LONGUET-HIGGINS, H. C. & COULSON, C. A. (1946). *Trans. Faraday Soc.* **42**, 756–764.
MILLS, W. H. & NIXON, I. G. (1930). *J. Chem. Soc.* pp. 2510–2524.
MURRAY-RUST, P. & MOTHERWELL, S. (1978). *Acta Cryst.* B**34**, 2518–2526.
NORRESTAM, R. & SCHEPPER, L. (1978). *Acta Chem. Scand. Ser. A*, **32**, 889–890.
SANTIAGO, C., GANDOUR, R. W., HOUK, K. N., NUTAKUL, W., CRAVEY, W. E. & THUMMEL, R. P. (1978). *J. Am. Chem. Soc.* **100**, 3730–3737.
STREITWEISER, A. JR, ZIEGLER, G. R., MOWERY, P. C., LEWIS, A. & LAWLER, R. G. (1968). *J. Am. Chem. Soc.* **90**, 1357–1358.
TSUKADA, H., SHIMANOUCHI, H. & SASADA, Y. (1978). *Bull. Chem. Soc. Jpn*, **51**, 985–991.

Acta Cryst. (1981). B**37**, 906–910

Structures of the Neuroleptic Drugs α- and β-Clopenthixol

BY PETER G. JONES AND GEORGE M. SHELDRICK

Anorganisch-Chemisches Institut der Universität, Tammannstrasse 4, 3400 *Göttingen, Federal Republic of Germany*

AND ALAN S. HORN

Department of Pharmacy, University of Groningen, Groningen, The Netherlands

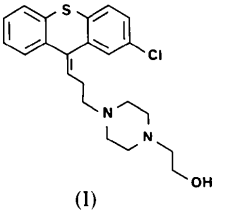
(*Received* 22 *September* 1980; *accepted* 3 *November* 1980)

Abstract

The tricyclic neuroleptic drug α-clopenthixol ($C_{22}H_{25}ClN_2OS$) is monoclinic, $P2_1/n$, with a = 11·549 (4), b = 15·739 (6), c = 11·627 (5) Å, β = 109·47 (2)°, U = 1992·6 Å^3, Z = 4. Its less potent β isomer is triclinic, $P\bar{1}$, with a = 6·493 (2), b = 7·758 (3), c = 21·881 (8) Å, α = 90·11 (2), β = 91·48 (2), γ = 92·81 (2)°, U = 1100·5 Å^3, Z = 2, and crystallizes as a dihydrate. The structures have been refined to R = 0·051 for 2503 reflexions (α) and 0·039 for 3170 reflexions (β). Various structural features of these drugs and those of the closely related α- and β-flupenthixol are compared.

Introduction

The thioxanthenes are an important group of neuroleptic drugs used in the treatment of psychotic patients. A member of this class which has recently been receiving increasing clinical interest is clopenthixol, which can exist as α and β isomers differing in their conformation about the exocyclic double bond. The α (*cis*) isomer is shown here (I). Pharmacological (Petersen, Moller-Nielsen, Pedersen, Jorgensen & Lassen, 1977) and clinical (Gravem, Engstrand & Guleng, 1978) studies have shown that this isomer is much more potent than the β form. One reason for this X-ray study was to establish the geometry of these two isomers.



(I)

There has also been increasing interest in the structural and conformational factors responsible for

Table 1. *Additional crystal data and data-collection and refinement details*

	α Isomer	β Isomer
Formula	$C_{22}H_{25}ClN_2OS$	$C_{22}H_{25}ClN_2OS.2H_2O$
M_r	400·97	437·01
D_x (Mg m^{-3})	1·337	1·319
μ(Mo $K\alpha$) (mm^{-1})	0·3	0·3
Crystal size (mm)	0·4 × 0·35 × 0·2	0·75 × 0·4 × 0·25
Crystal form	Colourless blocks, elongated along [101]	Pale-yellow blocks, elongated along **a**
Data collection		
2θ limits (°)	7–50	7–50
Reflexions measured	3497	4166
Unique reflexions	3496	3881
Observed reflexions $\lvert F > 4\sigma(F)\rvert$	2503	3174
Refinement		
Final R	0·051	0·039
Final R'	0·049	0·042
Weighting: g =	0·0005	0·0004
Largest difference peak (e Å^{-3})	0·22	0·18

0567-7408/81/040906-05$01.00

Table 2. *Atom coordinates* ($\times 10^4$) *and isotropic temperature factors* ($Å^2 \times 10^3$)

For non-hydrogen atoms $U = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j$.

