Synthesis and Properties of the Stereoisomeric Diethyl 2-Aminocyclohexane-1,4-dicarboxylates

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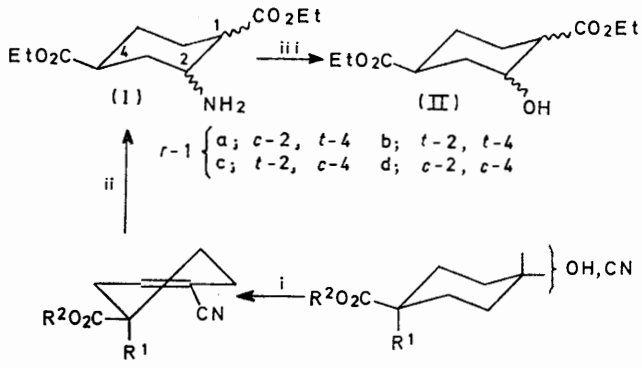
Nucleophilic addition of ammonia to ethyl 4-cyanocyclohex-3-enecarboxylate (III), followed by hydrolysis and esterification yielded the four stereoisomeric diethyl 2-aminocyclohexane-1,4-dicarboxylates (I). The conformations of these isomers were established by n.m.r. spectroscopy and by stereospecific deaminations to give cyclohexenes or diethyl 2-hydroxycyclohexane-1,4-dicarboxylates (II). *N*- and *O*-Benzoyl derivatives of the cyclohexanecarboxylates (I) and (II) respectively are discussed in relation to deshielding effects on α-protons. Diethyl *c*-2-aminocyclohexane-*r*-1,*c*-4-dicarboxylate (Id) undergoes intramolecular cyclisation to give ethyl 7-oxo-6-azabicyclo[3.2.1]octane-4-carboxylate (X).

OUR search for alicyclic compounds [1] possessing conformational features which promise exceptional reactivity and uses for pharmaceutical purposes has led us to the synthesis of the hitherto unknown stereoisomeric diethyl 2-amino- (I) and 2-hydroxycyclohexane-1,4-dicarboxylates (II). All four stereoisomers of (I)



(III) R^1 = H, R^2 = Et (IV) R^1 = H, R^2 = Et
(VI) R^1 = R^2 = H (V) R^1 = R^2 = H
(VIII) R^1 = CO_2Et, R^2 = Et (VII) R^1 = CO_2Et, R^2 = Et

Reagents: i, $SOCl_2$–C_5H_5N; ii, (a) 25% aq. NH_3, (b) HCl, (c) 3% HCl–EtOH; iii, $NaNO_2$–10% HOAc.

were obtained by nucleophilic addition of ammonia to ethyl 4-cyanocyclohex-3-enecarboxylate (III), followed by hydrolysis and esterification.

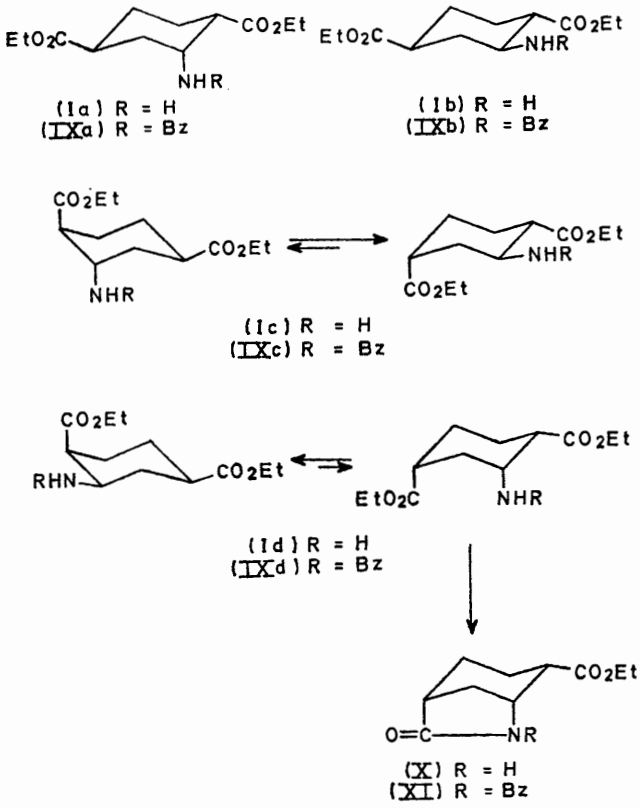
The cyanocyclohexene (III) was prepared by dehydration of the unstable ethyl 4-cyano-4-hydroxycyclohexanecarboxylate (IV) with thionyl chloride or phosphoryl chloride in pyridine.[2,3] The more stable hydroxy-carboxylic acid (V) similarly yielded the unsaturated acid (VI), and the hydroxy-1,1-dicarboxylate (VII), the most stable cyanohydrin in this series, gave the cyclohexene-1,1-dicarboxylate (VIII), in the highest yield (73%). The cyanohydrins (IV), (V), and (VII) were prepared from corresponding 4-ketones [4,5] by the procedure of Burdon *et al.*[6]

