

SUPPLEMENTARY MATERIAL FOR ETIFOXINE

Table S1. Hydrogen atoms coordinates ($\times 10^4$) and isotropic displacement parameters $U(\text{eq})/\text{\AA}^2 \times 10^3$ ^a

Atom	x	y	z	U(eq)
H2_1	10233	230	1577	62(8)
H5_1	9049	-3083	684	60
H7_1	4398	-2639	139	61
H8_1	4768	-1441	578	57
H10_1	10545	-910	2415	72
H11_1	10424	-1153	3489	90
H12_1	9743	-2346	3806	102
H13_1	9289	-3295	3051	106
H14_1	9329	-3051	1973	85
H15A_1	8626	1166	1725	66
H15B_1	7173	617	1559	66
H16A_1	7063	1542	792	157
H16B_1	8746	1303	640	157
H16C_1	7291	754	474	157
H17A_1	11430	-2673	1204	92
H17B_1	11453	-2016	701	92
H17C_1	12364	-1925	1409	92
H2_2	5107	-140	1277	73(9)
H5_2	5161	368	4218	55
H7_2	639	1108	3862	60
H8_2	522	810	2783	55
H10_2	5943	-1271	2189	79
H11_2	5296	-2542	2155	95
H12_2	4047	-3069	2955	88
H13_2	3599	-2340	3819	88
H14_2	4210	-1068	3848	73
H15A_2	2020	-80	853	69
H15B_2	3339	30	412	69
H16A_2	1769	1103	375	121
H16B_2	2197	1196	1129	121
H16C_2	3516	1306	688	121
H17A_2	7234	-163	3809	87
H17B_2	7889	-281	3154	87
H17C_2	7335	524	3342	87

^aesd's in parentheses are given for experimentally found H-atoms.

Table S2. Bond lengths [Å] for monoclinic racemic etifoxine^a

Molecule 1		Molecule 2	
Cl1_1-C6_1	1.745(2)	Cl1_2-C6_2	1.743(2)
O1_1-C4_1	1.356(2)	O1_2-C4_2	1.358(3)
O1_1-C1_1	1.451(2)	O1_2-C1_2	1.455(3)
N1_1-C4_1	1.301(3)	N1_2-C4_2	1.301(3)
N1_1-C3_1	1.405(3)	N1_2-C3_2	1.398(3)
N2_1-C4_1	1.330(3)	N2_2-C4_2	1.332(3)
N2_1-C15_1	1.448(3)	N2_2-C15_2	1.460(3)
C1_1-C2_1	1.511(3)	C1_2-C2_2	1.511(3)
C1_1-C17_1	1.523(3)	C1_2-C17_2	1.526(3)
C1_1-C9_1	1.526(3)	C1_2-C9_2	1.533(3)
C2_1-C5_1	1.384(3)	C2_2-C5_2	1.383(3)
C2_1-C3_1	1.403(3)	C2_2-C3_2	1.403(3)
C3_1-C8_1	1.395(3)	C3_2-C8_2	1.403(3)
C5_1-C6_1	1.383(3)	C5_2-C6_2	1.387(3)
C6_1-C7_1	1.382(3)	C6_2-C7_2	1.380(3)
C7_1-C8_1	1.382(3)	C7_2-C8_2	1.375(3)
C9_1-C10_1	1.380(3)	C9_2-C14_2	1.377(3)
C9_1-C14_1	1.385(3)	C9_2-C10_2	1.377(3)
C10_1-C11_1	1.379(4)	C10_2-C11_2	1.387(4)
C11_1-C12_1	1.374(4)	C11_2-C12_2	1.377(4)
C12_1-C13_1	1.366(5)	C12_2-C13_2	1.363(4)
C13_1-C14_1	1.375(4)	C13_2-C14_2	1.384(4)
C15_1-C16_1	1.466(4)	C15_2-C16_2	1.499(4)

