

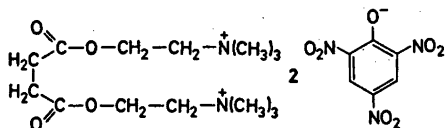
The Crystal Structure of Succinylcholine Picrate

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Succinylcholine picrate, $C_{26}H_{34}N_2O_{18}$, crystallizes in space group $P\bar{1}$ with a unit cell having dimensions $a=11.147(7)$, $b=7.091(8)$, $c=11.332(8)$ Å, $\alpha=101.59^\circ(5)$, $\beta=109.08^\circ(5)$, and $\gamma=94.68^\circ(13)$. $Z=1$. The structure was determined from a sharpened origin removed three-dimensional Patterson synthesis and refined by full matrix least squares technique to an R index of 0.063, using 1870 diffractometer-collected single crystal X-ray diffraction intensity data. The torsion angle $O-C-C-N^+$ is $\pm 87^\circ$. A correlation of the three known crystal structures of succinylcholine salts provides a picture of the readiness with which changes from the preferred conformation take place in different parts of the succinylcholine ion.

The crystal structure of succinylcholine picrate has been determined as a part of an investigation¹⁻³ of the influence of different surroundings on the conformation of the succinylcholine ion.



EXPERIMENTAL

Succinylcholine picrate, $C_{26}H_{34}N_2O_{18}$, was prepared by mixing saturated aqueous solutions of succinylcholine chloride and of picric acid, and single crystals were grown by slow evaporation of an aqueous solution of the compound. M.p. $158.5-159^\circ\text{C}$. The crystals are yellow, triclinic needles elongated in the b -direction. The unit cell parameters, obtained from precession photographs ($\text{MoK}\alpha$ radiation, $\lambda=0.7107$ Å) and refined by the least squares method using the program CELSIUS,⁴ are: $a=11.147(7)$, $b=7.091(8)$, $c=11.332(8)$ Å, $\alpha=101.59^\circ(5)$, $\beta=109.08^\circ(5)$, and $\gamma=94.68^\circ(13)$. The space group is $P\bar{1}$. The calculated density for one formula

unit per unit cell is 1.515 g cm^{-3} and the density measured by flotation in a mixture of tetrachloromethane and chloroform is 1.51 g cm^{-3} . The linear absorption coefficient, $\mu(\text{MoK}\alpha)$, is 1.4 cm^{-1} .

All X-ray data were measured from a crystal with the dimensions $0.35 \times 0.4 \times 0.5$ mm with quartz monochromatized $\text{MoK}\alpha$ -radiation using a NONIUS 3-circle automatic diffractometer. The ω -scanning mode was used with a scan speed of $0.6^\circ/\text{min}$, each reflection being scanned over a range of 1.4° . Of the about 4000 independent reflections within the range of $2.5^\circ \leq \theta \leq 28.0^\circ$, 1870 reflections with intensities greater than 2.5 standard deviations were considered as observed. The diffraction data were reduced to structure amplitudes by the use of an ALGOL-program OUTDIFF-5, written by A. M. Sørensen of this laboratory. No absorption corrections were applied.

DETERMINATION AND REFINEMENT OF THE STRUCTURE

An attempt to solve the structure applying symbolic addition procedures, using the Σ_2 relationship⁵ was made, but without success. A program system written for centrosymmetric structures by Dewar and Stone⁶ was used. The signs of 328 reflections were defined in terms of 7 symbols, 3 of which were origin defining. After the structure had been solved it became clear, that the correct combination of signs had a very low internal consistency.

The sharpened three-dimensional origin removed Patterson synthesis gave the orientation of the benzene ring of the picrate ion. Two picrate ions related by a center of symmetry give rise to a set of eight vectors equal to the imaginary vector between the centers of the two rings, and further 6 sets each consisting of eight practically equal vectors exist between the picrate ions. The Patterson synthesis was scan-

Table 1. Continued.

