# 153. 7-Bromocavernicolenone, a New α-Bromoenone from the Mediterranean Sponge *Aplysina* (= *Verongia*) *cavernicola*. Implied, Unprecedented Involvement of a Halogenated Dopa in the Biogenesis of a Natural Product

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A novel, mildly antibacterial, α-bromoenone (7-bromocavernicolenone) has been isolated from the Mediterranean sponge *Aplysina* (= *Verongia*) *cavernicola*. Its structure, 7-bromo-1,5-dihydroxy-2-azabicyclo[3.3.1]non-6-en-3,8-dione (**3**), is based on X-ray and NMR analysis and on the observation that acetylation of **3** affords two monoacetates. An unprecedented phenol oxidative biogenetic pathway is suggested leading to 7-bromocavernicolenone *via* 3-bromotyrosine and 5-bromodopa.

**1. Introduction.** – Among the living organisms affording secondary metabolites, a special position is occupied by marine sponges belonging to the order Verongida. In fact, such sponges, besides producing unusual fatty acids [1a], sterols [1b], free amino acids [1c], carotenoid sulfates [1d], and quinoline derivatives [1e], also give a wide variety of metabolites of proven [2] or presumable [3] [4] halotyrosine origin. Such products have been recently reviewed from both the chemotaxonomical [3] and the chemical [4a] points of view.

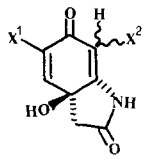
In the course of our search for novel metabolites from a Mediterranean member of the Verongida, *Aplysina* (= *Verongia*) *cavernicola* [4], we have now isolated a novel α-bromoenone whose structure has been elucidated. The formation of this product suggests a novel biogenetic pathway evolving through 3-bromotyrosine and 5-bromodopa.

**2. Results and Discussion**[1]). – The polar extracts of the sponge [4a] were reverse-phase flash-chromatographed to give, besides metabolites already known from this sponge [4], a new microcrystalline compound.

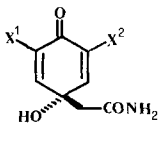
The compound proved mildly antibacterial, *in vitro*, inhibiting the growth of the phytopathogenic, gram-negative bacterium *Pseudomonas cichorii*, whilst it proved inactive against the gram-positive *Bacillus subtilis*.

A $^{13}$C-NMR study of this new compound revealed eight resonances. The multiplicities are essentially equal to those of either 5-bromo- (**1**; $X^1$ = Br, $X^2$ = H) [4c] or 5-chlorocavernicolin (**1**; $X^1$ = Cl, $X^2$ = H) [4d], except for the fact that a *d* is replaced by a *s*. Br-Atom was clearly revealed in the MS, while also the UV and $^1$H-NMR spectra were

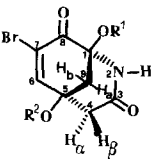
[1]) No absolute-configuration significance is to be attached to any of the structural formulae given.



**1** $X^1$ = Br or Cl
$X^2$ = H, Br or Cl



**2** $X^1$ = Br or Cl
$X^2$ = H, Br or Cl



(±)-**3** $R^1 = R^2 = H$
(±)-**4a** $R^1$ = Ac; $R^2$ = H
or *vice versa*
(±)-**4b** $R^1$ = H; $R^2$ = Ac
or *vice versa*

reminiscent of those for the cavernicolins **1** [4a] [4c] [4d]. This established a 2-bromo-2-cyclohexen-1-one partial structure, with quaternary C(6) and C(4), the latter bonded to the C-atom of a $CH_2CONH$ fragment. The compound was named accordingly *7-bromocavernicolenone* (**3**)[2]).

However, the mass-spectroscopic investigation proved difficult. We were unable to obtain reliable high-resolution measurements on the weak highest mass peaks (*m/z* 262 and 261) in the DEI [6] spectrum. Of our major concern, experiments carried out under charge-exchange conditions revealed a very weak signal (0.3% with respect to *m/z* 261 as the base peak) at *m/z* 522 with the pattern for two Br-atoms. This, and the fragmentation pattern *(Exper. Part)*, are compatible with a structure having two bromocyclohexenone groups joined through quaternary C-atoms. Actually, a dimeric tyrosine metabolite could have well been expected on the basis of the phenol oxidative pathways proposed for the biogenesis of the verongiaquinols **2** and the cavernicolins **1** [4d]. In fact, there is ample precedent for oligomeric tyrosine derivatives (bastadins [4a]) among the Verongida products[3]).