The stereoisomeric aminocyclohexanecarboxylates (Ia—d) were separated (ratios 1 : 7 : 1·5 : 5) by silica gel chromatography, and characterized as *N*-benzoyl derivatives and as hydrochlorides (see Table 1). The major amination products (Ib and d) are those with the amino-group equatorial since the addition of ammonia takes place more readily from the less hindered side of the cyclohexene ring. The equatorial benzamido-derivatives (IXb—d) are formed in higher yields and in a shorter time than the axially substituted isomer (IXa).

The n.m.r. spectra clearly indicated the geometry of the cyclohexylamines (Ia—d) and their benzamido-derivatives (IXa—d) (see Table 2). Thus, the *c*-2-amino-*t*-4-carboxylate (Ia) showed an unresolved multiplet (width 9·5 Hz) centred at τ 6·35 due to the equatorial

[1] V. Škarić, L. Stuhne, D. Škarić, and V. Turjak-Zebić, *J. Chem. Soc.* (*C*), 1969, 2783.
[2] R. P. Linstead and A. F. Millidge, *J. Chem. Soc.*, 1936, 478.
[3] T. Holm, *Acta Chem. Scand.*, 1964, **18**, 1577.
[4] E. Hardegger, P. A. Plattner, and F. Blanck, *Helv. Chim. Acta*, 1944, **27**, 793.
[5] T. Kutsuma and S. Sugasawa, *Tetrahedron*, 1958, **3**, 175.
[6] J. Burdon, T. J. Smith, and J. C. Tatlow, *J. Chem. Soc.*, 1961, 4519.

C-2 proton. The benzoylated product (IXa) showed the corresponding signal as a wider downfield multiplet, τ 5·11—5·52. The amide proton doublet at τ 3·23 disappeared on addition of deuterium oxide and the C-2 proton multiplet, partially obscured by the H_2O signal,



seemed to become narrower. Thus the isomer (Ia), obtained in the lowest yield, has the amino-group in the axial configuration.

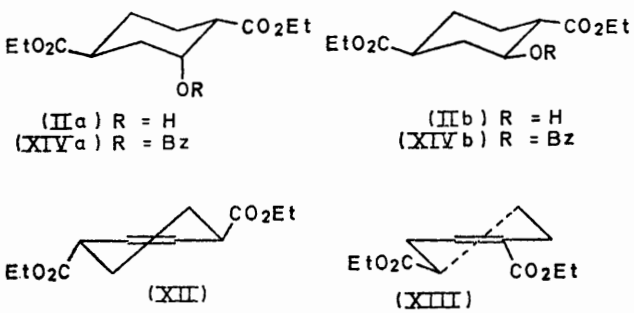
The spectra of the *t*-2-amino-isomers (Ib and c) showed octets centred at τ 7·01 and 6·82 (widths 24·5 and 23·9 Hz) in the region expected for axial C-2 protons [7] ($2J_{ax,ax} + J_{ax,eq}$). The stereoisomer (Ic), which originated in the 1,2-diaxial conformation and was therefore obtained in much lower yield than (Ib), was completely converted by conformational equilibration into the lower energy 1,2-diequatorial conformation.[8] The C-4 proton of (Ic) gave rise to an unresolved multiplet (width 11 Hz) centred at τ 7·22, indicating its equatorial configuration.