-5 112 108	1 44 47	-6 90 46	4 284 288	2 119 102	-6-6e.L	-6 51 47	-4-7e.L
-6 113 107	3 66 62	-8 37 58	3 36 61	1 102 86	7 66 64		1 45 46
-8 65 73		-9 62 70	2 53 39	-1 196 195	6 173 155	5-9e.L	2 34 26
-9 74 79	9-4e.L		1 59 63	-2 177 168	5 46 51	-7 53 50	5 37 30
	4 74 72	-0-4e.L	0 120 126	0 120 126	1 85 87	-6 35 43	5 65 59
3-3e.L	1 46 42	-6 52 57	-1 134 132	-6 71 68	-1 40 38	-4 83 74	8 55 56
-11 58 54	0 55 43	-5 73 71				-3 38 39	-2 40 34
-10 69 59	-1 71 65	-4 246 243		-1-5e.L	-5-6e.L	-2 40 34	8-5-7e.L
-9 96 99	-3 81 66	-3 121 119	-2 45 47	-1 153 157	0 60 61	-1 99 103	8 82 88
-7 201 206	-4 58 53	-2 183 186	-1 100 113	-5 52 58	1 69 72	0 35 27	7 71 71
-6 30 20	-5 85 82	-1 185 166	0 54 54	-4 43 45	2 43 49	1 101 117	5 35 40
-5 49 55	-7 101 99	0 153 155	3 105 106	3 43 36	3 166 176	2 64 53	1 43 39
-3 175 161		1 101 97	4 62 55	-2 64 55	4 50 50	4 91 104	
-2 212 211	8-4e.L	2 102 119	5 174 172	-1 162 157	5 107 110	5 32 29	-3-7e.L
-1 42 50	-8 43 41	3 176 171	6 153 155	0 39 38	6 85 88	7 39 44	4 74 68
0 38 51	-6 108 101	4 334 330	7 86 84	1 158 169	7 41 37		-2-8e.L
1 108 108	-5 177 179	5 65 57		2 85 102			5 42 31
2 181 179	-3 34 27	6 155 150		-9-4e.L	-4-6e.L	7 7 54	4 44 27
3 317 313	-2 73 77	7 38 30	5 86 94	4 199 201	10 37 32	6 59 59	2 51 74
4 27 29	-1 217 213	8 33 43	4 57 51	6 49 51	9 51 47	3 67 79	
5 87 91	0 169 161	9 244 238	3 114 111	8 129 133	8 100 99	2 36 47	
6 70 70	6 59 53	10 127 133	2 41 37	9 73 71	5 36 27	1 52 60	-1-9e.L
7 59 50		11 44 48	0 55 47		4 39 40	-1 108 114	0 77 78
8 127 124			-1 55 57	2-5e.L	1 80 80	-2 99 100	3 49 44
9 102 107	6 50 40	-1-4e.L		10 105 100	0 62 51	-6 137 138	4 96 92
	5 59 53	11 81 77		-10-4e.L	9 115 113	-1 33 34	5 64 76
4-3e.L	4 53 50	9 51 45	5 44 52	7 116 123	-2 41 44	-5 52 60	0-8e.L
8 126 124	0 79 84	7 165 162	5 86 92	6 65 67	-3 37 41	-3 87 88	5 8 8
7 111 103	-1 156 153	6 128 127	6 36 29	4 51 59		-2 39 42	0 57 43
6 157 154	5 52 58	5 153 141		5 41 29		0 38 49	3 74 75
5 56 58	-3 39 32	3 150 141		-11-4e.L	0 67 67	-1 38 29	
4 89 90	-4 34 28	2 219 189		-11-4e.L	-2 41 53	0 38 49	
2 57 59	2 57 56	1 219 189		-12-4e.L	2 35 14	-1 83 81	
1 86 76	-6 73 74	0 314 283		-9-5e.L	-3 59 56	2 39 31	-1 165 180
0 217 231		-1 149 155		-2 79 85	-5 112 119	4 118 123	1 36 37
-1 154 170	5-4e.L	1 280 287		5 39 39	6 65 62	6 65 62	3 49 44
-2 100 107	-10 42 45	-3 39 40		-8-5e.L	7 49 45	2 59 51	5 36 41
-3 269 272	-9 65 65	-4 100 106		10 47 49	8 74 68	1 40 44	
-4 107 107	-5 52 52	-5 280 285		-7 38 40	9 64 63		
-5 43 45	-5 43 45	-6 78 67		-7 96 99	10 45 56	9-6e.L	5 42 51
-7 41 42	-5 136 128	-7 84 67		-3 36 58		0 44 44	1 51 47
	-3 79 73			-2 10 38			2-9e.L
	-1 36 38			-1 135 141	8 61 56	8-6e.L	0 63 74
5-3e.L	0 195 193	-6 55 47	4 45 56	1 36 27	5 112 109	-3 59 53	
-11 51 56	-8 147 147	-4 147 140	5 44 48	4 48 43	4 48 43	-4 75 66	4-8e.L
-8 100 95	-2 92 90	-4 198 199	6 94 89	3 75 76	3 160 143	-5 44 47	1 73 88
-7 49 42	3 104 95	-3 201 211	7 65 68	4 146 156	2 48 46		
-6 135 135	4 57 59	-2 125 123	5 49 47	5 159 157	1 13 53	9-6e.L	5-9e.L
-4 35 24	6 122 117	-1 39 24	6 122 117	7 53 45	0 78 80	-4 121 122	1 41 57
-2 115 101		0 83 74		8 54 54	-1 52 64	-3 63 65	
-1 235 237	5-4e.L	1 352 326		9 63 62	-2 152 117	-2 66 61	
1 151 153	6 117 121	2 35 41	8 74 78	4-5e.L	-3 59 56	-1 48 45	
2 173 176	5 148 148	3 125 114	7 77 79	7 51 35	-4 53 64	1 69 74	
3 47 59	4 227 208	4 126 136	6 126 136	5 100 112	-5 68 76	7-7e.L	
5 96 86	2 133 139	5 204 197	5 176 181	6 66 61		1 39 39	
7 85 93	1 45 41	6 35 37	4 158 166	4 37 44	-1-6e.L	-1 56 59	