A deceptively simple $^1$H-NMR spectrum *(Exper. Part)*, though revealing long-range couplings suggestive of a rigid polycyclic structure, proved inadequate to solve the point. Therefore, we deemed that it was necessary to carry out an X-ray diffraction analysis of the tiny crystals which were obtained from MeOH after considerable effort.

Although affected by twinning, the structure could be solved as the relative orientation of the two lattices was properly identified (see *Exper. Part*). A drawing of the

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[2]) This compound, lacking optical rotation *(Exper. Part)* and revealing symmetry in the crystal *(Fig. 2)*, was originally submitted as racemic. More recently, while starting photochemical experiments with circularly polarized light, devised at resolving the racemate [5a], we have noticed that the compound, as isolated here *(Exper. Part)*, gives a negative $n \rightarrow \pi^*$ dichroic band centered at 335 nm in MeOH [5b]. According to very rough preliminary estimates, this only allows *ca.* 1% optical purity for the compound, *i.e.* well below the detection limit of either the X-ray analysis *(Exper. Part)* or NMR techniques [4c, d], or, finally, at least at the concentration used *(Exper. Part)*, of polarimetric measurements. Work is in progress [5b], using our previously developed photochemical techniques [5a], devised both at fully assigning the chiroptical properties of this compound, and at understanding the origin of the weak enantiomeric excess. Whilst the nature of the compound, as it will be clear later, does not leave room for racemization during extraction [4c, d], we can not, at the moment, rule out that optical resolution occurred during the process of crystallization *(Exper. Part)*. However, there are two precedents (actually the only two so far recorded for the marine environment) for products having low enantiomeric purity with the sponge studied here. These are 5-bromocavernicolin (**1**, $X^1$ = Br, $X^2$ = H) [4c] and 5-chlorocavernicolin (**1**, $X^1$ = Cl, $X^2$ = H) [4d]. Quite probably, the new compound described here represents the third such case, which is well allowed by the biogenetic mechanism proposed here *(Scheme)*.

[3]) However, in the light of the following experiments, the peak at *m/z* 522 must be the result of ion-molecule reactions giving dimers under the high-pressure conditions in the ion source during these MS experiments.

skeleton of 7-bromocavernicolenone (**3**), as determined from the X-ray study is shown in *Fig. 1*. Descriptively, the compound consists of a bicyclo[3.3.1]system, which has no precedent in previously known products of the Verongida [4]. It is worth mentioning that the assignment of the heteroatom types in the process of structure solution was by no means straightforward and was finally accomplished as follows. The examination

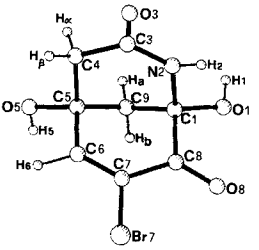


Fig. 1. *A PLUTO drawing of the molecule of 7-bromocavernicolenone* (**3**)

of the geometrical-bonding network as well as the behaviour of the thermal ellipsoids upon least squares refinement (*Exper. Part*) showed that the exocyclic groups attached to C(1) and C(5) behave best if treated as OH groups. This was fully confirmed by the fact that the monoacetylated derivatives **4a** and **4b** prepared from **3** preserve the two C=O functions of the precursor[4]). Moreover, the lactam group of **3** is attributed to N(2),C(3),O(3) on the basis of the relatively short N(2),C(3) (1.353(12) Å) and the relatively long C(3), O(3) (1.252(11) Å) distances (see *Table 1*). All other bond distances and angles between non-H-atoms are consistent with the structure **3**. Some H-bonding network is found between bromocavernicolenone molecules in the crystal lattice. In particular, the OH H-atoms H(1) and H(5) form short contacts with Br, O(8), and O(3) of an adjacent molecule. The distances H(1)···Br(7), H(1)···O(8), and H(5)···O(3) are as short as 2.80, 2.22, and 2.11 Å, respectively.