The isomer (Id) showed unresolved multiplets at τ *ca.* 6·78—7·33 for the C-1 and C-2 protons, which did not allow configurational assignment. However the compound was slowly converted into the azabicyclo-octanone (X), characterized as the *N*-benzoyl derivative (XI). The n.m.r. spectrum of compound (X) showed the C-2 proton signal shifted downfield to τ *ca.* 6·0 as a consequence of intramolecular elimination from the thermodynamically less stable 2,4-diaxial conformation.

The equatorial configurations of the benzamido-groups of (IXb—d) were confirmed by the relative ease of benzoylation, giving high yields (*ca.* 90%), and by concomitant shifts of the α-proton signals to lower field (τ 5·65—5·75).

The stereoisomers (Ib and d), having equatorial 2-amino-groups, offered additional stereochemical information in their reactions with nitrous acid.[9,10] Each isomer gave a 30% yield of unsaturated compounds and a 65% yield of the two possible stereoisomeric cyclohexanols (II). Thus, the *t*-2-amino-carboxylate (Ib) afforded diethyl cyclohex-2-ene-*r*-1,*t*-4-dicarboxylate (XII), diethyl cyclohex-1-ene-1,4-dicarboxylate (XIII), and the *cis*- and *trans*-2-hydroxy-diesters (IIa and b) (see Table 3). The n.m.r. signals of the C-2 and C-3 protons of the cyclohexenes (XII) and (XIII) showed the expected differences (see Table 2). The yield of the lower energy cyclohexanol (IIb) was twice that of the stereoisomer (IIa). N.m.r. data for (IIb) confirmed the axial configuration of the C-2 proton (multiplet at τ 6·05—6·42), and a multiplet in the spectrum of (IIa) centred at τ *ca.* 5·7 and partly overlapped by the $O{\cdot}CH_2$ resonances was assigned to the equatorial C-2 proton. The equatorial C-2 proton of the *O*-benzoyl derivative (XIVa) gave rise to a downfield multiplet at τ 4·27 ($2J_{eq,ax} + J_{eq,eq}$; width 9 Hz), whereas the epimeric *O*-benzoyl derivative (XIVb), obtained from the equatorial cyclohexanol in 98% yield, showed a sextet centred at τ 4·83 (width 25 Hz) for the axial C-2 proton.

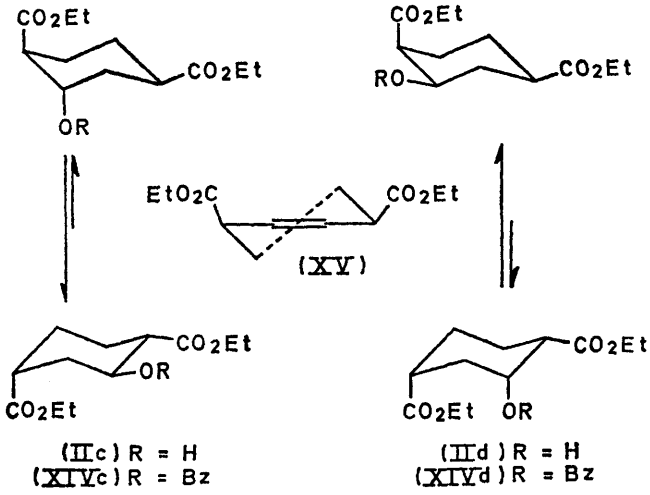
Treatment of the *c*-2-amino-carboxylate (Id) with nitrous acid afforded diethyl cyclohex-2-ene-*r*-1,*c*-4-dicarboxylate (XV) (as an unstable oil), the cyclohexene (XIII) already described, and the isomeric cyclohexanols (IIc and d) (see Table 3). The unsymmetrical cyclohexene (XV) showed n.m.r. signals at τ 4·04 and 4·07



due to the olefinic C-2 and C-3 protons in slightly different environments. The cyclohexanol (IId), obtained in a larger yield than (IIc), persisted as the 2-equatorially substituted stereoisomer. By conformational equilibration, however, the epimeric cyclohexanol (IIc) was converted into the isomer with the hydroxy-group equatorial, as indicated by the similar n.m.r. signals at τ *ca.* 6·05 for (IIc) and at *ca.* 6·1 for

