SHORT STRUCTURAL PAPERS

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2-Diethylamino-2′,6′-acetoxylidide (Lidocaine)

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Abstract. $C_{14}H_{22}N_2O$, monoclinic, $P2_1/c$; $a=13{\cdot}24(2)$, $b=14{\cdot}06(2)$, $c=19{\cdot}25(3)$ Å, $\beta=123{\cdot}7(1)°$ (20°C); F.W. 234·3, $D_m=1{\cdot}04$ g cm^{-3}, $Z=8$, $D_x=1{\cdot}03$ g cm^{-3}. Each of the two independent molecules is found to have the *trans*-amide configuration. The amidic proton of each molecule participates in a bifurcated bonding system, of which one branch is intramolecular and the other intermolecular.

Introduction. Transparent needle-like crystals (elongated along **c**) were grown from dimethylformamide–water solution at about −20°C. Single-crystal photographs indicated the systematic absences $h0l$ for l odd, and $0k0$ for k odd. They also revealed a rapid decrease of intensity with scattering angle, such that no reflexions could be observed beyond $\sin\theta/\lambda=0{\cdot}5$ Å^{-1}. The specimen was roughly cylindrical, 0·6 mm long and of mean diameter 0·3 mm. The intensities of the 3053 independent reflexions for which $\sin\theta/\lambda<0{\cdot}5$ Å^{-1} were measured with a Picker four-circle diffractometer, nickel-filtered Cu $K\alpha$ radiation, and a scintillation-counter. The θ–2θ scan mode was used; the detector was scanned through 2° over a period of one minute, and background counts were accumulated for 20 s at the beginning and end of each scan. 556 reflexions were considered to be unobserved, as their net intensities were less than either 5 deca-counts or 10% of the corresponding background. No correction was made for absorption ($\mu=5{\cdot}2$ cm^{-1}).

The structure was determined by symbolic addition procedures. The first E map revealed the positions of all the non-hydrogen atoms except those of the ethyl groups. The latter were subsequently identified in an F_o synthesis. Refinement was by the block-diagonal least-squares method. The quantity minimized was $\sum w\Delta F^2$ where

$$\begin{aligned} w &= 100/F_o^2 && \text{for } F_o>10, \text{ and} \\ &= F_o^2/100 && \text{otherwise.} \end{aligned}$$

For the six most intense reflexions, the observed structure amplitudes were found to be consistently smaller than the calculated values. The discrepancies were attributed to extinction, and these reflexions given zero weight. The hydrogen atoms were included in the structure-factor calculations (but without refinement) provided that they could be assigned chemically reasonable positions, or could be located in ΔF syntheses. Nine methyl hydrogen atoms were omitted. Refinement was slow, with oscillation of parameters and was terminated at an R of 0·11 (for observed reflexions only).* Final atomic parameters are given in Table 1.

Further refinement was possible but, in view of the very large thermal motion of this structure, was not expected to be useful. Bond lengths and angles are consistent with expectation but are not sufficiently accurate to merit detailed presentation. A summary of interatomic distances is given in Table 2.

The computer programs used in this work were those of Ahmed, Hall, Pippy & Huber (1966). Atomic scattering-factor curves were taken from Stewart, Davidson & Simpson (1965) (for hydrogen) and from Hanson, Herman, Lea & Skillman (1964).

Discussion. Both molecules are in the *trans*-amide configuration, in agreement with one spectroscopic assignment (Chupp, 1970) and in disagreement with another (Neville & Cook, 1969). The conformations of the independent molecules are very similar; in each case the amide group is planar, and the amino nitrogen atom [N(13)] lies quite close to the amide plane (Table 3). The relative positions of the nitrogen atom and the amidic proton are consistent with the intramolecular NH···N bond inferred by Chupp (1970) (Fig. 1, Table 2). This bond presumably stabilizes the conformation (*anti*) about C(10)–C(12), since the corresponding conformation in lidocaine molecules protonated at N(13) is quite different: 'nearly eclipsed' in the hydrohexa-

