Table 3. *Torsion angles* (°) *and dihedral angles* (°) *between planes*

Torsion angles

	(I)	(II)	(III)	(IV)
C(1)—C(2)—C(3)—C(4)	−148 (1)	−146 (2)	−90 (5)	−137·0 (6)
C(1)—C(2)—C(3)—C(7)	141 (2)	141 (2)	−161 (4)	151·0 (6)
C(3)—C(7)—C(8)—O(9)	41 (2)	36 (3)	39 (6)	26·2 (4)
C(4)—C(7)—C(8)—O(9)	−30 (3)	−36 (3)	−36 (6)	−45·0 (5)
O(9)—C(8)—O(10)—C(11)	5 (2)	6 (2)	7 (5)	7·0 (4)
C(8)—O(10)—C(11)—C(12)	93 (2)	95 (2)	104 (3)	159·6 (5)
O(10)—C(11)—C(12)—C(13)	7 (2)	3 (2)	−106 (3)	−106·2 (5)
C(13)—C(14)—O(18)—C(19)	−30 (2)	−27 (3)	−136 (3)	−160·0 (6)
C(14)—O(18)—C(19)—C(24)	−55 (2)	−56 (2)	21 (5)	−132·3 (6)

Dihedral angles between planes

Planes*	(I)	(II)	(III)	(IV)
(1)—(2)	114	116	35	48
(1)—(3)	137	134	90	54
(1)—(4)	115	116	92	64
(2)—(3)	81	80	78	75
(2)—(4)	11	10	126	61
(3)—(4)	73	72	124	118

* These planes are defined in the deposited material.

The resulting atomic coordinates appear in Table 1* and the atom numbering in Fig. 1. Table 2 shows the bond lengths and angles. The absolute configuration of (IV) has not been established for this structure determination but is known to be *cis* (1*R*,2*R*) for the cyclopropane and *S* for the benzylic α-C atom.

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and least-squares planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53356 (27pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. According to the substituents (X = Br, Cl and R = CN, H), we have four different pyrethroid molecules. Planes and torsion angles are defined as in Owen (1976). From Table 3, it is seen that two molecular conformations dominate in these four molecules. (I) is similar to (II) but different from (III) and (IV). The conformation of the molecule is certainly more dependent on the R substituent (CN, H) than the X one (Cl, Br).

Molecule (IV) (X = Cl, R = CN, our study) is more elongated than (III) where the Br atoms are pushed far away from the CN group due to electronic repulsion [torsion angles C(1)—C(2)—C(3)—C(4) and C(1)—C(2)—C(3)—C(7) are −90 (III), −137 (IV), −161 (III), 151° (IV)]. The crystal structures of the pyrethroids evoked here show that there is a certain degree of flexibility at each end of the molecule with the ester linkage in the middle forming a fairly rigid entity.

No intermolecular distances between molecules are less than the sum of the van der Waals radii of the atoms involved.

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Structure of 5-Methoxy-3-(1-methylethoxy)-1-phenyl-*N*-(1*H*-tetrazol-5-yl)-1*H*-indole-2-carboxamide–Diethylamine, a Potential Anti-Allergy Agent

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Abstract. $C_{24}H_{31}N_7O_3$, M_r = 465·56, monoclinic, $P2_1/n$, a = 14·439 (3), b = 9·147 (2), c = 19·207 (5) Å, β = 90·89 (2)°, V = 2536·4 Å^3, Z = 4, D_x = 1·219 Mg m^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, μ = 0·078 mm^{-1}, $F(000)$ = 992, T = 293 K, final R = 0·052 for 2731 observed reflections with $I > 3\sigma(I)$. The indole moiety is essentially planar, with the phenyl ring inclined at 68·03 (8)° to it. The tetrazole

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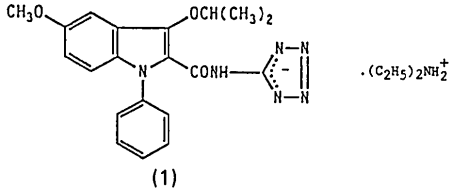
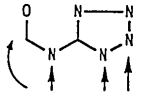
ring is also planar with the mean planes of the tetrazole ring and the indole moiety lying at 10·8 (4)°. The carboxamide chain is fully extended with a CC—NC torsion angle of 174·9 (3)°. The drug anion and the diethylammonium cation are hydrogen bonded.