8 50 46	3 90 86	9 50 56	3 72 85	3 49 57	-4 32 35	-2 34 37	
10 92 89	-2 152 115	10 50 46	-1 71 80	1 108 125	-3 112 114		-6-7e.L
	-4 102 102	11 87 85		-1 99 49	-2 111 107		-3 41 44
	-6 9 64		-2 83 94	-5 53 61	-1 98 102		-1 48 40
5 76 79	-7 107 111	11 141 139	0 43 41	-6 75 77	2 28 20		2 30 43
4 66 63	-8 45 55	10 64 52	2 28 20	-7 57 64	-8 41 45	2 165 146	
2 82 70		8 43 40	5 93 99	5 91 91		8 111 108	
1 100 92		7 287 284	8 105 111	5-5e.L	9 46 40	5 39 43	
0 60 59		4 63 71		-8 41 47	10 101 95	-1 40 42	
-1 118 122	-8 102 108	4 65 56		-7 40 39	11 42 43	-4 73 79	
-2 190 188	-7 75 81	3 98 101		-2 36 40		0-6e.L	
-4 151 153	-4 51 53	3 98 101	12 55 49	-4 30 32	8 09 90	-2 42 47	
-6 177 179	-3 195 140	1 138 112	10 87 92	-2 36 40	7 112 107	0 113 125	
-7 183 184	-1 103 110	0 85 86	8 182 179	7 93 101	5 31 28	2 59 58	
-8 91 91	1 49 39	-1 136 136	7 93 101	6 34 46	4 62 78	4 39 47	
-9 63 53	4 111 110	-2 137 144	5 176 184	2 90 102	3 60 52	6 78 82	
-7 216 218	5 88 83	-4 183 188	6 240 244	3 60 52	7 46 57	2 96 86	
-6 62 62	7 85 85	-5 36 37	0 158 159	0 59 54		2 96 86	
-4 81 83	7 46 35	-6 48 48	-1 61 46	6-5e.L	0 81 86		
-1 84 84	10 61 51		-3 39 42	6 46 40	-1 53 52	3-7e.L	
0 132 125		-4 86 97		5 102 103	-2 158 160	7 47 55	
1 64 44	3-4e.L	-5 44 47		1 76 81	-3 152 146	2 69 120	
2 44 46	9 72 65	-2 32 31	-3-5e.L	0 128 128	-4 75 62	-1 70 75	
3 33 41	8 49 51	-1 36 29	-5 61 55	-2 39 55		-3 44 42	
	7 56 63	0 75 75	-2 38 47	-1 35 34		-5 75 89	
8-3e.L	5 25 44	2 189 186	1 176 184	-1 54 45			
4 69 10	3 222 226	3 215 215	2 240 244	-5 75 76	-3 132 129	2-7e.L	
4 165 159	2 342 371	4 180 176	4 55 54	-6 40 46	-1 85 84	3 41 56	
3 52 46	1 115 139	5 124 118	6 32 30	-8 53 44	2 47 54	1-7e.L	
1 58 57	0 77 89	6 158 122	7 48 42		4 48 45	8 60 56	
-1 131 125	-1 257 254	7 47 31	9 36 37	7-5e.L	5 125 131	7 57 58	
-3 51 51	-2 307 284	8 50 37	10 35 25	-6 43 30	6 82 91	4 52 58	
-2 81 52	-3 31 32	10 31 13	12 45 21	-9 98 98	7 43 44	3 75 76	
-6 89 87	-4 93 97	12 73 68		-2 115 108	9 47 57	2 44 38	
-7 108 107	-5 33 38			0 135 135		-1 80 83	
	-7 122 125			3 81 80	2-6e.L	-2 40 34	
9-3e.L	-8 81 81			4 35 41	9 45 47	-3 105 94	
-9 72 69		11 54 59	9 64 59	4 45 31	8 36 31		
-8 62 60		10 60 58	7 85 75		7 58 58		
-6 69 54	2-4e.L	9 132 141	6 122 120	8-5e.L	6 51 49	-3 73 70	
-4 62 58	-7 152 147	8 71 73	5 30 29	2 50 43	5 215 232	-2 38 35	
-2 93 85	-6 137 140	7 63 63	3 46 47	1 110 117	4 47 49	-1 42 37	
-1 98 98	-5 42 38	6 116 111	2 221 218	1 47 54	2 32 44	0 103 137	
0 67 46	-4 104 97	4 66 69	1 47 54	-2 94 95	1 35 59	1 43 54	
1 58 53	-3 98 92	3 53 54	0 98 90	-3 69 66	0 140 164	3 60 53	
	-2 125 124	0 78 82	-1 96 101	-5 77 81	-1 116 128	4 95 122	
10-3e.L	-1 161 148	-1 29 25	-2 87 95	-6 86 70	-6 74 82		
0 128 122	1 163 159	-2 127 136	-3 63 39	-7 48 43			
-1 91 93	3 017 315		-4 181 180	-8 68 57			
-3 86 75	4 305 293		-7 34 38				
-6 59 50	5 41 50	-4-3e.L					
-9 66 51	6 90 85	-3 64 70					
	7 37 30	-2 60 67					
11-3e.L	8 147 128	-1 47 72					
-4 74 75	9 101 94	0 61 60					
-3 55 46	10 85 80	1 69 73					
-2 81 72	11 55 52	2 97 96					
0 68 56		3 69 73					
3 50 41	1-4e.L	4 113 115					
	9 352 56	5 33 25					
11-4e.L	8 111 110	6 91 97					
-2 111 101	7 58 59	7 105 101					
-1 59 49	5 75 71	8 71 70					
-3 85 80	4 213 214	10 50 48					
	3 505 503	11 47 45					
	2 46 49	12 53 48					
10-4e.L							
-8 47 35	1 75 71						
-6 84 72	0 422 398						
-4 70 65	-1 70 65	11-4e.L					
-3 63 60	-2 338 327	9 103 112					
2 84 71	-3 175 175	6 59 69					
0 49 51	-5 36 37	5 63 63					