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* A list of observed and calculated structure amplitudes has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30513 (14 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

fluoroarsenate, and *gauche* in the hydrochloride monohydrate (Hanson & Röhrl, 1972†). Each amidic proton participates also in an intermolecular NH···O bond; adjacent molecules are thereby joined to form chains parallel to **c** (Fig. 2). The proton is thus three-coordinated, and the hydrogen bond is bifurcated. The molecular packing is such as to achieve maximum hydrogen bonding, but is otherwise inefficient in that

Table 1. *Final atomic parameters*

Quantities given are: for non-hydrogen atoms, fractional coordinates × 10^4; $U_{ij} \times 10^3$ Å^2 (T.F. = exp $[-2\pi^2(U_{11}a^{*2}h^2 + \ldots 2U_{12}a^*b^*hk + \ldots)]$; e.s.d.'s are given in parentheses. For hydrogen atoms, fractional coordinates × 10^3; Debye–Waller factors *B*, in Å^2.

	x	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1*A*)	4251 (5)	2409 (5)	3907 (3)	97 (4)	105 (5)	75 (4)	−4 (4)	56 (4)	−14 (4)
C(2*A*)	5385 (5)	1952 (5)	4352 (4)	96 (4)	101 (5)	91 (4)	3 (4)	56 (4)	−10 (4)
C(3*A*)	6409 (6)	2509 (6)	4841 (4)	97 (5)	171 (7)	104 (5)	−4 (5)	56 (4)	−26 (5)
C(4*A*)	6329 (8)	3446 (6)	4891 (5)	144 (6)	125 (6)	137 (6)	−14 (5)	76 (5)	−48 (5)
C(5*A*)	5247 (8)	3893 (6)	4466 (5)	194 (8)	101 (6)	141 (7)	−16 (5)	105 (7)	−36 (6)
C(6*A*)	4144 (7)	3391 (5)	3958 (4)	139 (6)	98 (5)	110 (5)	−7 (4)	78 (5)	−16 (5)
C(7*A*)	2910 (8)	3867 (7)	3469 (6)	150 (7)	141 (8)	163 (8)	26 (6)	82 (6)	47 (6)
C(8*A*)	5473 (7)	910 (6)	4315 (5)	126 (6)	148 (7)	126 (6)	10 (5)	66 (5)	28 (5)
N(9*A*)	3180 (4)	1858 (4)	3431 (3)	88 (3)	114 (4)	70 (3)	−9 (3)	47 (3)	−16 (3)
C(10*A*)	2772 (6)	1525 (5)	2666 (4)	94 (4)	137 (6)	75 (4)	6 (4)	47 (3)	−12 (4)
O(11*A*)	3330 (4)	1610 (4)	2326 (3)	126 (3)	210 (5)	83 (3)	2 (3)	68 (3)	−25 (4)
C(12*A*)	1613 (6)	1004 (6)	2241 (4)	112 (5)	194 (8)	87 (5)	−25 (5)	54 (4)	−40 (5)
N(13*A*)	1011 (4)	987 (4)	2667 (3)	92 (3)	147 (5)	93 (4)	−1 (3)	47 (3)	−25 (3)
C(14*A*)	671 (13)	38 (8)	2755 (7)	348 (16)	173 (9)	173 (10)	−13 (8)	155 (11)	−72 (10)
C(15*A*)	1250 (16)	−313 (11)	3499 (9)	394 (20)	199 (14)	217 (14)	70 (11)	58 (13)	−75 (14)
C(16*A*)	−42 (11)	1602 (10)	2252 (8)	199 (10)	289 (14)	226 (12)	8 (10)	142 (10)	54 (10)
C(17*A*)	−292 (12)	2102 (13)	2768 (14)	168 (11)	306 (19)	459 (27)	−68 (18)	148 (14)	15 (12)
C(1*B*)	1573 (5)	2403 (5)	416 (3)	73 (3)	134 (6)	60 (3)	12 (4)	39 (3)	13 (4)
C(2*B*)	921 (6)	3176 (5)	420 (4)	84 (4)	137 (6)	98 (5)	10 (4)	49 (4)	16 (4)
C(3*B*)	−353 (7)	2991 (6)	25 (5)	109 (6)	171 (7)	133 (6)	11 (5)	63 (5)	40 (5)
C(4*B*)	−851 (6)	2152 (7)	−341 (4)	78 (5)	203 (9)	105 (5)	2 (5)	35 (4)	−8 (5)
C(5*B*)	−165 (7)	1430 (6)	−325 (4)	130 (5)	151 (7)	102 (5)	−22 (5)	62 (5)	−29 (5)
C(6*B*)	1076 (5)	1517 (5)	48 (4)	98 (4)	117 (5)	80 (4)	−7 (4)	46 (4)	−21 (4)
C(7*B*)	1856 (7)	716 (6)	83 (6)	159 (7)	102 (6)	190 (8)	−21 (6)	114 (7)	6 (5)
C(8*B*)	1516 (8)	4098 (6)	839 (7)	156 (7)	118 (7)	207 (10)	−37 (7)	105 (7)	13 (6)
N(9*B*)	2855 (4)	2516 (4)	828 (3)	79 (3)	114 (4)	66 (3)	8 (3)	45 (2)	3 (3)
C(10*B*)	3366 (5)	2934 (5)	469 (4)	88 (4)	132 (6)	75 (4)	21 (4)	51 (3)	22 (4)
O(11*B*)	2783 (4)	3250 (4)	−234 (3)	119 (3)	219 (6)	98 (3)	68 (3)	73 (3)	45 (4)
C(12*B*)	4726 (6)	2983 (6)	989 (4)	102 (5)	172 (8)	100 (5)	32 (5)	65 (4)	5 (5)
N(13*B*)	5267 (4)	2598 (4)	1802 (3)	78 (3)	138 (5)	88 (3)	11 (3)	34 (3)	−1 (3)
C(14*B*)	6135 (17)	3191 (13)	2435 (9)	365 (21)	383 (23)	167 (12)	79 (13)	115 (13)	33 (17)
C(15*B*)	5620 (15)	3750 (14)	2625 (8)	360 (18)	406 (23)	171 (10)	84 (13)	155 (12)	156 (16)
C(16*B*)	6035 (12)	1735 (9)	1931 (8)	252 (13)	216 (12)	237 (13)	112 (10)	166 (11)	101 (10)
C(17*B*)	6221 (14)	1147 (10)	2519 (10)	310 (17)	212 (14)	288 (15)	91 (11)	183 (14)	94 (12)