^aesd's in parentheses

Table S3. Bond angles [°] for monoclinic racemic etifoxine^a

Molecule 1		Molecule 2	
C4_1-O1_1-C1_1	117.04(15)	C4_2-O1_2-C1_2	116.32(15)
C4_1-N1_1-C3_1	115.55(17)	C4_2-N1_2-C3_2	115.36(17)
C4_1-N2_1-C15_1	124.53(19)	C4_2-N2_2-C15_2	124.24(19)
O1_1-C1_1-C2_1	106.91(16)	O1_2-C1_2-C2_2	106.92(16)
O1_1-C1_1-C17_1	103.86(17)	O1_2-C1_2-C17_2	103.76(17)
C2_1-C1_1-C17_1	114.39(19)	C2_2-C1_2-C17_2	114.53(18)
O1_1-C1_1-C9_1	109.57(17)	O1_2-C1_2-C9_2	108.69(17)
C2_1-C1_1-C9_1	110.49(17)	C2_2-C1_2-C9_2	110.71(17)
C17_1-C1_1-C9_1	111.24(19)	C17_2-C1_2-C9_2	111.74(18)
C5_1-C2_1-C3_1	120.42(19)	C5_2-C2_2-C3_2	120.75(19)
C5_1-C2_1-C1_1	123.14(19)	C5_2-C2_2-C1_2	123.13(19)
C3_1-C2_1-C1_1	116.38(18)	C3_2-C2_2-C1_2	115.97(18)
C8_1-C3_1-C2_1	118.44(19)	N1_2-C3_2-C8_2	119.30(18)
C8_1-C3_1-N1_1	119.47(18)	N1_2-C3_2-C2_2	122.55(18)

C2_1-C3_1-N1_1	122.09(18)	C8_2-C3_2-C2_2	118.14(19)
N1_1-C4_1-N2_1	124.94(19)	N1_2-C4_2-N2_2	124.9(2)
N1_1-C4_1-O1_1	124.92(19)	N1_2-C4_2-O1_2	124.92(19)
N2_1-C4_1-O1_1	110.07(18)	N2_2-C4_2-O1_2	110.09(18)
C6_1-C5_1-C2_1	119.6(2)	C2_2-C5_2-C6_2	119.3(2)
C7_1-C6_1-C5_1	121.0(2)	C7_2-C6_2-C5_2	121.0(2)
C7_1-C6_1-Cl1_1	120.23(18)	C7_2-C6_2-Cl1_2	120.54(18)
C5_1-C6_1-Cl1_1	118.74(18)	C5_2-C6_2-Cl1_2	118.49(17)
C6_1-C7_1-C8_1	119.2(2)	C8_2-C7_2-C6_2	119.6(2)
C7_1-C8_1-C3_1	121.1(2)	C7_2-C8_2-C3_2	121.1(2)
C10_1-C9_1-C14_1	118.3(2)	C14_2-C9_2-C10_2	118.5(2)
C10_1-C9_1-C1_1	122.1(2)	C14_2-C9_2-C1_2	120.6(2)
C14_1-C9_1-C1_1	119.5(2)	C10_2-C9_2-C1_2	120.9(2)
C11_1-C10_1-C9_1	121.0(3)	C9_2-C10_2-C11_2	120.5(3)
C12_1-C11_1-C10_1	119.9(3)	C12_2-C11_2-C10_2	120.2(3)
C13_1-C12_1-C11_1	119.4(3)	C13_2-C12_2-C11_2	119.5(3)
C12_1-C13_1-C14_1	120.9(3)	C12_2-C13_2-C14_2	120.3(3)
C13_1-C14_1-C9_1	120.3(3)	C9_2-C14_2-C13_2	120.9(3)
N2_1-C15_1-C16_1	113.6(2)	N2_2-C15_2-C16_2	113.4(2)

^a esd's in parentheses

Table S4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for monoclinic racemic etifoxine^{a,b}