Table 2. Final positional parameters and their estimated standard deviations. Parameters and e.s.d. of non-hydrogen atoms are $\times 10^4$, parameters and e.s.d. of hydrogen atoms are $\times 10^3$.

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C(11)	4114(5)	0158(7)	2535(4)	C(5)	-1271(6)	4119(8)	1309(5)
C(12)	5313(4)	1482(6)	3389(4)	C(6)	-2531(5)	4772(7)	0732(5)
C(13)	5514(4)	2480(6)	4609(4)	N(7)	-2435(4)	6862(5)	0607(3)
C(14)	4519(5)	2427(6)	5083(4)	C(8)	-1731(5)	8258(8)	1889(5)
C(15)	3333(5)	1245(7)	4368(5)	C(9)	-3797(5)	7274(9)	0109(6)
C(16)	3163(4)	0183(7)	3153(4)	C(10)	-1778(6)	7142(8)	-0327(5)
O(11)	3988(4)	-0879(5)	1474(3)	H(11)	128 (6)	448 (8)	517 (6)
N(12)	6398(4)	1590(5)	2947(4)	H(12)	007 (5)	265 (9)	497 (5)
O(121)	6193(4)	1612(5)	1821(3)	H(51)	-054 (6)	417 (9)	102 (6)
O(122)	7474(4)	1666(6)	3721(4)	H(52)	-139 (6)	264 (9)	098 (6)
N(14)	4722(5)	3519(6)	6366(4)	H(61)	-299 (5)	383 (8)	-032 (5)
O(141)	3803(4)	3582(6)	6735(4)	H(62)	-301 (5)	464 (7)	129 (5)
O(142)	5815(4)	4373(6)	7034(3)	H(81)	-170 (5)	967 (9)	184 (5)
N(16)	1953(4)	-1187(6)	2484(5)	H(82)	-070 (6)	804 (8)	226 (5)
O(161)	1462(4)	-1918(6)	3141(4)	H(83)	-209 (6)	809 (8)	251 (6)
O(162)	1477(4)	-1493(7)	1324(4)	H(91)	-383 (5)	856 (8)	-018 (5)
H(13)	636 (5)	302 (7)	512 (5)	H(92)	-431 (5)	743 (8)	079 (5)
H(15)	259 (5)	136 (7)	468 (5)	H(93)	-426 (5)	628 (8)	-074 (5)
C(1)	0348(5)	4270(8)	4741(5)	H(101)	-187 (6)	845 (9)	-048 (6)
C(2)	0029(5)	3752(8)	3318(5)	H(102)	-211 (6)	595 (9)	-114 (6)
O(3)	0541(4)	2615(7)	2772(4)	H(103)	-069 (6)	698 (9)	010 (6)
O(4)	-0898(3)	4603(5)	2689(3)				

Table 3. Final thermal parameters and their estimated standard deviations $\times 10^3$. The anisotropic temperature factors are defined by the equation

$$T.F. = \exp[-\frac{1}{2}(h^2a^{*2}B_{11} + k^2b^{*2}B_{22} + l^2c^{*2}B_{33} + 2hka^*b^*B_{12} + 2hla^*c^*B_{13} + 2klb^*c^*B_{23})]$$