	X	*Y*	*Z*	*B*		*X*	*Y*	*Z*	*B*
H(3*A*)	725	222	519	11·0	H(173*A*)	38	242	316	25·0
H(4*A*)	712	378	527	11·0	H(3*B*)	−86	352	1	11·0
H(5*A*)	515	461	452	11·0	H(4*B*)	−167	208	−61	11·0
H(81*A*)	520	62	467	20·0	H(5*B*)	−53	77	−59	11·0
H(82*A*)	515	62	377	20·0	H(9*B*)	332	231	144	11·0
H(83*A*)	630	62	453	20·0	H(121*B*)	498	366	103	11·0
H(9*A*)	277	171	373	11·0	H(122*B*)	507	264	70	11·0
H(121*A*)	102	129	169	11·0	H(141*B*)	666	361	227	25·0
H(122*A*)	176	35	216	11·0	H(142*B*)	685	286	297	25·0
H(141*A*)	78	−43	238	25·0	H(151*B*)	632	414	308	25·0
H(142*A*)	−20	0	260	25·0	H(152*B*)	502	411	213	25·0
H(151*A*)	105	−103	352	25·0	H(153*B*)	520	335	283	25·0
H(152*A*)	208	−40	359	25·0	H(161*B*)	676	179	197	25·0
H(153*A*)	116	3	380	25·0	H(162*B*)	547	126	137	25·0
H(161*A*)	−76	132	181	25·0	H(171*B*)	663	50	257	25·0
H(162*A*)	17	219	201	25·0	H(172*B*)	672	146	302	25·0
H(171*A*)	−102	252	247	25·0	H(173*B*)	542	93	242	25·0
H(172*A*)	−55	155	297	25·0					

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† Fig. 2. of this reference is in error in that the nitrogen atom specified in the Newman projections of C(12)–C(10) should be labelled 13, not 9.

Table 2. *Summary of interatomic distances*

Nominal e.s.d.'s are about 0·01 Å.