	U11	U22	U33	U23	U13	U12
Cl1_1	87(1)	52(1)	67(1)	-15(1)	-1(1)	-7(1)
O1_1	37(1)	41(1)	62(1)	4(1)	9(1)	0(1)
N1_1	37(1)	43(1)	49(1)	-2(1)	7(1)	0(1)
N2_1	41(1)	40(1)	68(1)	-3(1)	2(1)	-3(1)
C1_1	39(1)	38(1)	57(1)	0(1)	5(1)	3(1)
C2_1	42(1)	43(1)	43(1)	1(1)	6(1)	-1(1)
C3_1	41(1)	42(1)	38(1)	1(1)	7(1)	-1(1)
C4_1	41(1)	42(1)	44(1)	4(1)	7(1)	3(1)
C5_1	51(1)	47(1)	51(1)	-2(1)	5(1)	3(1)
C6_1	62(1)	43(1)	45(1)	-2(1)	4(1)	-6(1)
C7_1	49(1)	55(1)	48(1)	1(1)	1(1)	-9(1)
C8_1	42(1)	50(1)	51(1)	0(1)	6(1)	-1(1)
C9_1	40(1)	45(1)	55(1)	3(1)	-2(1)	1(1)
C10_1	69(2)	50(1)	55(1)	2(1)	-7(1)	3(1)
C11_1	92(2)	74(2)	53(2)	-2(1)	-8(1)	13(2)
C12_1	92(2)	104(3)	55(2)	16(2)	3(2)	-1(2)
C13_1	105(2)	81(2)	73(2)	24(2)	-3(2)	-27(2)
C14_1	88(2)	56(2)	64(2)	6(1)	-2(1)	-17(1)
C15_1	48(1)	43(1)	74(2)	-10(1)	7(1)	-2(1)

C16_1	134(3)	97(3)	76(2)	3(2)	-6(2)	55(2)
C17_1	45(1)	59(2)	81(2)	-7(1)	10(1)	8(1)
C11_2	89(1)	81(1)	41(1)	-5(1)	8(1)	22(1)
O1_2	39(1)	58(1)	47(1)	3(1)	8(1)	1(1)
N1_2	39(1)	46(1)	42(1)	-2(1)	6(1)	-2(1)
N2_2	50(1)	67(1)	43(1)	-4(1)	11(1)	5(1)
C1_2	40(1)	48(1)	44(1)	1(1)	5(1)	2(1)
C2_2	42(1)	36(1)	45(1)	1(1)	6(1)	-2(1)
C3_2	40(1)	35(1)	42(1)	2(1)	7(1)	-2(1)
C4_2	43(1)	42(1)	44(1)	0(1)	5(1)	-2(1)
C5_2	49(1)	43(1)	45(1)	2(1)	2(1)	2(1)
C6_2	63(1)	43(1)	41(1)	1(1)	9(1)	3(1)
C7_2	52(1)	51(1)	50(1)	1(1)	14(1)	9(1)
C8_2	42(1)	49(1)	46(1)	3(1)	6(1)	4(1)
C9_2	41(1)	47(1)	49(1)	0(1)	1(1)	8(1)
C10_2	77(2)	57(2)	66(2)	-5(1)	19(1)	12(1)
C11_2	102(2)	54(2)	80(2)	-14(1)	11(2)	21(2)
C12_2	77(2)	45(1)	95(2)	1(1)	0(2)	11(1)
C13_2	83(2)	51(2)	89(2)	13(1)	22(2)	5(1)
C14_2	76(2)	48(1)	60(2)	3(1)	15(1)	6(1)
C15_2	52(1)	80(2)	42(1)	-9(1)	8(1)	-4(1)
C16_2	88(2)	91(2)	63(2)	25(2)	12(2)	4(2)
C17_2	42(1)	68(2)	61(2)	-4(1)	1(1)	0(1)

^aesd's in parentheses

^bThe anisotropic displacement factor exponent takes the form:

$$-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$$

Table S5. Torsion angles [°] for monoclinic racemic etifoxine^a

Molecule 1		Molecule 2	
C4_1-O1_1-C1_1-C2_1	46.6(2)	C4_2-O1_2-C1_2-C2_2	-47.8(2)
C4_1-O1_1-C1_1-C17_1	167.90(18)	C4_2-O1_2-C1_2-C17_2	-169.17(18)
C4_1-O1_1-C1_1-C9_1	-73.2(2)	C4_2-O1_2-C1_2-C9_2	71.8(2)
O1_1-C1_1-C2_1-C5_1	146.7(2)	O1_2-C1_2-C2_2-C5_2	-148.15(19)
C17_1-C1_1-C2_1-C5_1	32.3(3)	C17_2-C1_2-C2_2-C5_2	-33.8(3)
C9_1-C1_1-C2_1-C5_1	-94.1(2)	C9_2-C1_2-C2_2-C5_2	93.6(2)
O1_1-C1_1-C2_1-C3_1	-36.3(2)	O1_2-C1_2-C2_2-C3_2	36.3(2)
C17_1-C1_1-C2_1-C3_1	-150.7(2)	C17_2-C1_2-C2_2-C3_2	150.59(19)
C9_1-C1_1-C2_1-C3_1	82.9(2)	C9_2-C1_2-C2_2-C3_2	-82.0(2)
C5_1-C2_1-C3_1-C8_1	4.7(3)	C4_2-N1_2-C3_2-C8_2	166.58(19)
C1_1-C2_1-C3_1-C8_1	-172.34(19)	C4_2-N1_2-C3_2-C2_2	-14.8(3)
C5_1-C2_1-C3_1-N1_1	-174.55(19)	C5_2-C2_2-C3_2-N1_2	177.15(19)
C1_1-C2_1-C3_1-N1_1	8.4(3)	C1_2-C2_2-C3_2-N1_2	-7.1(3)
C4_1-N1_1-C3_1-C8_1	-165.47(19)	C5_2-C2_2-C3_2-C8_2	-4.2(3)
C4_1-N1_1-C3_1-C2_1	13.8(3)	C1_2-C2_2-C3_2-C8_2	171.53(18)

C3_1-N1_1-C4_1-N2_1	172.6(2)	C3_2-N1_2-C4_2-N2_2	-172.6(2)
C3_1-N1_1-C4_1-O1_1	-3.8(3)	C3_2-N1_2-C4_2-O1_2	3.2(3)
C15_1-N2_1-C4_1-N1_1	-7.3(4)	C15_2-N2_2-C4_2-N1_2	10.6(4)
C15_1-N2_1-C4_1-O1_1	169.6(2)	C15_2-N2_2-C4_2-O1_2	-165.8(2)
C1_1-O1_1-C4_1-N1_1	-29.1(3)	C1_2-O1_2-C4_2-N1_2	30.6(3)
C1_1-O1_1-C4_1-N2_1	154.02(18)	C1_2-O1_2-C4_2-N2_2	-153.01(18)
C3_1-C2_1-C5_1-C6_1	-3.1(3)	C3_2-C2_2-C5_2-C6_2	2.5(3)
C1_1-C2_1-C5_1-C6_1	173.8(2)	C1_2-C2_2-C5_2-C6_2	-172.9(2)
C2_1-C5_1-C6_1-C7_1	-0.8(3)	C2_2-C5_2-C6_2-C7_2	0.7(3)
C2_1-C5_1-C6_1-C11_1	179.94(17)	C2_2-C5_2-C6_2-C11_2	-178.44(16)
C5_1-C6_1-C7_1-C8_1	2.9(3)	C5_2-C6_2-C7_2-C8_2	-2.1(3)
C11_1-C6_1-C7_1-C8_1	-177.83(17)	C11_2-C6_2-C7_2-C8_2	176.99(18)
C6_1-C7_1-C8_1-C3_1	-1.2(3)	C6_2-C7_2-C8_2-C3_2	0.3(3)
C2_1-C3_1-C8_1-C7_1	-2.6(3)	N1_2-C3_2-C8_2-C7_2	-178.5(2)
N1_1-C3_1-C8_1-C7_1	176.70(19)	C2_2-C3_2-C8_2-C7_2	2.7(3)
O1_1-C1_1-C9_1-C10_1	-10.8(3)	O1_2-C1_2-C9_2-C14_2	-155.0(2)
C2_1-C1_1-C9_1-C10_1	-128.3(2)	C2_2-C1_2-C9_2-C14_2	-37.8(3)
C17_1-C1_1-C9_1-C10_1	103.5(3)	C17_2-C1_2-C9_2-C14_2	91.1(3)
O1_1-C1_1-C9_1-C14_1	171.5(2)	O1_2-C1_2-C9_2-C10_2	25.6(3)
C2_1-C1_1-C9_1-C14_1	53.9(3)	C2_2-C1_2-C9_2-C10_2	142.7(2)
C17_1-C1_1-C9_1-C14_1	-74.2(3)	C17_2-C1_2-C9_2-C10_2	-88.3(3)
C14_1-C9_1-C10_1-C11_1	-2.8(4)	C14_2-C9_2-C10_2-C11_2	2.9(4)
C1_1-C9_1-C10_1-C11_1	179.5(2)	C1_2-C9_2-C10_2-C11_2	-177.6(2)
C9_1-C10_1-C11_1-C12_1	1.2(4)	C9_2-C10_2-C11_2-C12_2	-0.6(5)
C10_1-C11_1-C12_1-C13_1	1.4(5)	C10_2-C11_2-C12_2-C13_2	-2.2(5)
C11_1-C12_1-C13_1-C14_1	-2.4(5)	C11_2-C12_2-C13_2-C14_2	2.7(5)
C12_1-C13_1-C14_1-C9_1	0.9(5)	C10_2-C9_2-C14_2-C13_2	-2.5(4)
C10_1-C9_1-C14_1-C13_1	1.7(4)	C1_2-C9_2-C14_2-C13_2	178.1(2)
C1_1-C9_1-C14_1-C13_1	179.5(3)	C12_2-C13_2-C14_2-C9_2	-0.3(4)
C4_1-N2_1-C15_1-C16_1	-83.0(3)	C4_2-N2_2-C15_2-C16_2	66.1(3)