Introduction. Our efforts to discover anti-allergy drugs have led to the identification of a series of indolecarboxamidotetrazoles which are potent inhibitors of allergic mediator release from human basophils and from guinea pig and human chopped lung tissue challenged with anti-IgE (Unangst, Connor, Stabler, Weikert, Carethers, Kennedy, Thueson, Chestnut, Adolphson & Conroy, 1989). The title compound (1) was selected from this series



(1)

and evaluated in the clinic as its arginine salt (CI-949). A search of version 3.5 of the Cambridge Crystallographic Database (Allen, Kennard & Taylor, 1983) using fragment (2) (single, delocalized or aromatic bond types allowed) resulted in no entries found containing (2). The crystal and molecular structure of (1), as its diethylamine salt, was determined to assist molecular-modeling studies in understanding the structural and conformational features necessary for inhibition of allergic mediator release.



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(2)

Experimental. A suspension of 5·0 g (0·013 mol) of the parent carboxamidotetrazole (Unangst, Connor, Stabler, Weikert, Carethers, Kennedy, Thueson, Chestnut, Adolphson & Conroy, 1989) in 20 ml of absolute ethanol was warmed on the steam bath and treated with 5·0 ml (3·5 g; 0·048 mol) of diethylamine. The warm mixture was alternately treated with methanol and water until homogeneous (final volume ~225 ml). After hot filtration and cooling to room temperature, crystals of the diethylamine salt suitable for analysis were collected and washed with acetone to yield 4·1 g (69% yield), m.p. 488 K dec.

Table 1. *Summary of data collection and structure refinement*

Crystal size (mm)	0·16 × 0·27 × 0·45
Diffractometer	Enraf–Nonius CAD-4
Monochromator	Graphite
Cell constants	25 reflections, $10 < \theta < 15°$
θ_{max} (°)	25
Scan method	$\omega/2\theta$
ω-scan width (°)	$0{\cdot}75 + 0{\cdot}35\tan\theta$
Variable scan speed (° min^{-1})	1·25–3·30
Scan ranges of h, k, l	0→17, 0→10, −22→22
Intervals of standard reflections (s)	7200
Crystal decay (%)*	1·8
Data correction applied†	Lorentz and polarization
Unique data measured	4452
Data used [$I > 3\sigma(I)$]	2731
R_{int}	0·013
Parameters refined	307
R, wR	0·052, 0·076
Weighting scheme	$w = [\sigma^2(F_o) + (0{\cdot}080\ F_o)^2]^{-1}$
$(\Delta/\sigma)_{max}$ in last cycle	< 0·1
$\Delta\rho$, in final ΔF map (e Å^{-3})	± 0·16
S	1·556

* Linear decay, corrected for by appropriate scaling.
† Absorption ignored.

Details of data collection and structure refinement are given in Table 1. The structure was solved by direct methods (*MULTAN*11/82; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and refined by full-matrix least-squares calculations on F's. H atoms were located from a difference map and included at these positions in the structure-factor calculations with the overall isotropic temperature factor $B_{iso} = 4{\cdot}0$ Å^2; C, N and O had anisotropic temperature factors. Scattering factors used in the calculations were taken from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965). Computer programs used in this study were from the Enraf–Nonius *Structure Determination Package* (B. A. Frenz & Associates, Inc., 1985) and *ORTEP*II (Johnson, 1976).

Discussion. Final fractional coordinates and equivalent isotropic thermal parameters with e.s.d.'s are listed in Table 2.* Table 3 contains bond lengths and angles. Fig. 1 shows the molecular structure of the title compound. Fig. 2 is a stereoview of the unit-cell packing. The indole moiety is essentially planar with maximum deviation of any atom 0·026 (3) Å. The phenyl ring is also planar [max. deviation 0·005 (4) Å] and is oriented at 68·03 (8)° to the indole moiety. The tetrazole ring is planar to within 0·005 (3) Å and is linked to the indole moiety through a fully extended carboxamide group which exhibits a C7C9—N2C10 torsion angle of 174·9 (3)°.