[7] H. Feltkamp, N. C. Franklin, F. Koch, and T. N. Thanh, *Annalen*, 1967, **707**, 87.
[8] W. Naegele and D. Wendisch, *Org. Magnetic Resonance*, 1970, **2**, 439.
[9] W. Hückel and K. D. Thomas, *Annalen*, 1961, **645**, 177.
[10] H. Feltkamp, F. Koch, and T. N. Thanh, *Annalen*, 1967, **707**, 95.

(IId) corresponding to the axial C-2 protons. The same conclusions were drawn from the n.m.r. spectra of



(IIc) R = H (XIVc) R = Bz (IId) R = H (XIVd) R = Bz

the *O*-benzoyl derivatives (XIVc and d), which showed parallel downfield shifts of their C-2 proton signals to τ *ca.* 4·37 and 4·53 (widths 15 and 14 Hz). The band widths indicated the participation of both conformational isomers. The benzoylation of (IId) [to (XIVd)] proceeded much faster (and in 98% yield) than that of (IIc) [to (XIVc)] (94·9% yield). These results substantiated the tendency of the benzoyloxy-isomers to reach a similar equilibrium situation.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were obtained for potassium bromide pellets or liquid films with a Perkin-Elmer 137 spectrophotometer, u.v. spectra for solutions in 95% ethanol with a Beckman DU-2 spectrophotometer, and n.m.r. spectra for solutions in deuteriochloroform with a Varian A60 or JEOL JNM-C-60HL spectrometer (tetramethylsilane as internal standard). The neutralization equivalent was determined by potentiometric micro-titration in ethanol–water (1 : 1) with 0·1N-sodium hydroxide. Mass spectra were measured with a Varian MAT CH7 spectrometer. Column chromatography was performed over silica gel (Merck; 0·08 mm). The silica gel (Merck HF_{254}, type 60) which was used for t.l.c. and for preparative layer chromatography (20 cm plates) was activated at 110° for 60 min. The products were rendered visible by treatment with iodine vapour, by u.v. illumination, and by use of a ninhydrin spray.

Ethyl 4-cyano-4-hydroxycyclohexanecarboxylate (IV), an unstable oil, $\nu_{max.}$ 3448, 2950, 1724, and 1712 cm^{-1}; 4-cyano-4-hydroxycyclohexanecarboxylic acid (V), m.p. 125—

TABLE 1

Stereoisomeric diethyl 2-aminocyclohexane-1,4-dicarboxylates, their hydrochlorides, and their *N*-benzoyl derivatives

