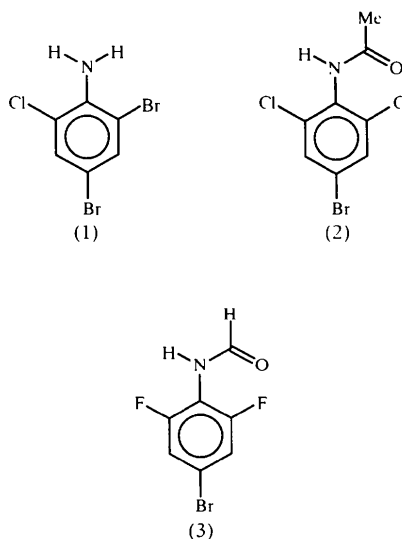


- Ferguson, G. (1998). *PREP8. A WordPerfect-5.1 Macro to Merge and Polish CIF Format Files from NRCVAX and SHELXL97 Programs*. University of Guelph, Canada.
- Ferguson, G., Carroll, C. D., Glidewell, C., Zakaria, C. M. & Lough, A. J. (1995). *Acta Cryst.* **B51**, 367–377.
- Ferguson, G., Gallagher, J. F., Glidewell, C., Low, J. N. & Scrimgeour, S. N. (1992). *Acta Cryst.* **C48**, 1272–1275.
- Ferguson, G., Glidewell, C. & Patterson, I. L. J. (1996). *Acta Cryst.* **C52**, 420–423.
- Ferguson, G., Glidewell, C. & Zakaria, C. M. (1994). *Acta Cryst.* **C50**, 928–931.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
- Glidewell, C. & Ferguson, G. (1994). *Acta Cryst.* **C50**, 924–928.
- Johnson, C. K. (1976). *ORTEP II*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Lindner, H. J. & von Gross, B. (1973). *Chem. Ber.* **106**, 1033–1037.
- Morton, A. A. & Brachman, A. E. (1954). *J. Am. Chem. Soc.* **76**, 2973–2980.
- Seip, H. M. & Seip, R. (1973). *Acta Chem. Scand.* **27**, 4024–4027.
- Sheldrick, G. M. (1997a). *SHELXL97. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
- Sheldrick, G. M. (1997b). *SHELXS97. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
- Spek, A. L. (1998). *PLATON. Molecular Geometry and Graphics Program*. Version of June 1998. University of Utrecht, The Netherlands.
- Wilson, A. J. C. (1993). *Acta Cryst.* **A49**, 795–806.

Comment

The aniline derivatives (1) and (2) arose as minor by-products in a synthetic scheme; compound (3) was synthesized by an unequivocal route. The X-ray analyses were undertaken to establish their structures and to provide details of their conformation and hydrogen bonding. Molecule (1) is isomorphous with 2,4,6-tribromoaniline (Christensen & Stromme, 1969). Molecule (2) is isostructural with *N*-acetyl-2,4,6-trichloroaniline, (4) (Nyburg *et al.*, 1987).



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2,4,6-Halogeno-Aniline Derivatives

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Abstract

The title compounds, 2,4-dibromo-6-chloroaniline, C₆H₄-Br₂ClN, (1), *N*-acetyl-4-bromo-2,6-dichloroaniline [alternative name: 4'-bromo-2',6'-dichloroacetanilide], C₈H₆-BrCl₂NO, (2), and *N*-formyl-4-bromo-2,6-difluoroaniline [alternative name: *N*-(4-bromo-2,6-difluorophenyl)formamide], C₇H₄BrF₂NO, (3), all have at least one short cell axis (in the range 4.2–4.7 Å) and contain molecules which are linked to form infinite chains along the short-axis directions via N—H...N or N—H...O hydrogen bonds. Compound (1) has halogen disorder at the 2 and 6 positions.

Views of the three molecules are presented in Fig. 1. In (1), the sizes of the electron-density maxima at the *ortho* sites were consistent with an unequal disorder of Br and Cl atoms; refinement showed that the ratio was 0.639 (4)/0.361 (4). This disorder effectively precludes any meaningful discussion of ring dimensions. Compounds (2) and (3) show the typical variation in benzene ring internal angles found in polyatomic substituted benzene rings, with the rings showing *2mm* symmetry about the Cl...C4 axis at a 3σ significance level (Domenicano, 1992); the mean internal angles at the *ortho* and *para* sites exceed 120°, while those at the 1 and *meta* positions are smaller (Table 1).