	α Isomer				β Isomer			
	x	*y*	*z*	*U*	*x*	*y*	*z*	*U*
S	3744 (1)	−3747 (1)	6070 (1)	48 (1)	13594 (1)	3875 (1)	5928 (1)	50 (1)
Cl	4554 (1)	−4185 (1)	1056 (1)	57 (1)	6601 (1)	978 (1)	4139 (1)	58 (1)
N(1)	5706 (2)	−196 (1)	2978 (2)	31 (1)	5092 (2)	1201 (2)	8055 (1)	37 (1)
N(2)	6280 (2)	1244 (1)	1752 (2)	36 (1)	3448 (2)	2466 (2)	9180 (1)	40 (1)
O	6082 (2)	993 (1)	−982 (2)	53 (1)	757 (2)	2561 (3)	10638 (1)	78 (1)
C(1)	5132 (2)	−3543 (2)	3324 (2)	34 (1)	8118 (3)	1912 (2)	5253 (1)	40 (1)
C(2)	4364 (3)	−4086 (2)	2473 (2)	39 (1)	8503 (3)	1857 (2)	4638 (1)	42 (1)
C(3)	3472 (3)	−4552 (2)	2734 (3)	42 (1)	10359 (3)	2472 (2)	4409 (1)	48 (1)
C(4)	3331 (3)	−4454 (2)	3855 (3)	41 (1)	11865 (3)	3126 (2)	4815 (1)	48 (1)
C(5)	5443 (3)	−3641 (2)	8322 (3)	40 (1)	13287 (3)	5865 (2)	6933 (1)	54 (1)
C(6)	6570 (3)	−3435 (2)	9160 (3)	47 (1)	12308 (4)	6536 (3)	7425 (1)	65 (1)
C(7)	7470 (3)	−3101 (2)	8758 (3)	46 (1)	10285 (4)	6038 (3)	7531 (1)	64 (1)
C(8)	7232 (3)	−2936 (2)	7535 (3)	39 (1)	9284 (3)	4790 (2)	7166 (1)	50 (1)
C(9)	5779 (2)	−2831 (2)	5379 (2)	29 (1)	9283 (3)	2532 (2)	6336 (1)	37 (1)
C(11)	4977 (2)	−3419 (2)	4456 (2)	31 (1)	9633 (3)	2544 (2)	5669 (1)	37 (1)
C(12)	4061 (2)	−3889 (2)	4701 (3)	35 (1)	11527 (3)	3158 (2)	5441 (1)	40 (1)
C(13)	5207 (2)	−3482 (2)	7085 (3)	33 (1)	12271 (3)	4622 (2)	6558 (1)	43 (1)
C(14)	6085 (2)	−3094 (2)	6675 (2)	32 (1)	10275 (3)	3989 (2)	6690 (1)	40 (1)
C(16)	6196 (2)	−2080 (2)	5134 (2)	33 (1)	8183 (3)	1223 (2)	6588 (1)	41 (1)
C(17)	5972 (3)	−1637 (2)	3939 (2)	36 (1)	7731 (3)	937 (2)	7250 (1)	43 (1)
C(18)	5805 (3)	−688 (2)	4078 (2)	37 (1)	5513 (3)	1320 (2)	7399 (1)	43 (1)
C(19)	6893 (3)	−106 (2)	2788 (3)	39 (1)	6117 (3)	2620 (2)	8406 (1)	44 (1)
C(20)	6771 (3)	403 (2)	1653 (3)	38 (1)	5668 (3)	2448 (3)	9077 (1)	47 (1)
C(21)	5093 (3)	1160 (2)	1910 (3)	41 (1)	2385 (3)	1100 (2)	8815 (1)	47 (1)
C(22)	5215 (3)	654 (2)	3051 (3)	38 (1)	2865 (3)	1279 (2)	8148 (1)	44 (1)
C(23)	6294 (3)	1836 (2)	791 (3)	44 (1)	3069 (3)	2262 (3)	9835 (1)	51 (1)
C(24)	5516 (3)	1634 (2)	−505 (3)	47 (1)	883 (3)	2566 (3)	9999 (1)	53 (1)
					W(1) 3893 (3)	2241 (2)	11516 (1)	60 (1)
					W(2) −2804 (3)	3884 (2)	10918 (1)	66 (1)
H(O)	5566 (28)	749 (20)	−1534 (28)	50	−240 (34)	3000 (29)	10761 (10)	80 (6)
H(1)	5777	−3250	3137	41	6795	1511	5397	49
H(3)	2958	−4938	2144	51	10597	2445	3978	58
H(4)	2721	−4781	4053	50	13162	3566	4664	57
H(5)	4821	−3894	8590	49	14676	6256	6848	66
H(6)	6725	−3524	10015	58	13036	7351	7693	78
H(7)	8269	−2983	9333	54	9575	6557	7859	77
H(8)	7872	−2706	7272	48	7868	4464	7241	60
H(16)	6718	−1780	5833	40	7610	359	6309	50
H(17*a*)	6661	−1728	3668	44	7955	−245	7349	53
H(17*b*)	5244	−1864	3348	44	8653	1678	7493	53
H(18*a*)	6498	−481	4735	45	4598	506	7183	53
H(18*b*)	5069	−603	4275	45	5254	2467	7264	53
H(19*a*)	7457	178	3480	47	7579	2601	8353	54
H(19*b*)	7204	−660	2707	47	5630	3695	8258	54
H(20*a*)	6224	115	955	47	6355	3394	9295	58
H(20*b*)	7563	461	1561	47	6174	1380	9225	58
H(21*a*)	4776	1714	1980	52	2816	2	8958	56
H(21*b*)	4538	872	1216	52	925	1162	8862	56
H(22*a*)	4422	600	3141	46	2410	2367	8003	54
H(22*b*)	5761	946	3745	46	2151	358	7924	54
H(23*a*)	6028	2377	991	52	3375	1109	9953	63
H(23*b*)	7129	1878	809	52	3969	3072	10058	63
H(24*a*)	5423	2137	−995	58	−23	1667	9827	65
H(24*b*)	4722	1442	−520	58	494	3662	9842	65
					Hw(1) 4044 (31)	1251 (24)	11629 (9)	84 (5)
					Hw(2) 2927 (34)	2265 (27)	11299 (10)	68 (6)
					Hw(3) −2962 (33)	4926 (28)	10971 (10)	73 (6)
					Hw(4) −3704 (29)	3392 (24)	11094 (9)	52 (5)