Isomers	M.p. (°C) [B.p. (°C): mmHg]	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl	$\lambda_{max.}$/nm (log ε) [$\lambda_{min.}$/nm (log ε)]	$\nu_{max.}$/cm^{-1}
(Ia)		6·6 [a]											3367, 2924, 1718
N-Bz (IXa)	122—123 [b]	79·4			3·7		$C_{19}H_{25}NO_5$			4·05		225·5 (4·03) [212 (3·87)]	3333, 2933, 1721, 1634, 1600, 1580, 1527, 696
(Ib)	43·5—45 [70—80; 0·05]	47·9 [a]	59·05	8·4	5·95		$C_{12}H_{21}NO_4$ [c]	59·25	8·7	5·75			3356, 3322, 3185, 2882, 1709
HCl	188—189 [d]		51·5	7·95	5·1	12·9	$C_{12}H_{22}ClNO_4$	51·5	7·95	5·0	12·65		3367, 2825, [e] 1721
N-Bz (IXb)	161—162 [f]	88·9	65·55	7·25	3·9		$C_{19}H_{25}NO_5$	65·7	7·25	4·05		227 (4·06) [212 (3·88)]	3333, 2941, 2882, 1721, 1634, 1600, 1577, 1534, 698
(Ic)	[70—90; 0·05]	10·2 [a]	59·1	9·0	5·35		$C_{12}H_{21}NO_4$	59·25	8·7	5·75			3636, 3436, 2959, 1727
HCl	132—133 [g]		51·7	8·2	5·15		$C_{12}H_{22}ClNO_4$	51·5	7·95	5·0			3448, 2924, [e] 1721
N-Bz (IXc)	150—151 [h]	88·7	65·75	7·6	4·0		$C_{19}H_{25}NO_5$	65·7	7·25	4·05		227 (4·05) [212 (3·88)]	3390, 2959, 2890, 1718 1634, 1603, 1577, 1534, 692
(Id)	[75—83; 0·0005]	35·2 [a]	59·2	8·95	5·6		$C_{12}H_{21}NO_4$	59·25	8·7	5·75			3663, 3448, 2976, 1730
HCl	161—163 [g]		51·6	8·1	5·15	12·75	$C_{12}H_{22}ClNO_4$	51·5	7·95	5·0	12·65		3367, 3067, 3021, 2809, 1724
N-Bz (IXd)	124—125 [f]	90	65·9	7·2	4·05		$C_{19}H_{25}NO_5$	65·7	7·25	4·05		227 (4·07) [212 (3·88)]	3390, 2967, 1718, 1639 1608, 1582, 1536, 688

[a] Based on total amount of isolated stereoisomers. [b] From methylene chloride–n-hexane. [c] Found: equiv. wt., 245. Required: 243·3. [d] From chloroform–ether. [e] Broad band. [f] From acetone. [g] From chloroform–ether–n-hexane. [h] From methylene chloride–ether–n-hexane.

TABLE 2

N.m.r. spectra [a,b] (τ values)

Compound	H-1, 3, 4, 5, 6 *[c]	H-2 [W] [d]	NH_2 [NHCO]	OCH_2 (q) [e]	CH_3 (t) [e]
(Ia)	*ca.* 6·99—8·35	6·35 (m)[f] [9·5]	8·43 (s)	5·82	8·75
				5·86	8·77
(Ib)	7·42—8·50	7·01 (o) [24·5] $\left(J_{2ax,\,1ax}\right\}$ 11·5 + 9·5) $J_{2ax,\,3ax}$ ($J_{2ax,\,3eq}$ 3·5)	8·62 (s)	5·81	8·74
				5·84	8·76
(Ic)	7·43—8·51 (H-4 at 7·05—7·43)	6·82 (o) [23·9] $\left(J_{2ax,\,1ax}\right\}$ 11·0 + 9·0) $J_{2ax,\,3ax}$ ($J_{2ax,\,3eq}$ 3·9)	8·56 (s)	5·82	8·75
(Id)	6·78—7·33—8·55		8·31 (s)	5·82	8·74
	H-1, 2 H-3, 4, 5, 6			5·86	8·77
(IIa)	7·10—8·58	*ca.* 5·7		5·84	8·76
				5·90	8·79
(IIb)	7·30—8·52	*ca.* 6·05—6·42 (m)		5·81	8·74
				5·86	8·77
(IIc)	7·02—8·58	*ca.* 6·05 (m)		5·84	8·77
				5·86	
(IId)	7·13—8·56	*ca.* 6·1 (m)		5·82	8·75
				5·87	8·77
(IXa)	*ca.* 6·94—8·58	5·11—5·52 (m) [21·0]	[3·23 (d)]	5·84	8·76
					8·79
(IXb)	7·20—8·58	*ca.* 5·75 (m)	[3·67 (d)]	5·92	8·74
					8·82
(IXc)	7·07—8·54	*ca.* 5·65 (m)	[3·73 (d)]	5·87	8·72
				5·95	8·83
(IXd)	6·97—8·57	*ca.* 5·75 (m)	[obscured]	5·85	8·73
				5·96	8·78
(XIVa)	7·07—8·53	4·27 (m) [9]		5·95	8·77
				5·99	8·89
(XIVb)	7·07—8·60	4·83 (sx) [25] ($2J_{ax,\,ax}$ 2 × 10·5) ($J_{ax,\,eq}$ 4·0)		5·94	8·78
				5·98	8·90
(XIVc)	6·95—7·45; 7·67—8·51	4·37 (sx) [15]		5·84	8·74
	H-1, 4 H-3, 5, 6				8·79
(XIVd)	7·00—8·67	4·53 (m) [14]		5·92	8·91
					8·99
Cyclohexenes	H-1, 4 H-2, 3 *	H-5, 6 *			
(XII)	6·72—7·13 (m) 4·10 (s)	7·88—8·24 (m)		5·86	8·76
(XV)	6·80—7·13 (m) 4·04 (s) 4·07 (s)	7·88—8·20 (m)		5·87	8·77
(XIII)	3·07 (t)	7·36—8·52 (m)		5·83	8·73
	H-2	H-3, 4, 5, 6		5·85	8·76