^a esd's in parentheses

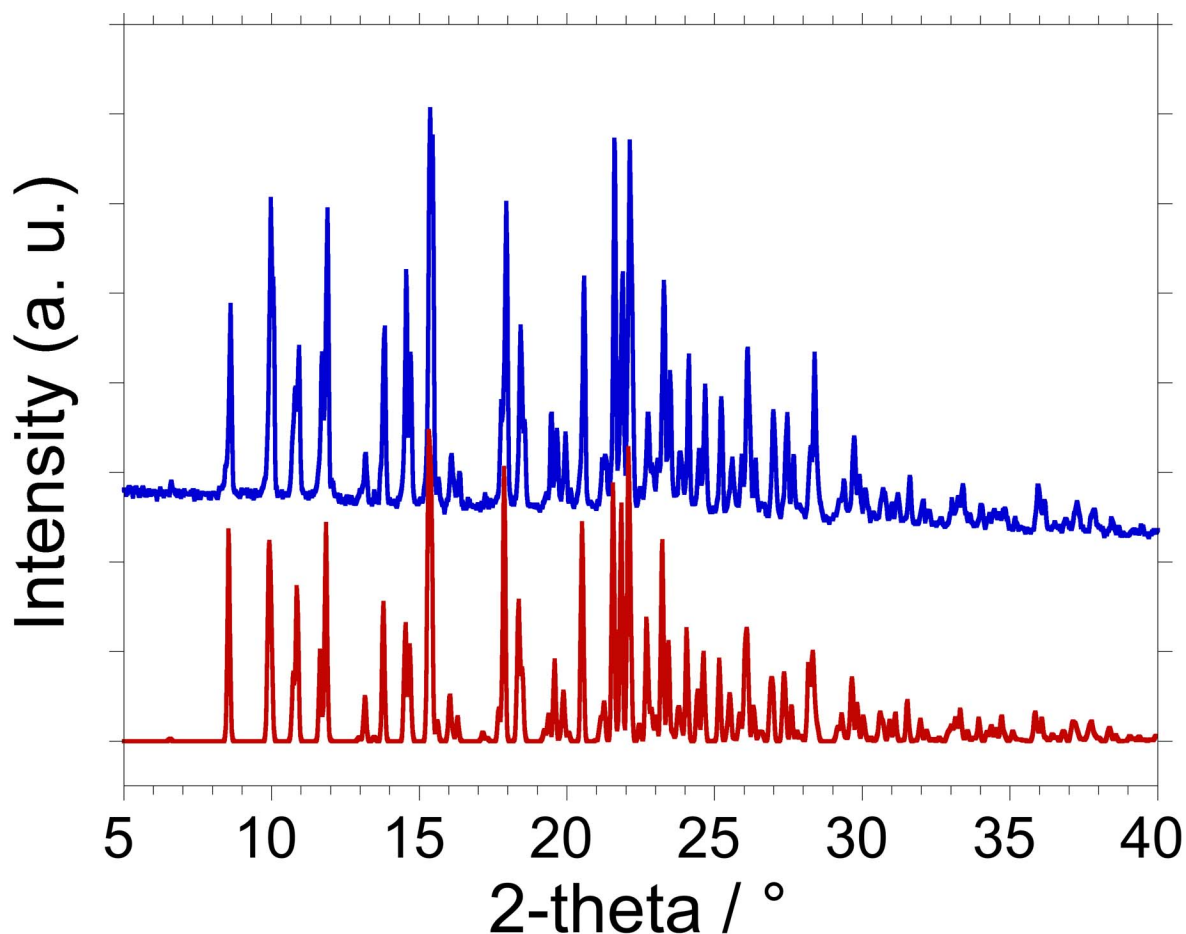


Figure S1. X-ray powder diffraction patterns of monoclinic racemic etifoxine. Blue: as-received sample, red: calculated.

Table S6. Lattice parameters and specific volume of monoclinic racemic etifoxine as a function of temperature^a

T/K	a/Å	b/Å	c/Å	β /°	$V_{\text{cell}}/\text{Å}^3$	$v/\text{cm}^3 \text{g}^{-1}$
100	8.3969(2)	17.4919(5)	20.6277(6)	98.326(3)	2997.83(16)	0.75024(4)
120	8.4053(2)	17.5078(5)	20.6464(6)	98.360(3)	3006.01(15)	0.75229(4)
140	8.4129(2)	17.5236(5)	20.6662(7)	98.387(3)	3014.13(16)	0.75432(4)
160	8.4219(2)	17.5387(5)	20.6874(7)	98.420(3)	3022.78(16)	0.75649(4)
180	8.4317(2)	17.5571(5)	20.7099(7)	98.471(3)	3032.37(16)	0.75888(4)
200	8.4411(2)	17.5771(6)	20.7369(7)	98.496(4)	3042.98(17)	0.76154(4)
220	8.4528(2)	17.5955(5)	20.7676(7)	98.561(3)	3054.39(16)	0.76439(4)
240	8.4640(3)	17.6196(6)	20.7975(7)	98.611(3)	3066.60(17)	0.76745(4)
260	8.4748(3)	17.6411(6)	20.8324(7)	98.677(4)	3078.91(17)	0.77053(4)
280	8.4826(3)	17.6591(6)	20.8626(8)	98.762(3)	3088.62(17)	0.77296(4)