the pharmacological activity of neuroleptic drugs (Horn, Post & Kennard, 1975; Bürki *et al.*, 1978; Reboul & Cristau, 1977*a*,*b*). We have studied the crystal and molecular structures of two other closely related thioxanthenes, α- and β-flupenthixol (Post, Kennard & Horn, 1975*a*,*b*; Post, Kennard, Sheldrick & Horn, 1975) in which the chloro group of clopenthixol is replaced by trifluoromethyl. It therefore seemed of interest to determine what effect this replacement has on the overall conformation, particularly since flupenthixol is more potent than clopenthixol (Moller-Nielsen *et al.*, 1973; Miller, Horn & Iversen, 1974).

Crystals of the free base of both isomers were provided by Dr N. Lassen of H. Lundbeck & Co., Copenhagen.

Experimental

Data were collected on a Stoe four-circle diffractometer with monochromated Mo $K\alpha$ radiation. Crystal data and details of data collection and refinement are given in the *Abstract* and in Table 1. Both structures were solved by multisolution direct methods, the α isomer automatically, the β isomer only when extra reflexions, chosen from a convergence map, were included in the starting set. In the final stages of

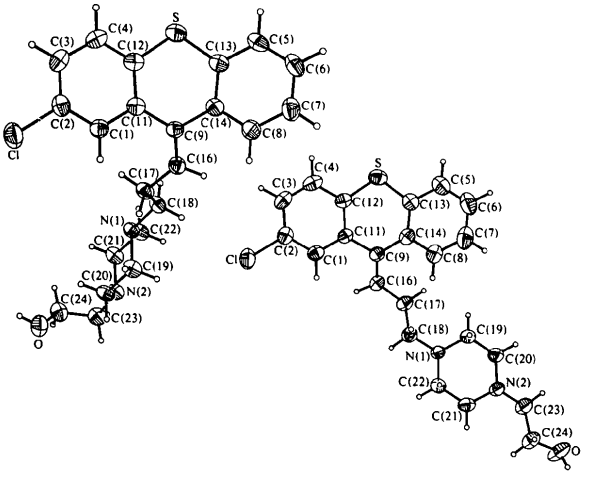


Fig. 1. Thermal-ellipsoid plots of (left) α- and (right) β-clopenthixol, perpendicular to the mean plane of C(11) to C(14). The wide difference in side-chain conformation is apparent (see also Table 5).