* Lists of structure factors, anisotropic thermal parameters, least-squares-planes data and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53305 (35 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Final fractional coordinates and equivalent isotropic thermal parameters* (Å^2) *with e.s.d.'s in parentheses*

$$B_{eq} = a^2B_{11} + b^2B_{22} + c^2B_{33} + ab\cos\gamma B_{12} + ac\cos\beta B_{13} + bc\cos\alpha B_{23}.$$

	x	y	z	B_{eq}
O1	−0·0749 (1)	0·0355 (3)	0·6200 (1)	4·69 (5)
O2	0·2269 (1)	0·4093 (3)	0·6798 (1)	3·66 (4)
O3	0·3022 (2)	0·6450 (3)	0·4975 (1)	5·53 (5)
N1	0·1664 (2)	0·4194 (3)	0·4994 (1)	3·25 (5)
N2	0·3491 (2)	0·5881 (3)	0·6068 (1)	3·80 (5)
N3	0·4443 (2)	0·7888 (3)	0·5690 (1)	4·01 (6)
N4	0·5103 (2)	0·8664 (3)	0·6033 (1)	4·22 (6)
N5	0·5198 (2)	0·8185 (3)	0·6666 (1)	4·43 (6)
N6	0·4611 (2)	0·7052 (3)	0·6763 (1)	4·06 (6)
N7	0·3846 (2)	−0·1162 (3)	0·4310 (1)	3·47 (5)
C1	0·1121 (2)	0·3021 (3)	0·5945 (1)	2·96 (5)
C2	0·0539 (2)	0·2050 (3)	0·6308 (1)	3·27 (6)
C3	−0·0148 (2)	0·1354 (4)	0·5933 (2)	3·59 (6)
C4	−0·0284 (2)	0·1635 (4)	0·5216 (2)	3·93 (7)
C5	0·0279 (2)	0·2556 (4)	0·4861 (1)	3·65 (6)
C6	0·0991 (2)	0·3243 (3)	0·5233 (1)	3·15 (6)
C7	0·2216 (2)	0·4593 (3)	0·5563 (1)	3·16 (6)
C8	0·1896 (2)	0·3905 (3)	0·6142 (1)	2·99 (6)
C9	0·2939 (2)	0·5714 (4)	0·5493 (1)	3·43 (6)
C10	0·4175 (2)	0·6929 (3)	0·6160 (1)	3·01 (6)
C11	−0·0516 (3)	−0·0230 (5)	0·6859 (2)	5·85 (9)
C12	0·1850 (2)	0·4416 (3)	0·4269 (1)	3·05 (6)
C13	0·1235 (2)	0·5189 (4)	0·3869 (2)	4·16 (7)
C14	0·1411 (3)	0·5379 (5)	0·3164 (2)	5·58 (9)
C15	0·2183 (3)	0·4794 (5)	0·2881 (2)	5·79 (9)
C16	0·2793 (2)	0·4028 (5)	0·3282 (2)	5·54 (9)
C17	0·2633 (2)	0·3816 (4)	0·3979 (2)	4·46 (7)
C18	0·1644 (2)	0·4723 (4)	0·7311 (2)	4·63 (8)
C19	0·2207 (4)	0·4903 (5)	0·7958 (2)	7·6 (1)
C20	0·1198 (3)	0·6099 (6)	0·7052 (2)	8·1 (1)
C21	0·4009 (3)	−0·2203 (4)	0·3730 (2)	4·92 (8)
C22	0·4907 (3)	−0·2970 (6)	0·3800 (2)	7·4 (1)
C23	0·2903 (2)	−0·0501 (4)	0·4307 (2)	4·36 (7)
C24	0·2742 (3)	0·0300 (5)	0·4967 (2)	5·77 (9)

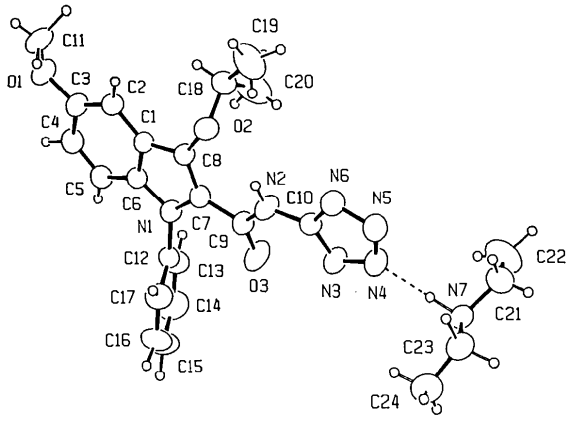

Fig. 1. *ORTEP* drawing of the drug anion and diethylammonium cation showing hydrogen bond.