The 2-azabicyclo[3.3.1]nonane skeleton is well known as a constituent part of morphine alkaloids. However, in unfused form it has only been known as synthetic products [7]. Also, at the best of our knowledge, there are no crystal structures reported for this skeleton, although a few azabicyclo[3.3.1]nonanes with the N-atom in a different position (3-, 7-, or 9-aza) have been investigated [8]. The latter further differ from bromocavernicolenone in having a saturated skeleton, thus lacking the near orthogonality between the planes formed by the lactam and enone moieties in **3** as discussed above[4]).

The nearly racemic nature of 7-bromocavernicolenone (**3**) suggests a phenol oxidative biogenetic pathway. As already discussed for the biogenesis of the verongiaquinols **2** and the cavernicolins **1** isolated from the same sponge [4c] [4d], the pathway allows either little

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[4]) The monoacetates also allowed us to evaluate, better than had been possible with **3**, the structurally significant long-range couplings among protons (*Exper. Part*). In fact, in agreement with the X-ray diffraction analysis for **3**, $^1$H-NMR spectra for the monoacetates **4**, under double irradiation, revealed long-range coupling constants of 2.4 Hz for a W relationship between $H_\alpha$–C(4) and $H_b$–C(9) and between H–C(6) and $H_a$–C(9). Also, in addition to the conclusions from the X-ray data, the $^1$H-NMR analysis of the monoacetates revealed a similar W relationship between the proton at the N-atom and $H_b$–C(9). This clearly indicates that the protons related in a W relationship lie in flattened portions of the molecule.

Table 1. *Bond Distances (Å) and Angles (deg.) of* **3**[a])

| | | | |
|---|---|---|---|
| C(1)–O(1) | 1.404(10) | C(1)–C(8)–O(8) | 122.6(8) |
| C(1)–C(9) | 1.502(12) | C(1)–N(2)–C(3) | 124.9(9) |
| C(1)–N(2) | 1.481(12) | C(4)–C(3)–O(3) | 120.7(8) |
| C(3)–N(2) | 1.353(12) | C(4)–C(5)–C(9) | 110.1(7) |
| C(3)–O(3) | 1.252(11) | C(4)–C(5)–O(5) | 107.2(7) |
| C(3)–C(4) | 1.480(13) | C(4)–C(3)–N(2) | 119.2(8) |
| C(5)–C(4) | 1.525(12) | C(6)–C(7)–Br(7) | 121.9(7) |
| C(5)–C(6) | 1.509(11) | C(6)–C(5)–C(4) | 109.1(8) |
| C(5)–C(9) | 1.521(13) | C(6)–C(5)–C(9) | 109.6(7) |
| C(5)–O(5) | 1.431(11) | C(6)–C(5)–O(5) | 110.1(7) |
| C(7)–Br(7) | 1.876(9) | C(7)–C(8)–O(8) | 124.5(8) |
| C(7)–C(8) | 1.501(12) | C(7)–C(8)–C(1) | 112.9(7) |
| C(7)–C(6) | 1.322(11) | C(8)–C(7)–C(6) | 122.0(9) |
| C(8)–C(1) | 1.558(11) | C(8)–C(7)–Br(7) | 116.1(6) |
| C(8)–O(8) | 1.220(10) | C(8)–C(1)–O(1) | 106.2(7) |
| | | C(8)–C(1)–C(9) | 110.9(7) |
| | | C(8)–C(1)–N(2) | 106.4(7) |
| | | C(9)–C(1)–N(2) | 109.9(8) |
| | | C(9)–C(5)–O(5) | 110.7(7) |
| | | C(9)–C(1)–O(1) | 114.7(7) |
| | | N(2)–C(3)–O(3) | 120.1(9) |
| | | O(1)–C(1)–N(2) | 108.3(7) |