Table 3. *Bond lengths* (Å)

	α Isomer	β Isomer		α Isomer	β Isomer		α Isomer	β Isomer
C(1)–C(2)	1·382 (5)	1·377 (3)	C(21)–N(2)	1·449 (5)	1·461 (3)	C(17)–C(18)	1·523 (5)	1·528 (4)
C(2)–Cl	1·740 (4)	1·739 (3)	C(22)–N(1)	1·465 (5)	1·470 (3)	C(19)–N(1)	1·466 (5)	1·463 (3)
C(3)–C(4)	1·375 (6)	1·381 (4)	C(23)–C(24)	1·509 (5)	1·503 (4)	C(20)–N(2)	1·459 (5)	1·466 (3)
C(6)–C(7)	1·378 (6)	1·377 (5)	C(1)–C(11)	1·400 (5)	1·393 (3)	C(21)–C(22)	1·513 (5)	1·505 (3)
C(11)–C(9)	1·484 (4)	1·482 (3)	C(2)–C(3)	1·377 (6)	1·380 (4)	C(23)–N(2)	1·459 (5)	1·468 (3)
C(12)–S	1·762 (4)	1·760 (3)	C(5)–C(6)	1·379 (5)	1·378 (4)	C(24)–O	1·413 (5)	1·402 (3)
C(13)–S	1·759 (4)	1·755 (3)	C(7)–C(8)	1·380 (5)	1·381 (4)	O–H(O)	0·812 (30)	0·799 (24)
C(13)–C(14)	1·397 (5)	1·401 (4)	C(11)–C(12)	1·397 (5)	1·402 (3)	H*w*(1)–*W*(1)		0·818 (20)
C(14)–C(9)	1·487 (5)	1·481 (3)	C(12)–C(4)	1·384 (5)	1·393 (4)	H*w*(3)–*W*(2)		0·828 (23)
C(16)–C(17)	1·498 (5)	1·500 (3)	C(13)–C(5)	1·394 (5)	1·395 (4)	H*w*(2)–*W*(1)		0·778 (23)
C(18)–N(1)	1·467 (5)	1·470 (3)	C(14)–C(8)	1·390 (5)	1·399 (4)	H*w*(4)–*W*(2)		0·791 (20)
C(19)–C(20)	1·510 (5)	1·509 (3)	C(16)–C(9)	1·342 (5)	1·340 (3)			

Table 4. *Bond angles* (°)