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(11)	3.00(23)	1.94(19)	2.35(20)	0.01(17)	0.67(18)	0.55(16)
C(12)	2.84(22)	1.92(19)	2.47(20)	0.02(17)	1.08(17)	0.61(16)
C(13)	2.71(21)	1.65(19)	2.32(20)	0.08(16)	0.48(17)	0.36(15)
C(14)	3.33(23)	1.61(19)	2.04(19)	0.57(17)	0.88(17)	0.34(15)
C(15)	2.81(22)	2.59(22)	2.78(21)	0.75(18)	1.13(18)	0.97(17)
C(16)	2.40(21)	2.37(21)	2.50(21)	-0.05(17)	0.46(17)	0.68(17)
O(11)	4.94(20)	2.82(16)	2.79(16)	-1.05(14)	1.54(14)	-0.69(12)
N(12)	3.35(21)	1.60(16)	3.27(20)	-0.09(14)	1.26(17)	0.30(14)
O(121)	4.73(20)	3.46(17)	3.47(18)	-0.02(15)	2.08(15)	1.07(14)
O(122)	2.73(17)	4.82(21)	4.40(19)	0.17(14)	0.94(15)	0.74(15)
N(14)	5.30(26)	2.32(19)	2.74(20)	0.69(19)	1.92(15)	0.31(15)
O(141)	6.55(25)	4.72(21)	4.13(20)	0.64(18)	3.33(19)	-0.24(16)
O(142)	5.86(24)	3.48(18)	2.80(16)	-0.62(17)	0.91(16)	-0.66(14)
N(16)	3.04(20)	3.39(22)	3.81(23)	-0.42(16)	0.59(18)	0.63(18)
O(161)	4.38(21)	6.17(25)	5.47(22)	-2.15(18)	0.92(18)	2.35(19)
O(162)	4.16(21)	6.78(25)	3.03(19)	-1.43(18)	0.15(16)	-0.38(16)
C(1)	3.47(25)	4.11(27)	3.23(23)	1.15(20)	0.41(20)	0.52(20)
C(2)	2.95(24)	3.26(24)	3.55(25)	0.62(20)	0.42(20)	0.64(20)
O(3)	6.65(26)	7.29(28)	4.64(21)	4.41(23)	1.36(20)	0.73(19)
O(4)	3.50(16)	2.79(15)	2.76(15)	0.72(13)	0.61(13)	0.71(12)
C(5)	5.21(30)	3.16(24)	2.55(22)	1.28(22)	1.21(20)	0.40(18)
C(6)	3.85(26)	1.61(19)	2.96(22)	-0.41(18)	0.66(20)	0.28(16)
N(7)	2.89(18)	1.93(15)	2.31(15)	-0.00(13)	0.70(14)	0.46(12)
C(8)	3.96(28)	2.35(21)	2.92(22)	-0.39(19)	0.50(19)	-0.45(17)
C(9)	2.92(24)	3.80(26)	3.52(25)	0.91(21)	0.64(20)	0.52(21)
C(10)	4.72(29)	4.83(29)	3.72(25)	0.06(23)	2.15(23)	1.97(22)

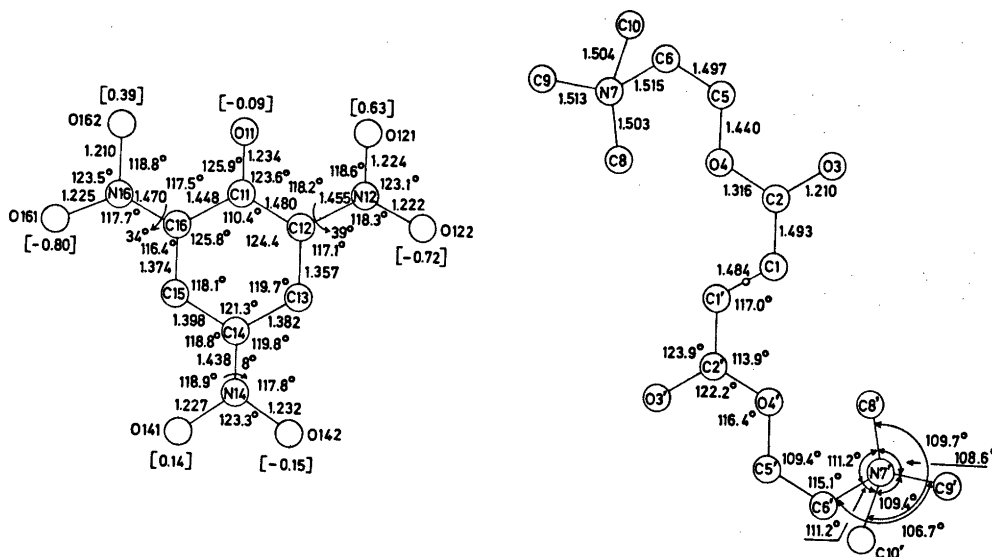


Fig. 1. Bond distances and angles. The e.s.d. on bonds are in the range 0.005–0.009 Å and on angles 0.4–0.5°. The numbers in angular parentheses are the distances in Ångström of the atoms from the least squares plane through the six carbon atoms in the ring.

ned for potential "center-center" peaks, and for each of them the fit of the additional 6 sets of vectors with the Patterson synthesis was examined. This, together with packing considerations, gave the clue to the solution. A three-dimensional electron density map calculated using the phases from the contributions of the atoms of the benzene ring and the three nitro groups (for the sake of simplicity arranged coplanar with the ring) indicated the positions of all ten non-hydrogen atoms in the succinylcholine ion and of the phenoxide oxygen atom.

The refinement was performed by the full-matrix least squares method. Positional parameters for all non-hydrogen atoms were varied together with their individual thermal parameters, initially isotropic but converted to anisotropic as the refinement neared convergence. When the R index had dropped to 0.1 a three-dimensional difference Fourier synthesis was calculated, from which the positions of all 17 hydrogen atoms in the asymmetric unit could be postulated. The positional parameters of the hydrogen atoms were added to the variables while their temperature factors were assumed to be equal to those of the atoms to which they are bonded. Some further cycles of least squares refinement were carried out, and after the last

cycle the final shifts of all varied parameters were less than one third of their corresponding estimated standard deviations. All atoms were treated as uncharged, and the form factors were taken from *International Tables for X-ray Crystallography*.⁷ The refinement was based on F_o , and the function minimized was $\sum w[|F_o| - |F_c|]^2$. Unit weight was given to each observed reflection with the exception of very weak reflections ($|F_o| < 10$), which were given weights less than 1.0. The final R value is 0.063. The observed structure amplitudes and the final calculated structure factors are given in Table 1. Nearly all calculations have been performed on the IBM 7094 computer at the NEUCC installation in Copenhagen with the use of the program systems *X-RAY 63*⁸ and *WATSUP*.⁹

DESCRIPTION AND DISCUSSION OF THE STRUCTURE

The final positional and thermal parameters together with their estimated standard deviations are given in Tables 2 and 3. The interatomic distances and angles are shown in Fig. 1, in which the atomic numbering used in this paper is also given. A number of least squares planes through parts of the ions were calculated.