* Unless otherwise stated.

[a] See introduction to Experimental section. [b] Aromatic proton signals of (IXa—d) and (XIVa—d) are not recorded. [c] Unresolved multiplet. [d] Band width (*W*) and coupling constants in Hz. [e] J_{Et} 7 Hz. [f] Unresolved multiplet (m); *ca.* refers to estimated positions when resonance is obscured by those of other protons.

TABLE 3

Stereoisomeric diethyl 2-hydroxycyclohexane-1,4-dicarboxylates and their *O*-benzoyl derivatives

Isomers	M.p. (°C) [B.p. (°C); mmHg]	Yield (%)	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H	$\lambda_{max.}$/nm (log ε)	$\nu_{max.}$/cm^{-1}
(IIa)	[70—76; 0·0005]	24·2 [a]	59·2	8·5	$C_{12}H_{20}O_5$	59·0	8·25		3546, 2941, 1718
O-Bz (XIVa)	69—70 [b]	57·4	65·5	6·85	$C_{19}H_{24}O_6$ [c]	65·5	6·95	230 (4·11)	2950, 1721, 1603, 1582, 712
(IIb)	44—45·5 [100—104; 0·05]	42·8 [a]	58·9	8·05	$C_{12}H_{20}O_5$	59·0	8·25		3367, 2933, 2882, 2809, 1718 [d]
O-Bz (XIVb)	[120—130; 0·005]	97·5	65·35	7·2	$C_{19}H_{24}O_6$ [e]	65·5	6·95	230 (4·14)	2924, 1721, 1597, 1577, 712
(IIc)	26·5—28 [95—100; 0·001]	19·5 [a]	59·15	8·45	$C_{12}H_{20}O_5$	59·0	8·25		3509, 2959, 1727
O-Bz (XIVc)	[120—130; 0·005]	94·9	65·6	6·65	$C_{19}H_{24}O_6$	65·5	6·95	230 (4·12)	2985, 1724, 1600, 1587, 712
(IId)	[85—90; 0·001]	44·2 [a]	59·2	8·55	$C_{12}H_{20}O_5$	59·0	8·25		3559, 2967, 1724 [e]
O-Bz (XIVd)	[125—130; 0·004]	98·2	65·45	7·05	$C_{19}H_{24}O_6$ [c]	65·5	6·95	230 (4·12)	2985, 1724, 1597, 1582, 712

[a] Based on total amount of isolated products. [b] From ether–n-hexane. [c] Found: M^+, 348. Required: *M*, 348·4. [d] Sharp band. [e] Broad band.

128° (from ether–hexane) (lit.,[11] 125—140°) (Found: C, 56·6; H, 6·8; N, 8·25. Calc. for $C_8H_{11}NO_3$: C, 56·8; H, 6·55; N, 8·3%), $\nu_{max.}$ 3356, 3125, 2924, 2232, 1695, and 1669 cm^{-1}; and *diethyl 4-cyano-4-hydroxycyclohexane*-1,1-*dicarboxylate* (VII), b.p. 118° at 5×10^{-4} mmHg, n_D^{24} 1·4618 (Found: C, 57·8; H, 7·05; N, 4·8. $C_{13}H_{19}NO_5$ requires C, 58·0; H, 7·1; N, 5·2%), $\nu_{max.}$ 3390, 2849, and 1724 cm^{-1}, were prepared by minor adaptations of the reported method.[6]