The amount by which the group at Cl1 is rotated out of the aromatic ring plane in each molecule is of interest. For (1), difference maps showed that the H atoms of the NH₂ group lay approximately in the aromatic ring plane. For (2), the plane of the *N*-acetyl group is rotated 60.97 (14)° from coplanarity with the aromatic ring; for (3), the corresponding value for the rotation of the *N*-formyl group is 57.3 (3)°. Details of the relevant torsion angles in (2) and (3), along with those of (4) for comparison, are given in Table 2. All three compounds adopt a conformation by which the carbonyl group is *cis* to the exocyclic C—N bond.

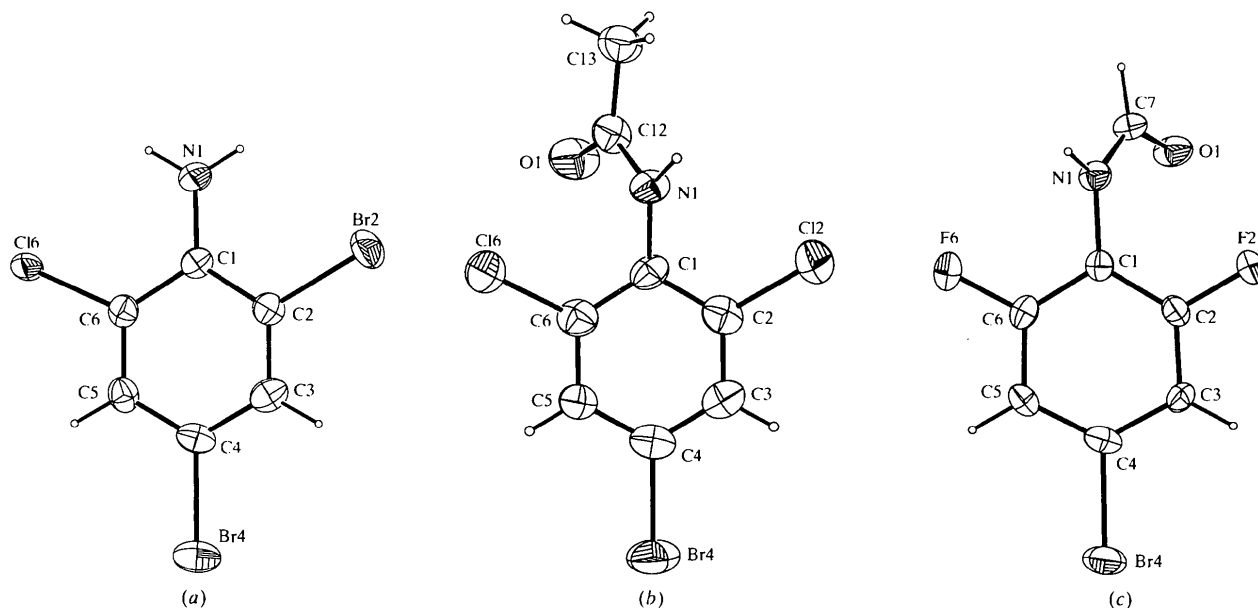


Fig. 1. Views of (a) compound (1), (b) compound (2) and (c) compound (3), with the adopted numbering schemes. Displacement ellipsoids are drawn at the 30% probability level. For (1), only the major components of the disordered Br and Cl atoms at C2 and C6 are shown. For (2), the methyl H atoms are disordered and only one orientation is shown.

Examination of the structures with *PLATON* (Spek, 1998) showed that there were no solvent-accessible voids in the crystal lattices and that the molecules of all three compounds are linked to form chains *via* N—H...N hydrogen bonds in (1), and N—H...O hydrogen bonds in (2) and (3) (details are given in Table 3). Although compound (4) crystallizes in space group *Pn*, its packing employs the N—H...O motif to generate chains *via* the *n*-glide operation.