	α Isomer	β Isomer		α Isomer	β Isomer		α Isomer	β Isomer
C(12)–S–C(13)	101·2 (2)	101·1 (2)	C(8)–C(14)–C(13)	117·3 (4)	117·1 (3)	C(14)–C(9)–C(16)	118·6 (3)	123·7 (2)
C(18)–N(1)–C(22)	110·5 (3)	109·8 (2)	C(9)–C(16)–C(17)	130·0 (3)	128·3 (3)	C(1)–C(11)–C(12)	117·4 (3)	118·1 (3)
C(20)–N(2)–C(21)	109·7 (3)	109·1 (2)	N(1)–C(18)–C(17)	113·6 (3)	113·3 (2)	S–C(12)–C(4)	117·6 (4)	117·7 (2)
C(21)–N(2)–C(23)	114·1 (3)	112·0 (2)	N(2)–C(20)–C(19)	109·7 (4)	111·2 (2)	C(4)–C(12)–C(11)	121·3 (4)	120·3 (3)
Cl–C(2)–C(1)	118·6 (4)	118·9 (2)	N(1)–C(22)–C(21)	110·7 (4)	110·9 (2)	S–C(13)–C(14)	121·2 (3)	121·8 (2)
C(1)–C(2)–C(3)	121·3 (4)	121·6 (3)	O–C(24)–C(23)	110·0 (3)	108·5 (3)	C(8)–C(14)–C(9)	121·8 (4)	122·2 (3)
C(3)–C(4)–C(12)	120·6 (4)	120·9 (3)	C(18)–N(1)–C(19)	112·2 (3)	112·2 (2)	C(9)–C(14)–C(13)	120·9 (3)	120·6 (3)
C(5)–C(6)–C(7)	119·4 (4)	120·0 (3)	C(19)–N(1)–C(22)	108·6 (3)	107·3 (2)	C(16)–C(17)–C(18)	110·3 (3)	112·4 (2)
C(7)–C(8)–C(14)	121·5 (4)	121·9 (3)	C(20)–N(2)–C(23)	114·5 (4)	109·6 (2)	N(1)–C(19)–C(20)	111·3 (3)	110·8 (2)
C(11)–C(9)–C(16)	125·3 (3)	120·1 (2)	C(2)–C(1)–C(11)	120·4 (4)	120·6 (3)	N(2)–C(21)–C(22)	110·1 (3)	111·4 (2)
C(1)–C(11)–C(9)	121·5 (4)	121·3 (2)	Cl–C(2)–C(3)	120·1 (3)	119·5 (2)	N(2)–C(23)–C(24)	118·4 (3)	113·3 (2)
C(9)–C(11)–C(12)	121·1 (4)	120·5 (2)	C(2)–C(3)–C(4)	118·9 (4)	118·5 (3)	C(24)–O–H(O)	109·6 (25)	113·9 (17)
S–C(12)–C(11)	121·1 (3)	121·9 (2)	C(6)–C(5)–C(13)	120·1 (4)	120·4 (3)	H*w*(1)–*W*(1)–H*w*(2)		109·5 (22)
S–C(13)–C(5)	117·6 (3)	117·7 (2)	C(6)–C(7)–C(8)	120·5 (4)	119·8 (3)	H*w*(3)–*W*(2)–H*w*(4)		106·0 (21)
C(5)–C(13)–C(14)	121·1 (3)	120·5 (3)	C(11)–C(9)–C(14)	116·0 (3)	116·1 (2)			

Table 5. *Torsion angles* (°)