Table 4. Least squares planes and angles between them. The equations of the planes are in direct (unit cell) space. Distances (Å) to atoms defining the plane are asterisked.

A.	$3.1826x - 6.4014y + 5.1107z - 2.4967\text{Å} = 0$
B.	$-0.6196x + 6.8770y + 0.2238z - 0.7650\text{Å} = 0$
C.	$-1.7944x + 6.6204y - 5.4084z + 1.9550\text{Å} = 0$
D.	$7.1335x - 5.7666y - 1.2873z - 1.7479\text{Å} = 0$
E.	$7.5084x + 4.7930y - 3.4255z - 0.6837\text{Å} = 0$

∠ Plane A Plane B 39°
 ∠ Plane A Plane C 8°
 ∠ Plane A Plane D 34°

Atom	A	B	C	D	E
C(11)	-0.006*				
C(12)	0.022*	-0.001*			
C(13)	-0.026*				
C(14)	0.014*		-0.002*		
C(15)	0.001*				
C(16)	-0.005*			0.003*	
O(11)	-0.088				
N(12)	-0.028	0.002*			
O(121)	0.627	-0.001*			
O(122)	-0.717	-0.001*			
N(14)	-0.007		0.006*		
O(141)	0.138		-0.002*		
O(142)	-0.150		-0.002*		
N(16)	-0.154			-0.010*	
O(161)	-0.801			0.004*	
O(162)	0.394			0.004*	
C(1)					0.000*
C(1')					0.000*
C(2)					0.000*
C(2')					0.000*
O(3)					-0.027
O(4)					0.073
C(5)					0.112
C(6)					0.547

The parameters of these planes, the deviations of the atoms from them and some angles between them are given in Table 4.

The dimensions of the picrate ion indicate a strong delocalisation of the negative charge of the phenoxide oxygen atom and are essentially as found by Maartmann-Moe¹⁰ in the mutually isomorphous salts, potassium picrate and ammonium picrate, and by Thewalt and Bugg in the structure of serotonin picrate monohydrate.¹¹ The benzene ring is not completely planar (*cf.* Table 4) and atoms bonded directly to the ring show considerable deviations, (up to 0.15 Å), from the least squares plane through the six carbon atoms. The planes of the two nitrogroups in the *ortho*-positions to O(11) are

twisted relative to the plane of the ring, the angles being 34 and 39°, respectively, and the distances O(121)–O(11) and O(162)–O(11) are 2.77 and 2.74 Å. The deviations of O(121) and O(162) from the ring plane have the same sign, while the deviation of O(11) from this plane has the opposite sign.

The bond lengths and angles of the succinylcholine ion show no deviations from the expected values. The central part of the ion, including the ten atoms C(1) to C(5) and C(1') to C(5'), is in this crystal structure approximately planar (*cf.* Table 4). The alcohol moiety of the ester group is situated *s-cis* to the carbonyl group, an arrangement which agrees with the most commonly found ester con-