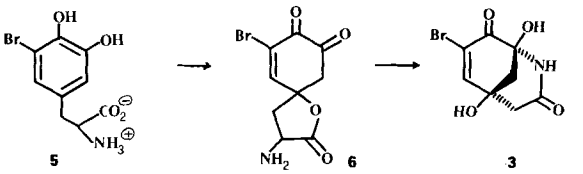
[a]) The C–H, N–H, and O–H distances are in the range 0.7–1.1 Å with an e.s.d. of *ca.* 0.1 Å.

or no control of the absolute configuration. In the present case, the nature of the product suggests 5-bromodopa (**5**) as a biogenetic precursor giving a similar type of spirolactone (see **6**), as a 1:1 diastereoisomeric mixture[5]), than the one which was proposed to rationalize the formation of the cavernicolins **1** from tyrosine [4d]. The difference here is that the vinyl-alcohol functionality, developing at C(2)–C(3) in the oxidative process of **5**, tautomerizes to a keto function. Hydrolysis of the spirolactone **6** [4d], followed by, in turn, nucleophilic attack of the amino-acid N-atom at the C(3) carbonyl group and decarboxylative oxidation may be seen to produce **3**.

Regarding the marine environment, 3,5-dibromotyrosine is a proven biogenetic precursor of both dibromoverongiaquinol (**2**, $X^1 = X^2 = Br$) and dibromohomogentisamide with sponges of the order Verongida [2]. Also, 3-bromo-, 3-chloro-, 3,5-dichloro-, and 3-bromo-5-chlorotyrosine are the likely precursors of a vast array of metabolites isolated from sponges of the same order [4]. In addition, free 3-chloro-, 3-bromo-, and 3-bromo-5-chlorotyrosine have been found in the marine crab *Limulus polyphemus* [9a], while tyrosine is certainly metabolized by marine phytoplancton [9b] as well as being involved in the formation of melanins and in other processes [9c]. Finally, dopa-3-sulfate has recently been found in *Ascophyllum nodosum* (Chromophycota, Fucales) [9d]. Actually, if we consider the whole area of natural products, dopa is well known to be involved in a

[5]) Spirolactone **14** in [4d] was similarly required to be a nearly 1:1 or a perfectly 1:1 diastereoisomeric mixture in order to rationalize the formation of, respectively, nearly-racemic or racemic cavernicolins **1**. The terminology 'racemic or nearly-racemic' for **14** in [4d] is incorrect. If the spirolactone mechanism applies, some degree of face selection is clearly expected even for a chemically achieved spirocyclization.

Scheme. *Hypothetical Biogenetic Scheme for 7-Bromocavernicolenone* (**3**) *of* A. cavernicola.




variety of processes. However, we have no knowledge either of naturally occurring free halodopas or of suggestions as to their possible implication in biogenetic pathways, though synthetic 5-bromodopa [10a] and 5-fluorodopa [10b] are known. Therefore, our proposal embodied in the *Scheme* stimulates to attempt a biosynthetic experiment by feeding *A. cavernicola* with labeled 5-bromodopa. The method devised in *Rinehart*'s group for carrying out biosynthetic studies with sponges of the order Verongida [2] offers opportunities for such an investigation.

We thank Dr. *H. Zibrowius* for aid in collecting the sponge, Mr. *A. Slomp* for skilled technical assistance with the mass spectra, Dr. *R. De Clauser* for the bioassays, and, for financial support, the *Provincia Autonoma di Trento, Assessorato Agricoltura* (project on the biological control of phytopathogenesis), *CNR* and *MPI* (Roma), and *NATO* (Bruxelles).