	α Isomer	β Isomer		α Isomer	β Isomer		α Isomer	β Isomer
C(13)–S–C(12)–C(4)	151·0 (3)	154·4 (2)	C(16)–C(9)–C(14)–C(8)	−39·0 (5)	−42·2 (4)	C(2)–C(1)–C(11)–C(12)	2·7 (5)	1·6 (3)
C(12)–S–C(13)–C(5)	−155·5 (3)	−155·8 (2)	C(11)–C(9)–C(16)–C(17)	1·1 (6)	177·3 (3)	C(1)–C(2)–C(3)–C(4)	1·6 (5)	1·2 (4)
C(19)–N(1)–C(18)–C(17)	−74·2 (4)	70·8 (3)	C(1)–C(11)–C(12)–S	−177·2 (3)	−176·5 (2)	C(3)–C(4)–C(12)–S	175·5 (3)	175·7 (2)
C(18)–N(1)–C(19)–C(20)	−179·9 (3)	−179·5 (2)	C(9)–C(11)–C(12)–S	4·7 (4)	2·0 (3)	C(13)–C(5)–C(6)–C(7)	−2·3 (6)	−3·0 (4)
C(18)–N(1)–C(22)–C(21)	−179·1 (3)	178·1 (2)	S–C(13)–C(14)–C(8)	−177·7 (3)	−173·9 (2)	C(6)–C(5)–C(13)–C(14)	−1·8 (5)	−2·6 (4)
C(21)–N(2)–C(20)–C(19)	−59·0 (4)	56·0 (3)	C(5)–C(13)–C(14)–C(8)	5·0 (5)	7·0 (4)	C(6)–C(7)–C(8)–C(14)	0·4 (6)	0·8 (4)
C(20)–N(2)–C(21)–C(22)	59·5 (4)	−55·9 (3)	C(9)–C(16)–C(17)–C(18)	140·2 (4)	105·2 (3)	C(7)–C(8)–C(14)–C(13)	−4·3 (5)	−6·1 (4)
C(20)–N(2)–C(23)–C(24)	64·1 (5)	170·2 (3)	N(1)–C(19)–C(20)–N(2)	58·8 (4)	−59·7 (3)	C(14)–C(9)–C(11)–C(12)	33·7 (5)	35·4 (3)
C(11)–C(1)–C(2)–Cl	177·4 (3)	177·5 (2)	N(2)–C(23)–C(24)–O	−76·4 (5)	−172·5 (3)	C(16)–C(9)–C(11)–C(12)	−143·4 (4)	−142·4 (3)
C(2)–C(1)–C(11)–C(9)	−179·2 (3)	−176·9 (3)	C(13)–S–C(12)–C(11)	−31·9 (3)	−29·2 (3)	C(11)–C(9)–C(14)–C(13)	−38·9 (5)	−39·9 (3)
Cl–C(2)–C(3)–C(4)	−179·2 (3)	−178·5 (2)	C(12)–S–C(13)–C(14)	27·1 (4)	25·1 (3)	C(16)–C(9)–C(14)–C(13)	138·5 (4)	137·9 (3)
C(2)–C(3)–C(4)–C(12)	0·9 (5)	0·3 (4)	C(22)–N(1)–C(18)–C(17)	164·4 (3)	−170·0 (2)	C(14)–C(9)–C(16)–C(17)	−176·0 (4)	−0·3 (4)
C(3)–C(4)–C(12)–C(11)	−1·6 (5)	−0·9 (4)	C(22)–N(1)–C(19)–C(20)	−57·5 (4)	59·8 (3)	C(1)–C(11)–C(12)–C(4)	−0·2 (5)	−0·1 (3)
C(6)–C(5)–C(13)–S	−179·2 (3)	178·2 (3)	C(19)–N(1)–C(22)–C(21)	57·4 (4)	−59·7 (3)	C(9)–C(11)–C(12)–C(4)	−178·3 (3)	178·4 (3)
C(5)–C(6)–C(7)–C(8)	3·0 (6)	3·9 (4)	C(23)–N(2)–C(20)–C(19)	171·2 (3)	178·9 (3)	S–C(13)–C(14)–C(9)	4·8 (5)	6·1 (3)
C(7)–C(8)–C(14)–C(9)	173·2 (4)	173·9 (3)	C(23)–N(2)–C(21)–C(22)	−170·5 (3)	−177·4 (2)	C(5)–C(13)–C(14)–C(9)	−172·6 (4)	−173·0 (3)
C(14)–C(9)–C(11)–C(1)	−144·4 (4)	−146·1 (3)	C(21)–N(2)–C(23)–C(24)	−63·4 (5)	−68·7 (3)	C(16)–C(17)–C(18)–N(1)	174·1 (3)	−174·7 (2)
C(16)–C(9)–C(11)–C(1)	38·5 (5)	36·1 (3)	C(11)–C(1)–C(2)–C(3)	−3·5 (5)	−2·2 (4)	N(2)–C(21)–C(22)–N(1)	−59·5 (4)	59·4 (3)
C(11)–C(9)–C(14)–C(8)	143·7 (4)	140·1 (3)						

refinement, water and hydroxyl H atoms refined freely, other H atoms with C–H = 0·96 Å, H–C–H = 109·5°. Weighting schemes were of the form $w^{-1} = \sigma^2(F) + gF^2$. Final atomic coordinates are given in Table 2, bond lengths and angles and torsion angles in Tables 3–5. Fig. 1 shows the molecules of both isomers.*

Discussion

The geometry of the *cis* and *trans* isomers has been unequivocally established; this is of importance, since errors have been made in assigning the correct geometry to other analogues. Table 6 compares clopenthixol and flupenthixol in terms of structural parameters thought to be of significance with regard to the mode of binding at receptor sites (Horn *et al.*, 1975; Post *et al.*, 1975*a*). Despite certain similarities, no clear pattern emerges and data from further analogous compounds must be sought.

* Lists of structure factors and anisotropic thermal parameters for both isomers have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35880 (37 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

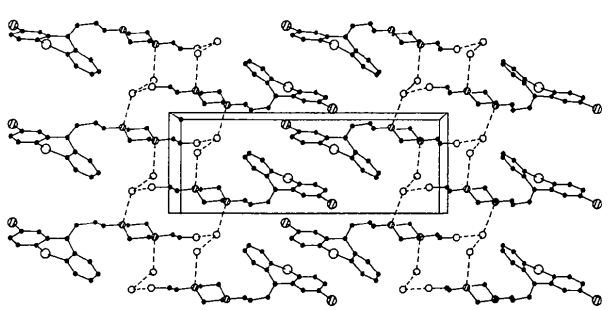


Fig. 2. Packing diagram of β-clopenthixol viewed down **a**. H atoms are omitted for clarity, hydrogen bonds are indicated by broken lines, and the origin is marked by a black spot.