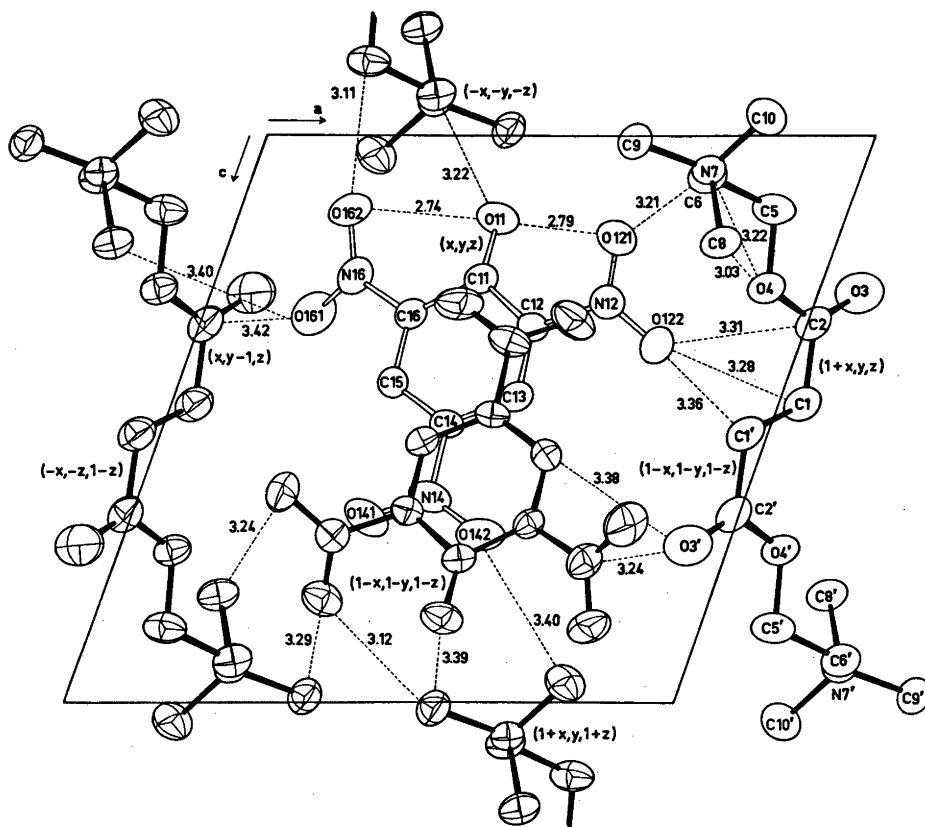


Fig. 2. Non-bonded distances less than or equal to the sum of the respective van der Waals radii of the atoms. The atoms are represented by their thermal ellipsoids scaled to enclose 50 % probability. The drawing was produced by ORTEP.³⁸

formation,¹² but the β -carbon atom of the acid moiety [C(1')] is situated in a more unusual manner, namely *s-trans* to the carbonyl group. As in most of the examined solid state structures containing the atomic arrangement O-C-C-N⁺, the system is in this structure found in an approximately *gauche* conformation, the torsion angle O(4)-C(5)-C(6)-N(7) being $\pm 87^\circ$ and the intramolecular distances N(7)-O(4) and C(8)-O(4) being 3.22 and 3.03 Å respectively. None of the hydrogen atoms bonded to C(8) are in a position favourable for a close contact to O(4). The distances H(82)-O(4) and H(83)-O(4) are 2.58 and 2.91 Å, respectively. This is in agreement with the situation found in *erythro- α,β -dimethylacetylcholine iodide*.¹³ The conformation about all

three N-C methyl bonds is staggered.

The structural packing on the whole is rather compact. Only few contacts (Fig. 2) between succinylcholine ions are found, whereas a number of close contacts between the picrate ions and between succinylcholine ions and picrate ions are observed. In agreement with the delocalisation of the negative charge of the phenoxide oxygen atom contacts to O(11) are not dominant and many contacts to the nitrogroups, especially the two in the *ortho*-positions to O(11), exist.

The crystal structures of three succinylcholine salts have been examined.²⁻⁴ Some indications concerning the preferred conformation of the succinylcholine ion and the readiness with which alterations from this conformation

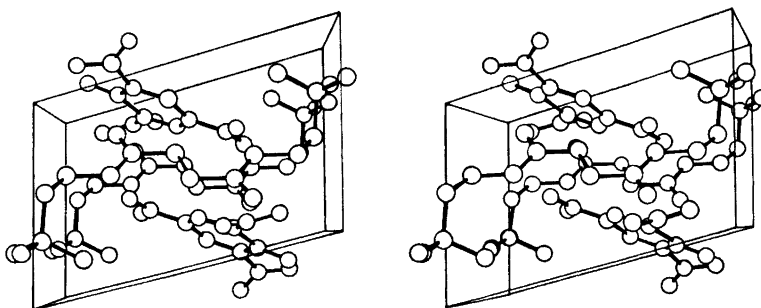


Fig. 3. Stereodiagram illustrating the packing. The b axis is \uparrow , the c axis is \leftarrow , and the a axis is directed upward. The drawing was produced by ORTEP.²³

take place in different parts of the ion can be seen from a correlation of the three structures. The immediate impression is that the three succinylcholine ions are very dissimilar: in the not very compact succinylcholine perchlorate structure the ion has a rather extended shape, while it is more or less crumpled up in the more compact succinylcholine iodide and succinylcholine picrate structures. Nevertheless the differences are concentrated in certain parts of the chain, while other parts of it are unchanged from structure to structure (*cf.* Table 5). The two main differences are found in the torsion around C(1)–C(2), and around O(4)–C(5). More constant are the following: (I) The torsion angle C(2')–C(1')–C(1)–C(2), in succinylcholine perchlorate and picrate 180° owing to the symmetry and in the iodide about 170°. (II) The torsion angle C(1)–C(2)–O(4)–C(5), which deviates from 180° with less than 10° in all three structures. (III) The torsion angle O(4)–C(5)–C(6)–N(7), which is of the magnitude characteristic for the system O–C–C–N⁺ in many solid state structures¹⁴ (although

deviations from this arrangement also have been reported.^{15–17})

It can be concluded that the *gauche* conformation of the choline moiety as expected from the numerous known structures¹⁸ is relatively stable and that alterations of the overall conformation of the succinylcholine ion preferably take place in other parts of the ion. This is in full agreement with Herdklotz and Sass,¹⁹ who found that the conformation of the acetylcholine ions in acetylcholine chloride crystals differs from that found in acetylcholine bromide.²⁰ Also here the *gauche* choline conformation was a common feature, while different ester conformations were observed.