Ethyl 4-cyanocyclohex-3-enecarboxylate (III), b.p. 70° at 10^{-1} mmHg (lit.,[12] 125—127° at 3 mmHg) (Found: C, 66·75; H, 7·5; N, 7·65. Calc. for $C_{10}H_{13}NO_2$: C, 67·0; H, 7·3; N, 7·8%), $\lambda_{max.}$ 207·5 nm (log ε 4·095), $\nu_{max.}$ 2924, 2212, 1721, and 1634 cm^{-1}, τ 8·77 (3H, t, Me), 7·08—8·57 (7H, m, 1-, 2-, 5-, 6-H), 5·83 (2H, q, $O{\cdot}CH_2$), and 3·36 (1H, m, 3-H); *4-cyanocyclohex-3-enecarboxylic acid* (VI), m.p. 133—135° (from ether–hexane) (Found: C, 63·7; H, 6·65; N, 9·2. $C_8H_9NO_2$ requires C, 63·55; H, 6·0; N, 9·25%), $\nu_{max.}$ 3521, 2924, 2232, 1770, and 1534 cm^{-1}; and *diethyl 4-cyanocyclohex-3-ene*-1,1-*dicarboxylate* (VIII), b.p. 95° at 10^{-3} mmHg, n_D^{23} 1·4708 (Found: C, 62·05; H, 7·0; N, 5·3. $C_{13}H_{17}NO_4$ requires C, 62·15; H, 6·8; N, 5·6%), $\lambda_{max.}$ 208 nm (log ε 4·05), $\nu_{max.}$ 2985, 2222, 1724, and 1639 cm^{-1}, τ 8·75 (6H, t, 2 × Me), 7·59—7·82 (4H, m, 5-, 6-H_2), 7·12—7·35 (2H, m, 2-H_2), 5·77 (4H, q, 2 × $O{\cdot}CH_2$), and 3·37 (1H, m, 3-H), were made by adapting reported methods.[2,3]

Stereoisomeric Diethyl 2-Aminocyclohexane-1,4-*dicarboxylates* (Ia—d).—A solution of ethyl 4-cyanocyclohex-3-ene-1-carboxylate (III) (750 mg, 4·18 mmol) in aqueous 25% ammonia (6·3 ml) was heated in a sealed tube at 150° for 60 h, then evaporated to dryness. To the residue dissolved in water (25 ml) activated carbon was added, then filtered off, and the filtrate was evaporated to a colourless foam (806 mg). This was refluxed in hydrochloric acid (81 ml) for 17 h. A crystalline product which separated from aqueous solution (30 ml) [m.p. 271—273° (103 mg, 14·5%)] was identified as cyclohex-1-ene-1,4-dicarboxylic acid. The residue (1·11 g) from the mother liquor was refluxed in ethanolic 3% hydrochloric acid for 17 h and neutralized with aqueous ammonia. From the chloroform extract an oil separated, which was chromatographed on silica gel (29 g). Methylene chloride–methanol (99 : 1) eluted the *amino-dicarboxylates* (Ia and b), methylene chloride–methanol (98·5 : 1·5) the *isomer* (Ic), and methylene chloride–methanol (98 : 2) the *isomer* (Id) (see Table 1).

Diethyl 2-Benzamidocyclohexane-1,4-*dicarboxylates* (IXa—d).—Each amino-diester (Ia—d) (0·123—0·41 mmol) dissolved in methylene chloride (0·1 ml) and anhydrous pyridine (1—3 ml) was treated with an equimolar amount of benzoyl chloride. Preparative t.l.c. (silica gel) [development in methylene chloride–ether (95 : 5) and elution with methylene chloride] gave crystalline *products* (IXa—d) (see Table 1).