Table 3. *Bond distances* (Å) *and bond angles* (°)

O1	C3	1·366 (4)		C1	C6	1·393 (4)	
O1	C11	1·409 (4)		C1	C8	1·427 (4)	
O2	C8	1·372 (3)		C2	C3	1·372 (4)	
O2	C18	1·465 (4)		C3	C4	1·412 (4)	
O3	C9	1·209 (4)		C4	C5	1·361 (4)	
N1	C6	1·387 (4)		C5	C6	1·393 (4)	
N1	C7	1·392 (3)		C7	C8	1·366 (4)	
N1	C12	1·435 (3)		C7	C9	1·470 (4)	
N2	C9	1·359 (4)		C12	C13	1·362 (4)	
N2	C10	1·385 (4)		C12	C17	1·381 (4)	
N3	N4	1·351 (4)		C13	C14	1·393 (4)	
N3	C10	1·322 (4)		C14	C15	1·357 (5)	
N4	N5	1·298 (4)		C15	C16	1·356 (5)	
N5	N6	1·353 (4)		C16	C17	1·377 (5)	
N6	C10	1·316 (3)		C18	C19	1·482 (5)	
N7	C21	1·487 (4)		C18	C20	1·495 (6)	
N7	C23	1·490 (4)		C21	C22	1·479 (6)	
C1	C2	1·414 (4)		C23	C24	1·486 (5)	
C3	O1	C11	116·6 (2)	N1	C7	C9	120·7 (2)
C8	O2	C18	115·5 (2)	C8	C7	C9	130·1 (3)
C6	N1	C7	107·4 (2)	O2	C8	C1	127·6 (2)
C6	N1	C12	123·5 (2)	O2	C8	C7	123·9 (3)
C7	N1	C12	127·7 (2)	C1	C8	C7	108·6 (2)
C9	N2	C10	126·1 (3)	O3	C9	N2	122·8 (3)
N4	N3	C10	103·1 (2)	O3	C9	C7	122·8 (3)
N3	N4	N5	110·1 (3)	N2	C9	C7	114·4 (2)
N4	N5	N6	109·3 (2)	N2	C10	N3	126·0 (2)
N5	N6	C10	103·7 (2)	N2	C10	N6	120·2 (3)
C21	N7	C23	114·3 (2)	N3	C10	N6	113·8 (3)
C2	C1	C6	120·2 (3)	N1	C12	C13	119·3 (3)
C2	C1	C8	134·0 (2)	N1	C12	C17	120·1 (3)
C6	C1	C8	105·7 (2)	C13	C12	C17	120·6 (3)
C1	C2	C3	117·6 (3)	C12	C13	C14	119·1 (3)
O1	C3	C2	124·8 (3)	C13	C14	C15	120·2 (3)
O1	C3	C4	114·1 (3)	C14	C15	C16	120·4 (3)
C2	C3	C4	121·0 (3)	C15	C16	C17	120·6 (3)
C3	C4	C5	121·8 (3)	C12	C17	C16	119·1 (3)
C4	C5	C6	117·7 (3)	O2	C18	C19	105·8 (3)
N1	C6	C1	109·4 (2)	O2	C18	C20	111·9 (3)
N1	C6	C5	128·9 (3)	C19	C18	C20	114·4 (4)
C1	C6	C5	121·6 (3)	N7	C21	C22	112·6 (3)
N1	C7	C8	108·8 (2)	N7	C23	C24	110·6 (3)

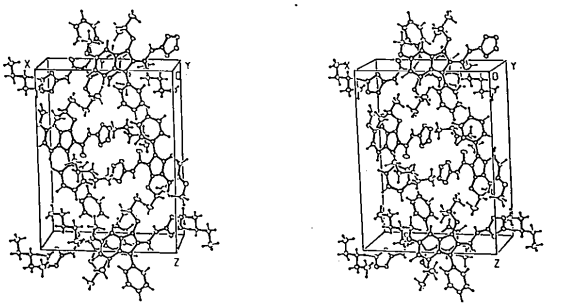

Fig. 2. Stereoview of a unit cell showing molecular packing.