The very many crystal structures of compounds, which in some or another way intervene in the normal biological functions of acetylcholine have given good information about the preferred conformation of this sort of compounds, and it has been observed that alterations from this preferred state, which may be induced by the crystal packing, will only seldom take place in the choline moiety. These results

Table 5. The numerical value of torsional angles (°) of succinylcholine iodide, succinylcholine perchlorate, and succinylcholine picrate.

	Suc. iodide	Suc. perchlorate	Suc. picrate
C(2')–C(1')–C(1)–C(2)	170	180	180
C(1')–C(1)–C(2)–O(4)	25	44	3
C(1)–C(2)–O(4)–C(5)	172	177	178
C(2)–O(4)–C(5)–C(6)	113	99	164
O(4)–C(5)–C(6)–N(7)	80	78	87

have been compared with measurements by IR²¹ and NMR spectroscopy²²⁻²⁴ in solution of compounds related to acetylcholine and with theoretical considerations,²⁵⁻²⁷ and more or less detailed agreement has been found. Nevertheless we are still concerned only with preferred conformations, and in biological systems we meet the possibility that the molecules may change conformation under influence of enzymes or receptors²⁸⁻²⁹ in a similar way as several enzymes³⁰⁻³² change conformation when acting on a substrate.

REFERENCES

1. Jensen, B. *Acta Chem. Scand.* 22 (1968) 2035.
2. Jensen, B. *Acta Chem. Scand.* 24 (1970) 2517.
3. Jensen, B. *Acta Chem. Scand.* 25 (1971) 3388.
4. Liminga, R. *Acta Chem. Scand.* 19 (1965) 1631.
5. Hauptman, H. and Karle, J. *Solution to the Phase Problem*, A.C.A. Monograph No. 3, Polycrystal Book Service, Pittsburgh 1953.
6. Dewar, R. K. B. *Use of Computers in the X-Ray Phase Problem*, Diss., University of Chicago, Chicago 1968.
7. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1962, Vol. III.
8. Stewart, J. M. *X-RAY-63, Crystal Structure Calculations System*, Computing Science Center, University of Maryland, Baltimore 1965.
9. Watson, K. J. *WATSUP*, A Set of Unified Computer Programmes for the Determination of Crystal Structures, Chemical Laboratory IV, H. C. Ørsted Institute, University of Copenhagen, Copenhagen 1969.
10. Maartmann-Moe, K. *Acta Crystallogr. B* 25 (1969) 1452.
11. Thewalt, U. and Bugg, C. E. *Acta Crystallogr. B* 28 (1972) 82.
12. Mathieson, M. McL. and Welsh, H. K. *Acta Crystallogr.* 18 (1965) 953.
13. Brennan, T. F., Ross, F. K., Hamilton, W. C. and Shefter, E. *A.C.A.-meeting, August 1970*, Carleton University, Ottawa, Abstract D. 1.
14. Sundaralingam, M. *Nature (London)* 217 (1968) 35.
15. Chotia, C. and Pauling, P. *Chem. Commun.* (1969) 746.
16. Shefter, E., Sackman, P., Stephen, W. F. and Smissman, E. E. *J. Pharm. Sci.* 59 (1970) 1118.
17. Barrans, Y. Thèse, L'Université de Bordeaux, Bordeaux 1971.
18. Shefter, E. In Trigger, D. J., Moran, J. F. and Barnard, E. A., Eds., *Cholinergic Ligand Interactions*, Academic, New York and London 1971.
19. Herdtklotz, J. K. and Sass, R. L. *Biochem. Biophys. Res. Commun.* 40 (1970) 583.
20. Canepa, F. G., Pauling, P. J. and Sörum, H. *Nature (London)* 210 (1966) 907.
21. Fellman, J. H. and Fujita, T. S. *Nature (London)* 211 (1966) 848.
22. Culvenor, C. C. J. and Ham, N. S. *Chem. Commun.* (1966) 537.
23. Casy, A. F., Hassan, M. M. A. and Wu, E. C. *J. Pharm. Sci.* 60 (1971) 67.
24. Partington, P., Feeney, J. and Burgen, A. S. V. *Mol. Pharmacol.* 8 (1972) 269.
25. Kier, L. B. *Mol. Pharmacol.* 3 (1967) 487.
26. Liquori, A. M., Damiani, A. and Elefante, G. J. *Mol. Biol.* 33 (1968) 439.
27. Pullman, B. and Courrière, P. *Theoret. Chim. Acta* 31 (1973) 19.
28. Phillips, D. C. *Sci. Amer.* 215 (1966) 78.
29. Koshland, D. E., Jr. and Neet, K. E. *Annu. Rev. Biochem.* 37 (1968) 388.
30. Ludwig, M. L., Hartsuck, J. A., Steitz, T. A., Muirhead, H., Coppola, J. C., Reeke, G. N. and Libscomb, W. N. *Proc. Nat. Acad. Sci. U.S.* 57 (1967) 511.
31. O'Sullivan, W. J. and Cohn, M. *J. Biol. Chem.* 241 (1966) 3116.
32. Yankeelov, J. A., Jr. and Koshland, D. E., Jr. *J. Biol. Chem.* 240 (1965) 1593.
33. Johnson, C. K. *ORTEP*, Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee 1965.

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