Experimental

2,4-Dibromo-6-chloroaniline, (1), and *N*-acetyl-4-bromo-2,6-dichloroaniline, (2), were isolated by chromatography as by-products in the synthesis of 4-bromo-2-chloro-6-iodoaniline from *N*-acetylaniline (acetanilide), using the following reaction sequence: (i) Br₂ in AcOH, (ii) HCl and NaClO₃ in AcOH, (iii) HCl, (iv) NaOH and (v) IBr in AcOH. Compound (1) was recrystallized from EtOH; m.p. 367–369 K [literature m.p. 368 K (Chattaway & Orton, 1901)]. Compound (2) was recrystallized from EtOH; m.p. 477–480 K [literature m.p. 481–482 K (Godfrey & Thrift, 1967) and 477–478 K (Reed & Orton, 1907)]. Compound (3) was prepared by formylation of 4-bromo-2,6-difluoroaniline (Aldrich) with acetic formic anhydride in acetic acid following the method of Heubner *et al.* (1966). Compound (1) was subsequently obtained by the bromination of 2-chloroaniline (Chattaway & Orton, 1901); (2) was readily synthesized directly from *N*-acetyl-4-bromophenylaniline (4-bromophenylacetanilide) and sodium chlorate (2 equivalents) in a hydrochloric acid/acetic acid medium at 273 K.

Compound (1)

Crystal data

C₆H₄Br₂ClN
M_r = 285.37
 Orthorhombic
*P*2₁2₁2₁
a = 4.1787 (5) Å
b = 13.245 (2) Å
c = 14.856 (3) Å
V = 822.2 (3) Å³
Z = 4
D_x = 2.305 Mg m⁻³
D_m not measured

Data collection

Enraf–Nonius CAD-4
 diffractometer
 $\theta/2\theta$ scans
 Absorption correction:
 Gaussian (*ABSO* in
NRCVAX; Gabe *et al.*,
 1989)
T_{min} = 0.107, *T_{max}* = 0.310
 3760 measured reflections
 1890 independent reflections

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.063
wR(*F*²) = 0.142

Mo *K*α radiation
 λ = 0.7107 Å
 Cell parameters from 25
 reflections
 θ = 10.02–17.28°
 μ = 10.104 mm⁻¹
T = 294 (1) K
 Plate
 0.42 × 0.24 × 0.12 mm
 Purple

951 reflections with
I > 2σ(*I*)
R_{int} = 0.054
 θ_{\max} = 27.43°
h = -5 → 5
k = -16 → 17
l = -18 → 19
 3 standard reflections
 frequency: 120 min
 intensity decay: 5.6%

$\Delta\rho_{\max}$ = 0.641 e Å⁻³
 $\Delta\rho_{\min}$ = -0.604 e Å⁻³
 Extinction correction: none

$S = 0.937$
1890 reflections
111 parameters
H atoms constrained
 $w = 1/[\sigma^2(F_o^2) + (0.07P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$

Compound (2)*Crystal data*

C₈H₆BrCl₂NO
 $M_r = 282.95$
Monoclinic
C2/c
 $a = 16.7289 (15) \text{ \AA}$
 $b = 4.6993 (5) \text{ \AA}$
 $c = 25.928 (3) \text{ \AA}$
 $\beta = 95.220 (14)^\circ$
 $V = 2029.9 (4) \text{ \AA}^3$
 $Z = 8$
 $D_x = 1.852 \text{ Mg m}^{-3}$
 D_m not measured

Data collection

Enraf-Nonius CAD-4
diffractometer
 $\theta/2\theta$ scans
Absorption correction:
Gaussian (ABS_O in
NRCVAX; Gabe *et al.*,
1989)
 $T_{\min} = 0.301$, $T_{\max} = 0.709$
2376 measured reflections
2315 independent reflections

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.043$
 $wR(F^2) = 0.112$
 $S = 0.968$
2315 reflections
119 parameters
H atoms constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0662P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$

Compound (3)*Crystal data*

C₇H₄BrF₂NO
 $M_r = 236.02$
Orthorhombic
 $P2_12_12_1$
 $a = 4.5575 (5) \text{ \AA}$
 $b = 11.4987 (12) \text{ \AA}$
 $c = 15.026 (2) \text{ \AA}$
 $V = 787.42 (16) \text{ \AA}^3$
 $Z = 4$
 $D_x = 1.991 \text{ Mg m}^{-3}$
 D_m not measured

Scattering factors from
*International Tables for
Crystallography* (Vol. C)
Absolute structure:
Flack (1983)
Flack parameter = 0.46 (4)
(747 Friedel pairs)

Mo $K\alpha$ radiation
 $\lambda = 0.7107 \text{ \AA}$
Cell parameters from 25
reflections
 $\theta = 9.03\text{--}12.22^\circ$
 $\mu = 4.534 \text{ mm}^{-1}$
 $T = 294 (1) \text{ K}$
Plate
 $0.4 \times 0.2 \times 0.1 \text{ mm}$
Colourless