The extended structures of both isomers show hydrogen-bonding interactions (Table 7). In the α isomer the molecules are linked in centrosymmetric pairs, whereas in the β isomer the molecules are

Table 6. *Selected structural features of clopenthixol and flupenthixol*

CPX = clopenthixol; FPX = flupenthixol. The values for FPX are taken from Post *et al.* (1975*a*,*b*) and Post *et al.* (1975). E.s.d.'s: 1° for dihedral angles, 0·02 Å for N–ring centroid distances.

		α Isomer	β Isomer
Dihedral angle (between the aromatic rings)	CPX	146°	148°
	FPX	151	143
N–ring centroids*			
N(1)–*A*	CPX	6·32 Å	7·46 Å
	FPX	5·82	6·09
N(1)–*B*	CPX	7·38	5·51
	FPX	7·46	6·45
N(2)–*A*	CPX	9·03	10·11
	FPX	7·75	8·24
N(2)–*B*	CPX	10·09	7·26
	FPX	10·26	9·30

* Ring *A* is the aromatic ring bearing the Cl or CF_3 group, *B* the other aromatic ring.

Table 7. *Hydrogen bonds*

E.s.d.'s: H···*Y*, 0·04, *X*···*Y* 0·01 Å.

X–H···*Y*	H···*Y*	*X*···*Y*	Symmetry operator of *Y*
α Isomer			
O–H(O)···N(1)	2·03 Å	2·83 Å	$1-x, -y, -z$
β Isomer			
W(1)–H(*w*2)···O	2·02	2·78	*x*,*y*,*z*
O–H(O)···*W*(2)	1·87	2·66	*x*,*y*,*z*
W(1)–H(*w*1)···N(1)	2·12	2·93	$1-x, -y, 2-z$
W(2)–H(*w*3)···N(2)	2·09	2·89	$-x, 1-y, 2-z$
W(2)–H(*w*4)···*W*(1)	2·01	2·80	$-1+x, y, z$

involved in bands of H-bonded atoms running parallel to **b** (Fig. 2). It can also be seen from Fig. 2 that S and Cl atoms of adjacent molecules are related by the translation 0,0·5,0; it is probably this pseudo-symmetry which caused problems in the automatic direct-methods procedures.

Crystallographic programs were written by GMS and Dr W. Clegg. We thank the Verband der Deutschen Industrie for financial support.

References

BÜRKI, H. R., FISCHER, R., HUNZIKER, F., KÜNZLE, F., PETCHER, T. J., SCHMUTZ, J., WEBER, H. P. & WHITE, T. G. (1978). *Eur. J. Med. Chem.* **13**, 479–485.

GRAVEM, A., ENGSTRAND, E. & GULENG, R. J. (1978). *Acta Psychiatr. Scand.* **58**, 384–388.

HORN, A. S., POST, M. L. & KENNARD, O. (1975). *J. Pharm. Pharmacol.* **27**, 553–563.

MILLER, R. J., HORN, A. S. & IVERSEN, L. L. (1974). *Mol. Pharmacol.* **10**, 759–766.

MOLLER-NIELSEN, I., PEDERSEN, V., NYMARK, M., FRANCK, K. F., BOECK, V., FJALLAN, B. & CHRISTENSEN, A. V. (1973). *Acta Pharmacol. Toxicol.* **33**, 353–362.

PETERSEN, P. V., MOLLER-NIELSEN, I., PEDERSEN, V., JORGENSEN, A. & LASSEN, N. (1977). *Psychopharmacology Series.* 2. *Psychotherapeutic Drugs.* Part 2. *Applications*, edited by E. USDIN & I. S. FOREST, pp. 827–867. New York: Marcel Dekker.

POST, M. L., KENNARD, O. & HORN, A. S. (1975*a*). *Nature (London)*, **256**, 342–343.

POST, M. L., KENNARD, O. & HORN, A. S. (1975*b*). *Acta Cryst.* B**31**, 2724–2726.

POST, M. L., KENNARD, O., SHELDRICK, G. M. & HORN, A. S. (1975). *Acta Cryst.* B**31**, 2366–2368.

REBOUL, J. P. & CRISTAU, B. (1977*a*). *Eur. J. Med. Chem.* **12**, 71–75.

REBOUL, J. P. & CRISTAU, B. (1977*b*). *Eur. J. Med. Chem.* **12**, 76–79.