300	8.4950(3)	17.6873(6)	20.9059(7)	98.841(3)	3103.88(18)	0.77678(4)
320	8.5080(3)	17.7164(6)	20.9506(7)	98.947(3)	3119.50(18)	0.78069(4)
340	8.5205(3)	17.7469(6)	21.0063(8)	99.087(3)	3136.55(19)	0.78496(5)

^aesd's in parentheses

Table S7. Specific volume of molten etifoxine as a function of temperature

T/K	Density/g cm ⁻³	v/cm ³ g ⁻¹
363.154	1.16203	0.860563
358.155	1.16632	0.857398
353.155	1.17057	0.854285
348.154	1.17524	0.850890
343.154	1.17978	0.847616
338.154	1.18406	0.844552
333.154	1.18828	0.841552
328.150	1.19235	0.838680
323.150	1.19590	0.836190

Table S8. Temperature, enthalpy of fusion, and glass transition (temperature at midpoint) of monoclinic racemic etifoxine

	T _{fus} /K (onset)	Δ _{fus} H/Jg ⁻¹	Tg/K
	362.69	80.85	297.46
	361.91	84.76	297.65
	362.39	81.47	296.04
	362.35	87.17	297.60
	362.53	89.51	
	361.97	87.47	
	362.81	84.93	
	362.77	82.25	
	362.77	85.63	
	362.76	87.33	
	362.81	83.36	
	362.77	86.05	
	362.83	84.47	
	362.83	84.41	
	362.71	91.54	
	362.77	88.41	
Mean values	362.6±0.3	85.60±2.91	297.2±0.8