## Experimental Part

1. *General Remarks. A. cavernicola* was collected in August 1984 in the place already described and was extracted accordingly [4a]. Reverse-phase flash chromatography: by suction on *Merck LiChrosorb-RP-18*, 25-40 μm. Reverse-phase HPLC: 25 × 1-cm or 25 × 0.4-cm *Merck-LiChrosorb-RP-18* (7 μm) columns, solvent flow 5 ml/min or 1 ml/min, resp. monitoring by UV absorption at 254 nm. Polarimetric measurements: *JASCO-DIP-181* polarimeter. UV spectra ($\lambda_{max}$ in nm, $\varepsilon$ in $mol^{-1}\,l\,cm^{-1}$): *Beckman-DB-4* spectrometer. $^1$H-NMR spectra: *Varian-XL-300* spectrometer (at 300 MHz); $\delta$'s (ppm) relative to internal $Me_4Si$ ( = 0 ppm), coupling constants $J$ in Hz; long-range couplings are fully supported by double-irradiation experiments. $^{13}$C-NMR spectra: *Varian-CFT20* spectrometer (at 20 MHz with a microinsert); multiplicities by off-resonance decoupling. MS (DEI [6] or charge-exchange): home-made spectrometer built on a *ELFS-4-162-8-Extranuclear* quadrupole or *VG ZAB2F* mass spectrometer, allowing both linked scans ($B/E$ and $B^2/E$) and accurate mass measurements (peak-matching technique); $m/z$ value (rel. intensity). Biassays were carried out by the *Petri*-disc zonal inhibition technique at the dosis of 100 μg of test compound per disc.

2. *7-Bromocavernicolenone* ( = *7-Bromo-1,5-dihydroxy-2-azabicyclo[3.3.1]non-6-en-3,8-dione*; **3**). The residue (18.8 g) from evaporation of the BuOH extract of the sponge [4a] was reverse-phase flash chromatographed (∅ = 6 cm, l = 6 cm; *LiChrosorb*) with $H_2O$/MeOH (increasing MeOH content). The fraction eluted with $H_2O$/MeOH 95:5 containing **3** together with the known [4d] *(±)-3-bromoverongiaquinol* ((±)-**2**; $X^1$ = Br, $X^2$ = H) and nearly racemic *5-bromo-* (**1**; $X^1$ = Br, $X^2$ = H) and *5-chlorocavernicolin* (**1**; $X^1$ = Cl, $X^2$ = H)[6]) was subjected to reverse-phase HPLC (25 × 1 cm) with $H_2O$/tetrahydrofuran 98:2 to give **3** as a viscous oil ($t_R$ 10.2 min) which slowly crystallized (0.016% of dry sponge weight). Recrystallization from MeOH at r.t. by slow evaporation gave **3** as colourless needles (*ca.* 0.2 × 0.1 mm), m.p. 165-170° (dec.), suitable for X-ray diffraction analysis. No [α] from 589 to 365 nm ($c$ = 0.23, MeOH). UV (MeOH): 254 (2600). $^1$H-NMR ($CD_3OD$): 7.43 (*X* of *ABMNX*, $J$(6, 9a) = 2.2, H–C(6)); 2.64 (*MN* of *ABMNX*, appearing as br. *s*, 2H–C(4)); 2.43 (*A* of *ABMNX*, $H_b$–C(9)); 2.31 (*B* of

[6]) Known [4d] dihaloverongiaquinols and dihalocavernicolins were eluted together with $H_2O$/MeOH either 9:1 or 8:2.

*ABMNX*, $H_a$–C(9)); $J$(9a, 9b) = 12.5, $J$(9a, 6) = 2.2, $J$(9b, 4α) too small to be measured. $^{13}$C-NMR ($(CD_3)_2SO$): 187.8 (*s*, C(8)); 168.3 (*s*, C(3)); 156.9 (*d*, C(6)); 118.8 (*s*, C(7)); 80.9 (*s*, C(1)); 69.5 (*s*, C(5)); 46.6 (*t*, C(9)); 43.1 (*t*, C(4)). MS: 264, 262 (2.7 each, $(M + 1)^+$); 263, 261 (1.4 each, $M^+$); 247,245 (7 each, $((M + 1) - 17)^+$); 246, 244 (1.5 each, $M^+ - 17$); 235, 233 (23 each, $M^+ - 28$); 218, 216 (19 each; HR: 215.9613±0.01, $C_7H_7BrNO_2$, calc. 215.9660; $(244 - CO)^+$); 204, 202 (5 each, 244 – 42); 203, 201 (16 each, 244 – 43); 182 (70; HR: 182.0439 ± 0.005; $C_8H_8NO_4$, calc. 182.0453; $(261 - Br)^+$); 165 (7, $(182 - 17)^+$); 154 (12, $(233 - 79)^+$); 136 (68; HR: 136.0480±0.01, $C_7H_6NO_2$, calc. 136.0398; $(216 - HBr)^+$); 59 (100); 53 (48); 44 (61); 43 (59); *B*/*E* on 261 gave 244, 233, and 182; *B*/*E* on 245 gave 217, 202, and 201; *B*/*E* on 216 gave 136; *B*/*E* on 182 gave 165; $B^2/E$ on 136 gave 154, 165, and 216; $B^2/E$ on 182 gave 261 and 263.