The bond distances and angles in the indole moiety and its substituents, phenyl, methoxy and methylethoxy groups, are unexceptional. There is a delocalized negative charge on the tetrazole ring resulting in essentially equivalent ring C—N distances [1·316 (3) and 1·322 (4) Å]. The distance N4—N5 1·298 (4) Å is clearly indicative of a double bond, which is significantly shorter than N3—N4 and N5—N6 bonds [1·351 (4) and 1·353 (4) Å, respectively]. There are no unusual intermolecular distances less than van der Waals distances and the crystal appears to be composed of hydrogen-bonded

drug anions and diethylammonium cations (Fig. 2) with the N4···H1N7 distance equal to 1·81 Å and the N4···H1N7—N7 bond angle equal to 168·5°.

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Structure of 3-(1-Methylethoxy)-7-phenyl-*N*-(1*H*-tetrazol-5-yl)-2-benzofurancarboxamide, a Potential Anti-Allergy Agent

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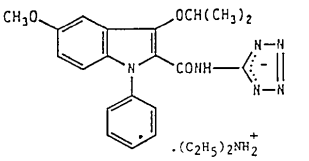
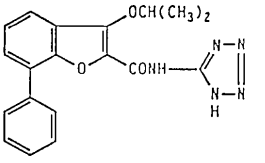
(*Received* 12 *April* 1990; *accepted* 18 *June* 1990)

Abstract. $C_{19}H_{17}N_5O_3$, $M_r = 363{\cdot}38$, monoclinic, $P2_1/n$, $a = 7{\cdot}243\ (6)$, $b = 11{\cdot}452\ (4)$, $c = 20{\cdot}552\ (4)$ Å, $\beta = 93{\cdot}93\ (3)°$, $V = 1701\ (2)$ Å^3, $Z = 4$, $D_x = 1{\cdot}419$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 0{\cdot}093$ mm^{-1}, $F(000) = 760$, $T = 293$ K, final $R = 0{\cdot}027$ for 1239 observed reflections with $I > 3\sigma(I)$. The benzofuran moiety is essentially planar with the phenyl ring inclined at 139·53 (7)° to it. The tetrazole ring is also planar with the mean planes of the tetrazole ring and the benzofuran moiety lying at 8·1 (2)°. The carboxamide chain is fully extended with a CC—NC torsion angle of 177·7 (2)°. H atoms on the N atoms are involved in short intramolecular contacts (O···H 2·058 and 2·236 Å).

Introduction. We have reported the crystal structure of 5-methoxy-3-(1-methylethoxy)-1-phenyl-*N*-(1*H*-tetrazol-5-yl)-1*H*-indole-2-carboxamide–diethylamine (1) (Parvez, Unangst, Connor & Mullican, 1991). Compound (1) is a potent inhibitor of allergic mediator release from human basophils and from guinea pig and human chopped lung tissue challenged with anti-IgE (Unangst, Connor, Stabler, Weikert, Carethers, Kennedy, Thueson, Chestnut, Adolphson & Conroy, 1989). The crystal structure of (2), a benzofuran analogue of (1), was determined to assist molecular-modeling studies in understanding the structural and conformational features necessary for inhibition of allergic mediator release.



(1)



(2)

Experimental. A mixture of 8·8 g (0·030 mol) of 3-(1-methylethoxy)-7-phenyl-2-benzofurancarboxylic acid (Connor, Cetenko, Unangst & Johnson, 1987) and 5·5 g (0·034 mol) of 1,1′-carbonylbis(1*H*-imidazole) in 180 ml of acetonitrile was stirred at reflux under a nitrogen atmosphere for 90 min. The cooled reaction mixture was treated with 3·0 g (0·035 mol) of anhydrous 5-aminotetrazole, followed by 10·0 ml (7·3 g; 0·072 mol) of triethylamine. The mixture was again stirred at reflux for 16 h, cooled, added to 750 g of ice and water, and acidified with acetic acid. The precipitated product was filtered, washed with water, and recrystallized from methanol/*N*,*N*-

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