Table S9. Onset temperatures of the melting peak of etifoxine and the corresponding pressures

P/MPa	T/K
0.1	362.75
22.42	369.05
31.71	372.65
55.86	378.55
86.32	386.95
112.49	393.85
141.37	400.65
164.62	406.85
190.21	412.25
214.14	418.05
233.28	421.15
257.33	425.25

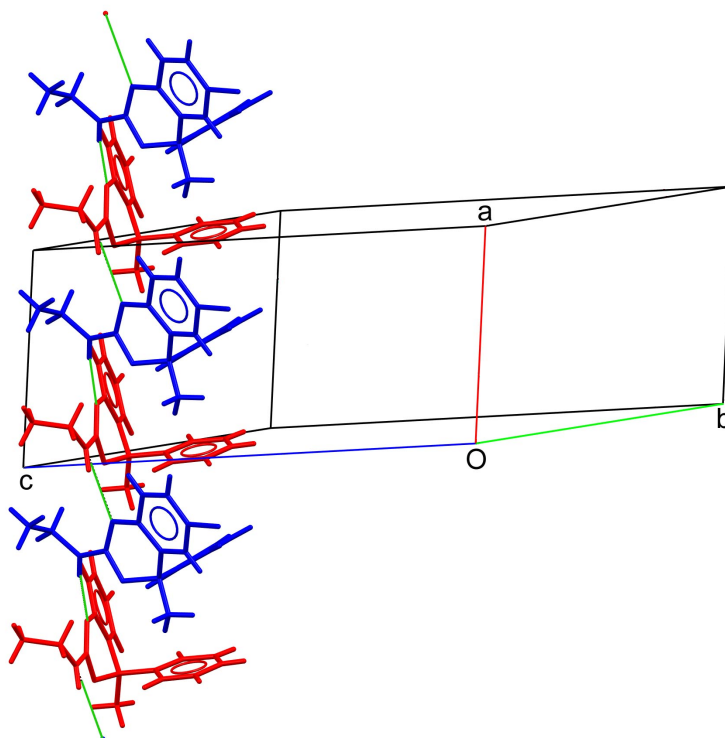


Figure S2. Hydrogen bonding in racemic etifoxine. Molecules 1 and 2 are linked by N1...H-N2 hydrogen bonds (green) that form infinite chains parallel to axis **a**.

Table S10. Distances d [Å] and angles [°] of intermolecular hydrogen bonds for monoclinic racemic etifoxine^a

D-H ... A ^b	d(D-H)	d(H ... A)	d(D ... A)	Angle D-H-A)
N2_1-H2_1...N1_2#1	0.86	2.25	3.080(3)	162.9
N2_2-H2_2...N1_1	0.86	2.26	3.112(3)	169.4
C15_2-H15A_2...O1_1#2	0.97	2.52	3.460(3)	162.4
C15_1-H15B_1...O1_2	0.97	2.57	3.471(3)	155.1
C15_1-H15B_1...N2_2	0.97	2.70	3.593(3)	153.7

^aesd's in parentheses.

^bSymmetry transformations used to generate equivalent atoms: #1: $x+1, y, z$ #2: $x-1, y, z$

Table S11. Polynomial $p = p_0 + p_1T + p_2T^2$ for the lattice parameters and reliability index R defined as $R = \sum(p_{exp} - p_c)^2 / p_c^2$, where p_{exp} and p_c are the measured and calculated lattice parameters.

Parameter	p_0	$p_1(\cdot 10^3)$	$p_2(\cdot 10^5)$	$R(\cdot 10^4)$
$a/\text{Å}$	8.3600(28)	0.322(27)	0.044(6)	1.1
$b/\text{Å}$	17.443(58)	0.342(57)	0.16(13)	1.1
$c/\text{Å}$	20.677(26)	-0.69(25)	0.49(6)	4.3
$\beta/^\circ$	98.41(4)	-1.74(42)	1.08(9)	1.5