C(ring)——C(ring)	1·33 to 1·44 Å
C(ring)——CH_3	1·48 to 1·52
CH_2——CH_3	1·22 to 1·40
N(13)——C(ethyl)	1·40 to 1·51
C(1)——N(9)	1·42 and 1·43
N(9)——C(10)	1·34 and 1·34
C(10)——O(11)	1·23 and 1·21
C(10)——C(12)	1·47 and 1·50
C(12)——N(13)	1·43 and 1·42
N(9)······N(13)	2·69 and 2·66
N(9*A*)····O(11*B*′)	2·90
N(9*B*)····O(11*A*)	2·89
N(13*A*)···O(11*B*′)	3·53
N(13*B*)···O(11*A*)	3·52

Table 3. *Distances* (Å × 10^2) *of some atoms from certain mean planes*

Atoms specified in bold type define the mean plane. Two distances are given, the first for molecule *A*, and the second for molecule *B*.

Phenyl ring: **C(1)**, 0,0; **C(2)**, 0,1; **C(3)**, 0, −1; **C(4)**, 0,1; **C(5)**, 1,0; **C(6)**, −1,0; C(7), 0, −3; C(8), −4, −2; N(9), −5, −4.

Amide group: C(1), 2,0; **N(9)**, −3,0; **C(10)**, 0,0; **O(11)**, −1,0; **C(12)**, 1,0; N(13), 9, −3; O(11)*, −45, −2.

* Oxygen atom in adjacent molecule. Angle between phenyl ring and amide group: 76° for *A*, 82° for *B*

the density is very low and the thermal motion (especially of the peripheral groups) very large. The importance of the hydrogen bond as a determinant of the crystal structure is thereby demonstrated.

We thank Dr M. Röhrl for growing the crystals and for a preliminary X-ray survey.

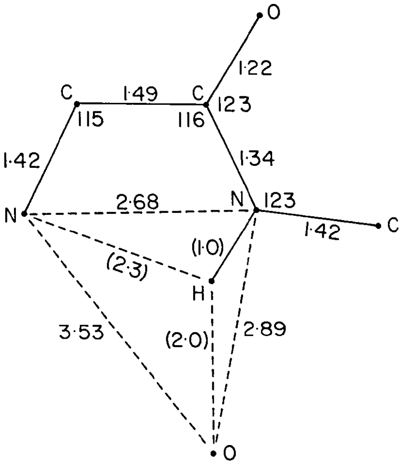

Fig. 1. Average environment of the amidic proton. e.d.s.'s are 0·01 Å and 1°. (The proton has been assigned a chemically reasonable position).

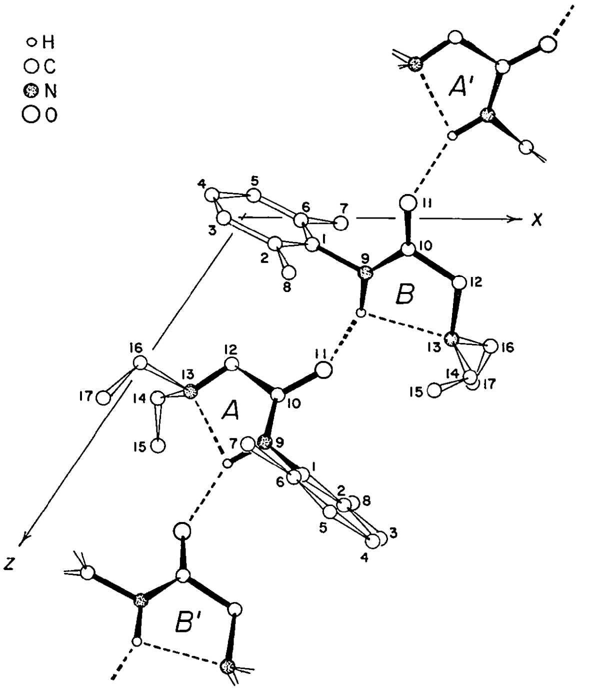

Fig. 2. Part of one hydrogen-bonded chain, viewed along **b**. (The centrosymmetrically related chain is not shown.) The solid bonds identify the planar central portions of the molecules. Hydrogen atoms other than amidic are not shown.

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