)–C(5a)–C(6)	120·3 (6)	C(51)–C(52)–C(53)	115·7 (5)	O(3)–Cl–O(4)	114·6 (4)

they have also been complemented with CNDO calculations (Grabe, 1972, 1974). N(3) and C(4) are found to be among the most positively charged atoms.

The structure of the cation, excluding the H atoms, is shown in Fig. 3. The molecule contains several planar parts (see Table 3). Planes 1 and 2 make an angle of 148·5°, very similar to the value found in fully reduced 1,5-dihydroflavins.

The bond lengths and angles are given in Tables 4 and 5. The distances within the molecule are close to expected values (Sutton, 1965), except those found in the pyrimidinoid and cyanine parts. Bond lengths involved in the cyanine part indicate strong delocalization of the π electrons over the chain N(5)–C(51)–C(52)–C(53)–N(54), which is characteristic for cyanine chains of so-called linear aromaticity (Matthews, Stenkamp & Colman, 1973).

The authors are indebted to Professor Peder Kierkegaard for his interest in this work and for all the facilities placed at their disposal, to Professor Peter Hemmerich for his valuable advice and encouragement in this work and to Dr Sven Westman for his correction of the English of this paper.

References

CHUANG, H. Y. K., PATEK, D. R. & HELLERMAN, L. (1974). *J. Biol. Chem.* **249**, 2381–2384.

DUDLEY, K. H., EHRENBERG, A., HEMMERICH, P. & MÜLLER, F. (1964). *Helv. Chim. Acta*, **47**, 1354–1383.

GÄRTNER, B. & HEMMERICH, P. (1975). *Angew. Chem.* **87**, 137–138.

GÄRTNER, B., HEMMERICH, P. & ZELLER, E. A. (1976). *Eur. J. Biochem.* **63**, 211–221.

GRABE, B. (1972). *Acta Chem. Scand.* **26**, 4084–4100.

GRABE, B. (1974). *Acta Chem. Scand.* A**28**, 363–374.

HELLERMAN, L. & ERWIN, V. G. (1968). *J. Biol. Chem.* **243**, 5234–5243.

HUGHES, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737–1752.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

KARLE, J. & KARLE, I. L. (1966). *Acta Cryst.* **21**, 849–895.

MATTHEWS, B. W., STENKAMP, R. E. & COLMAN, P. M. (1973). *Acta Cryst.* B**29**, 449.

MAYCOCK, A. L. (1975). *J. Amer. Chem. Soc.* **97**, 2270–2272.

NORRESTAM, R. (1972). *Acta Cryst.* A**28**, 303–308.

SUTTON, L. E. (1965). *Tables of Interatomic Distances and Configuration in Molecules and Ions*. London: The Chemical Society.

ZELLER, E. A., GÄRTNER, B. & HEMMERICH, P. (1972). *Z. Naturforsch.* **27B**, 1050–1052.