Ethyl 7-Oxo-6-azabicyclo[3.2.1]*octane-4-carboxylate* (X).—Diethyl *c*-2-aminocyclohexane-*r*-1,*c*-4-dicarboxylate (Id) cyclised spontaneously at room temperature to a crystalline *product*, m.p. 85—86° (from ether–hexane), obtained as needles (Found: C, 61·0; H, 7·7; N, 7·05. $C_{10}H_{15}NO_3$ requires C, 60·9; H, 7·65; N, 7·1%), *m/e* 197 (M^+), $\nu_{max.}$ 3165, 2924, 1724, and 1686br cm^{-1}, τ 8·76 (3H, t, Me), 7·25—8·54 (8H, m, 1-, 2-, 3-, 4-, 8-H), *ca.* 6·0 (1H, m, 5-H), 5·84 (2H, q, $O{\cdot}CH_2$), and 3·95br (1H, s, NH). The N-*benzoyl derivative* (XI) (66·9%) had m.p. 78—79° (from ether–hexane) (Found: C, 67·45; H, 6·1; N, 4·6. $C_{17}H_{19}NO_4$ requires C, 67·75; H, 6·35, N, 4·65%), $\lambda_{max.}$ 230 nm (log ε 4·00), $\lambda_{min.}$ 217 nm (log ε 3·89), $\nu_{max.}$ 2959br, 1739, 1721, 1658, 1592, 1575, and 698 cm^{-1}; τ 8·75 (3H, t, Me), 7·14—8·57 (8H, m, 1-, 2-, 3-, 4-, 8-H), 5·90 (2H, q, $O{\cdot}CH_2$), 5·00 (1H, d, 5-H), and 2·36—3·0 (5H, m, aromatic).

Deamination of Diethyl t-2-*Aminocyclohexane*-r-1,t-4-*dicarboxylate* (Ib) *with Nitrous Acid.*—To a solution of the amino-diester (Ib) (400 mg, 1·644 mmol) in 10% acetic acid (1·44 ml), sodium nitrite (164 mg, 2·377 mmol) in water (1 ml) was added. The mixture was heated for 90 min (water-bath) and then evaporated to a syrup. The residue from the chloroform extract was chromatographed on a silica gel (20 g) column. Methylene chloride eluted two cyclohexenes (90 mg, 27·5%) identified as diethyl cyclohex-2-ene-*r*-1,*t*-4-dicarboxylate (XII), an unstable oil, $\nu_{max.}$ 2959br and 1724 cm^{-1}, and *diethyl cyclohex-1-ene*-1,4-*dicarboxylate* (XIII), b.p. 95° at 5×10^{-2} mmHg (Found: C, 63·95; H, 8·3. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·05%), $\lambda_{max.}$ 217 nm (log ε 3·88), $\nu_{max.}$ 2915, 1721, 1701, and 1645 cm^{-1}, followed by oily *diethyl* c-2-*hydroxycyclohexane*-r-1,t-4-*dicarboxylate* (IIa) (79 mg, 24·2%). Methylene chloride–methanol (99·5 : 0·5) eluted the crystalline *diethyl* t-2-*hydroxycyclohexane*-r-1,t-4-*dicarboxylate* (IIb) (140 mg, 42·8%) (see Table 3).

Deamination of Diethyl c-2-*Aminocyclohexane*-r-1,c-4-*dicarboxylate* (Id).—The amino-diester (Id) was deaminated as described for (Ib). Methylene chloride eluted diethyl cyclohex-2-ene-*r*-1,*c*-4-dicarboxylate (XV) (unstable isomer), $\nu_{max.}$ 2993br and 1727 cm^{-1}, and diethyl cyclohex-1-ene-1,4-dicarboxylate (XIII) in 31·04% yield, and then *diethyl* c-2-*hydroxycyclohexane*-r-1,c-4-*dicarboxylate* (IId) (44·24%). Methylene chloride–methanol (99·5 : 0·5) eluted the crystalline *diethyl* t-2-*hydroxycyclohexane*-r-1,c-4-*dicarboxylate* (IIc) (19·52%) (see Table 3).

Diethyl 2-Benzoyloxycyclohexane-1,4-*dicarboxylates* (XIVa—d).—The hydroxy-diesters (IIa—d) were benzoylated as already described; for details of products see Table 3.

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