1534 reflections with
 $I > 2\sigma(I)$
 $R_{\text{int}} = 0.012$
 $\theta_{\max} = 27.39^\circ$
 $h = -21 \rightarrow 21$
 $k = 0 \rightarrow 6$
 $l = 0 \rightarrow 33$
3 standard reflections
frequency: 120 min
intensity decay: 1.8%

$(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.640 \text{ e \AA}^{-3}$
(adjacent to Br4)
 $\Delta\rho_{\min} = -0.333 \text{ e \AA}^{-3}$
Extinction correction: none
Scattering factors from
*International Tables for
Crystallography* (Vol. C)

Mo $K\alpha$ radiation
 $\lambda = 0.7107 \text{ \AA}$
Cell parameters from 25
reflections
 $\theta = 8.83\text{--}17.00^\circ$
 $\mu = 5.201 \text{ mm}^{-1}$
 $T = 294 (1) \text{ K}$
Lath
 $0.40 \times 0.17 \times 0.10 \text{ mm}$
Colourless

Data collection

Enraf-Nonius CAD-4
diffractometer
 $\theta/2\theta$ scans
Absorption correction:
Gaussian (ABS_O in
NRCVAX; Gabe *et al.*,
1989)
 $T_{\min} = 0.399$, $T_{\max} = 0.632$
2080 measured reflections
1792 independent reflections

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.054$
 $wR(F^2) = 0.137$
 $S = 0.975$
1792 reflections
109 parameters
H atoms constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0846P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$

1204 reflections with
 $I > 2\sigma(I)$
 $R_{\text{int}} = 0.033$
 $\theta_{\max} = 27.41^\circ$
 $h = -5 \rightarrow 5$
 $k = -14 \rightarrow 14$
 $l = -19 \rightarrow 19$
3 standard reflections
frequency: 120 min
intensity decay: 2.3%

$\Delta\rho_{\max} = 0.583 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.820 \text{ e \AA}^{-3}$
Extinction correction: none
Scattering factors from
*International Tables for
Crystallography* (Vol. C)
Absolute structure:
Flack (1983)
Flack parameter = $-0.02 (2)$
(714 Friedel pairs)

Table 1. *Internal ring angles* ($^\circ$) *in compounds (2) and (3)*

	(2)	(3)
C6—C1—C2	116.6 (3)	116.3 (6)
C1—C2—C3†	122.0 (3)	123.6 (6)
C2—C3—C4†	119.1 (3)	116.7 (6)
C3—C4—C5	121.1 (3)	123.2 (6)

† The angles at C2 and C3 are the means of (C1—C2—C3 + C1—C6—C5) and (C2—C3—C4 + C4—C5—C6), respectively.

Table 2. *Some exocyclic torsion angles* ($^\circ$) *defining the orientation of the substituent at the N atoms in (2), (3) and (4)†*

	(2)	(3)	(4)
C2—C1—N1—C7	62.0 (5)	59.2 (9)	70.7 (8)
C1—N1—C7=O	$-0.9 (6)$	$-2.8 (11)$	$-3.8 (5)$

† Nyburg *et al.* (1987).

Table 3. *Hydrogen-bond dimensions* (\AA , $^\circ$) *in compounds (1), (2) and (3)*

	D—H	H...A	D...A	D—H...A
(1)				
N1—H1A...Br2	0.86	2.61	3.033 (8)	112
N1—H1B...Cl6	0.86	2.73	3.108 (14)	109
N1—H1B...N1'	0.86	2.39	3.150 (11)	147
(2)				
N1—H1...O1 ⁱⁱ	0.86	2.01	2.829 (4)	159
(3)				
N1—H1...O1 ⁱⁱⁱ	0.86	2.00	2.802 (3)	154

Symmetry codes: (i) $-\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$; (ii) $x, y - 1, z$; (iii) $x - 1, y, z$.