3. *Acetylation of* **3.** To **3** (0.002 g) was added 1 drop of $Ac_2O$ and pyridine (20 µl) at r.t. After one night, the mixture was subjected to reverse-phase HPLC (25 × 0.4 cm) with $H_2O$/MeOH, gradient elution from 7:3 to 1:1 within 12 min, to give *bromocavernicolenone acetate-A* (**4a**) at 6.3 min and *bromocavernicolenone acetate-B* (**4b**) at 10.2 min. Data of **4a**: $^1$H-NMR ($CDCl_3$): 7.52 (*X* of *AFGMQX*, appearing as *d*, $J$(6, 9a) = 2.4, H–C(6)); 6.0 (*Q* of *AFGMQX*, appearing as br. *s*, NH); 4.7 (br. *s*, OH); 3.10 (*M* of *AFGMQX*, $J$(9b, 9a) = 12.2, $J$(9b, 4α) = 2.4, $J$(9b, 2) = 2.4, $H_b$–C(9)); 2.97 (*F* of *AFGMQX*, $J$(4α, 4β) = 17.1, $J$(4α, 9b) = 2.4, Hα–C(4)); 2.90 (*G* of *AFGMQX*; $J$(4β, 4α) = 17.1, $H_β$–C(4)); 2.52 (*A* of *AFGMQX*, $J$(9a, 9b) = 12.2, $J$(9a, 6) = 2.4, $H_a$–C(9)); 2.13 (*s*, $CH_3$). MS: 306, 304 (0.2 each, $(M + 1)^+$); 305, 303 (0.5 each, $M^+$); 246, 244 (3.5 each, $((M + 1) - AcOH)^+$); 245, 243 (21 each, $(M - AcOH)^+$); 218, 216 (5.6 each, $((M + 1) - AcOH - 28)^+$); 217, 215 (3.6 each, $(M - AcOH - 28)^+$); 203, 201 (18 each); 174, 172 (8 each); 164 (6); 136 (12); 121 (12); 57 (25); 55 (27); 43 (100).

Data of **4b**: $^1$H-NMR: practically superimposable to that for **4a.** MS: as for **4a** with only slight differences in intensities.

4. *Crystal Structure of* **3.** $C_8H_8BrNO_4$, $M$ = 262.06. The unit cell is monoclinic, space group $P2_1/c$, with dimensions $a$ = 10.827(6), $b$ = 11.300(6), $c$ = 7.328(6) Å, $\beta$ = 94.7(4)°, $V$ = 893.53 Å$^3$, $Z$ = 4, $D_c$ = 1.947 gcm$^{-3}$, $\mu$ = 45.4. The examination under polarized light provided the first evidence of crystalline twinning. This feature was confirmed by experimental X-ray work carried out on a *Philips PW 1100* automated diffractometer (graphite monochromator Mo$K_\alpha$ radiation). Twenty-five 'hunted' reflections [11] could be separated into two distinct groups which ultimately define two different orientation matrices ($UB_1$ and $UB_2$, respectively) of an identical unit cell. This type of twinning can be classified as TLQS (Twin Lattice Quasi Symmetry) according to

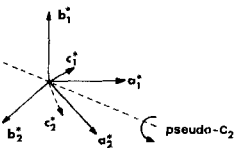



Fig. 2. *Relative orientation of two reciprocal cells for crystals of 7-bromocavernicolenone* (**3**)