Compound (1) crystallized in the orthorhombic system; space group $P2_12_12_1$ was indicated by the systematic absences. The 2-Br and 6-Cl atoms are mutually disordered, with the 2 site having occupancies Br 0.639 (4) and Cl 0.361 (4), with

complementary values at the 6 site. This was allowed for by use of suitable restraints during the refinement [with C—Br set to 1.885 (5) and C—Cl to 1.720 (5) Å]. Compound (2) crystallized in the monoclinic system; space groups *C2/c* or *Cc* were indicated by the systematic absences; *C2/c* was assumed, and confirmed by the analysis. A difference map showed the methyl H atoms as a torus of density and these H atoms were allowed for by placing six H atoms with 0.5 occupancy around the methyl C atom with appropriate geometry constraints. Compound (3) crystallized in the orthorhombic system; space group *P2₁2₁2₁* was indicated by the systematic absences. In all three compounds, H atoms were treated as riding atoms (C—H 0.93 and 0.96, N—H 0.86 Å). Compounds (1) and (3) are chiral; the analysis of (1) showed that it was best treated as a racemic twin [Flack (1983) parameter 0.46 (4)], while in the case of (3), the analysis unequivocally established the chirality of the crystal studied [Flack (1983) parameter -0.02 (2)].

For all compounds, data collection: *CAD-4-PC* (Enraf–Nonius, 1992); cell refinement: *SET4* and *CELDIM* in *CAD-4-PC*; data reduction: *DATRD2* in *NRCVAX96* (Gabe *et al.*, 1989); program(s) used to solve structures: *NRCVAX96*; program(s) used to refine structures: *NRCVAX96* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *NRCVAX96*, *ORTEPII* (Johnson, 1976) and *PLATON* (Spek, 1998); software used to prepare material for publication: *NRCVAX96*, *SHELXL97* and *PRCIF97* (Ferguson, 1997).

We are indebted to Dr J. F. Gallagher and Dublin City University for funds to purchase the X-ray tube used in the data collections. While no direct support for this work was provided by NSERC Canada, we do acknowledge that organization for partially funding the 1992 upgrade of the CAD-4 diffractometer.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1221). Services for accessing these data are described at the back of the journal.

References

- Chattaway, F. D. & Orton, K. J. P. (1901). *J. Chem. Soc.* **79**, 818–826.
 Christensen, A. T. & Stromme, K. O. (1969). *Acta Cryst.* **B25**, 657–664.
 Domenicano, A. (1992). *Accurate Molecular Structures*, edited by A. Domenicano & I. Hargittai, ch. 18, pp. 437–468. International Union of Crystallography and Oxford University Press.
 Enraf–Nonius (1992). *CAD-4-PC Software*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.
 Ferguson, G. (1997). *PRCIF97. A WordPerfect-5.1 Macro to Merge and Polish CIF Format Files from NRCVAX and SHELXL97 Programs*. University of Guelph, Canada.
 Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
 Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
 Godfrey, K. E. & Thrift, R. I. (1967). *J. Chem. Soc. C*, pp. 400–404.
 Heubner, C. F., Donoghue, E. M., Plummer, A. J. & Furness, P. A. (1966). *J. Med. Chem.* **9**, 830–832.
 Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
 Nyburg, S. C., Fawcett, J. K. & Szymanski, J. T. (1987). *Acta Cryst.* **C43**, 2452–2453.
 Recd, W. W. & Orton, K. J. P. (1907). *J. Chem. Soc.* **91**, 1543–1554.
 Sheldrick, G. M. (1997). *SHELXL97. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Spek, A. L. (1998). *PLATON. Molecular Geometry and Graphics Program*. Version of June 1998. University of Utrecht, The Netherlands.

Acta Cryst. (1998). **C54**, 1977–1980

(–)-Tetrahydropalmatine Monohydrate

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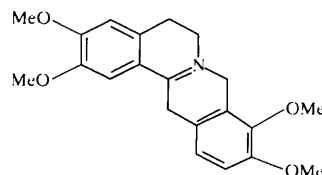
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Abstract

The title compound, C₂₁H₂₅NO₄·H₂O, was isolated from the rhizome of *Stefania rotunda* L. of Vietnam and its structure elucidated. An *S* configuration was found at the asymmetric C13 atom of the (–)-enantiomer. The water molecule generates infinite helically arranged molecular columns around the screw axes in the *z* direction through intermolecular hydrogen bonds.

Comment

Tetrahydropalmatine, (1), is an alkaloid of the protoberberine type which can be isolated from different plants (Glasby, 1975; Ribár *et al.*, 1993). The sample used for this study was isolated from the Vietnamese plant *Stefania rotunda* L. (Menispermaceae family), which grows wild among limestone rocks at Cuc Phuong National Park. It is used in Vietnamese folk medicine for its activity against insomnia, stomach-ache, headache, asthma and fever. The main alkaloid, (–)-tetrahydropalmatine, is preserved for neuroasthenia and psychoses. Since the chemical identity of (–)-tetrahydropalmatine was originally not known, its X-ray structure was elucidated.



(1)