*Donnay* and *Donnay* [12]. The relative orientation of the two reciprocal cells is shown in *Fig. 2*. The $a^*$ and $b^*$ vectors of both cells lie all in one plane. The relative rotation of the quadrants is 23.3°. The direct $c$ axes are common, although pointing in opposite directions. Ultimately the twins are related to each other by a pseudo two-fold axis which coincides with the bisector of the angle between the two $a^*$ axes. A complete set of data was recorded only for one twin. In order to identify the reflections which may be affected by some overlap with a reflection of the other twin, the following considerations were applied. The coordinates $x$, $y$, $z$ ($x$) of the general reflection $h$, $k$, $l$ ($h$) are given by the equation $x = UB \cdot h$. Two overlapping reflections correspond to a unique set of coordinates $x$, so that $UB_2 \cdot h_2 = UB_1 \cdot h_1$. For each $h_1$ reflection, a corresponding triple of values $h_2$ may be calculated by the equation: $h_2 = UB_2^{-1} \cdot UB_1 \cdot h_1$. Only when $h_2$ corresponds to a triple of integer numbers is there a net overlap between the two actual reflections. However, in order to account also for partial overlap, all the $h_2$ triples whose components are within ± 5% of the nearest integer were considered to affect the intensity of $h_1$. A computer program, written specifically for this problem, showed that such a condition is observed about 50 times. In such cases, the symmetry related reflection ($h$, $-k$, $l$) of $h_1$ was measured, because it was free of the overlap problem. Although all of the reflections used for calculations do not belong to an unique portion of the reciprocal space, this solution avoided the painful procedure or determining the relative weight of the overlapping $h_1$ and $h_2$ reflections.

Of the 2865 independent reflections which were collected up to a 2$\theta$ angle of 60° ($\omega - 2\theta$ scan technique) 1227 had $I > 3\sigma(I)$. The intensities were corrected also for absorption. This was technically possible because the

faces {−100} and {0 − 10} of one twin practically coincide with the faces {−1−10} and {−110} of the other twin, and the faces {001} are common. Ultimately, all of the faces of the crystal may be described by the indexes {001}, {00−1}, {−110}, {−1−10}, {100}, and {0−10} of one individual. The structure was solved by *Patterson* and *Fourier* methods by using the package of programs SHELX-76 [13]. The assignment of each individual atom was done not only on the basis of the chemical information available, but also on the basis of the behaviour of the thermal ellipsoids upon least-squares refinement. As an example, the OH groups were identified because N- in place of O-atoms led to unusually low temperature factors in the least-squares cycles. Practically all of the H-atoms could be located from $\Delta F$ maps. There was no apparent ill-behaviour in their refinement, although the associated standard deviations are high. The final $R$ factor is 0.062 ($R_w = 0.063$). Since a $\Delta F$ map at this stage did not reveal any unusual feature (highest peak 0.2 $e/Å^3$), the refinement was considered finished. *Table 2* reports the coordinates of all the non-H-atoms[7]).

Table 2. *Atomic Coordinates of the non-H-Atoms of* **3**[a])

| Atom | $x$ | $y$ | $z$ | Atom | $x$ | $y$ | $z$ |
|---|---|---|---|---|---|---|---|
| C(1) | 3865(8) | 9678(8) | 2351(12) | C(8) | 3771(8) | 11042(7) | 2614(11) |
| N(2) | 3276(8) | 9418(7) | 498(12) | C(9) | 3198(9) | 9030(9) | 3766(12) |
| C(3) | 2060(8) | 9171(8) | 111(12) | O(1) | 5134(6) | 9418(6) | 2368(10) |
| C(4) | 1289(9) | 8879(8) | 1627(13) | O(3) | 1607(7) | 9157(7) | 1517(9) |
| C(5) | 1828(8) | 9336(7) | 3481(12) | O(5) | 1151(7) | 8784(6) | 4847(10) |
| C(6) | 1667(9) | 10661(7) | 3546(13) | O(8) | 4627(6) | 11712(5) | 2375(11) |
| C(7) | 2520(8) | 11429(8) | 3130(12) | Br(7) | 2232(1) | 13066(1) | 3124(2) |

[a]) Coordinates multiplied by $10^4$, temperature factors by $10^3$.

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