

CYCLISATION OF N-BENZOYL-O-METHANESULPHONYL DERIVATIVES OF CONFORMATIONALLY BIASED DIEQUATORIAL 2-AMINOCYCLOHEXANOLS*

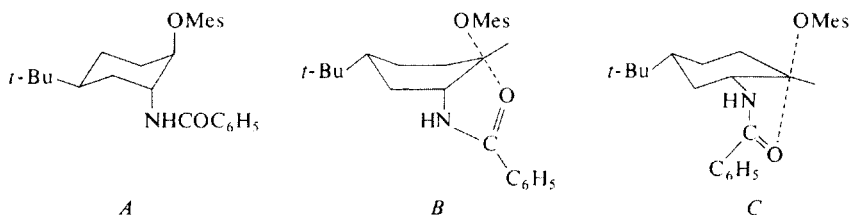
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The rates of Δ^2 -oxazoline formation from conformationally biased N-acyl-O-methanesulphonyl derivatives of 2-aminocyclohexanols and of 2-amino-3-hydroxydecalin with both functional groups in equatorial or axial positions have been measured. The comparison of the reaction rates of variously substituted derivatives of this type indicates that the (flattened) diequatorial chair transition state fits better the found data than the hitherto assumed boat transition state.

The cyclisation of N-benzoyl-O-methanesulphonyl derivatives of 2-amino alcohols to Δ^2 -oxazolines is a well known and thoroughly studied reaction (see *e.g.* ref.¹⁻³). The cyclisation proceeds *via* intramolecular S_N2 reaction with inversion on the carbon bearing the leaving methanesulphonyloxy group¹. It was shown that in the reaction of N-benzoyl-O-methanesulphonates of 2-aminocyclohexanols only the *trans* isomers afford Δ^2 -oxazolines, the *cis* epimers giving products of solvolysis. Study of derivatives, in which the cyclohexane ring was conformationally biased by introduction of tert-butyl group³, revealed that "diaxial" compounds, such as *Id*, react about 80 times (at 60°C in ethanol) faster than the corresponding "diequatorial" derivatives, such as *VId*. It was assumed that, whereas in *Id* the antiperiplanar arrangement of the



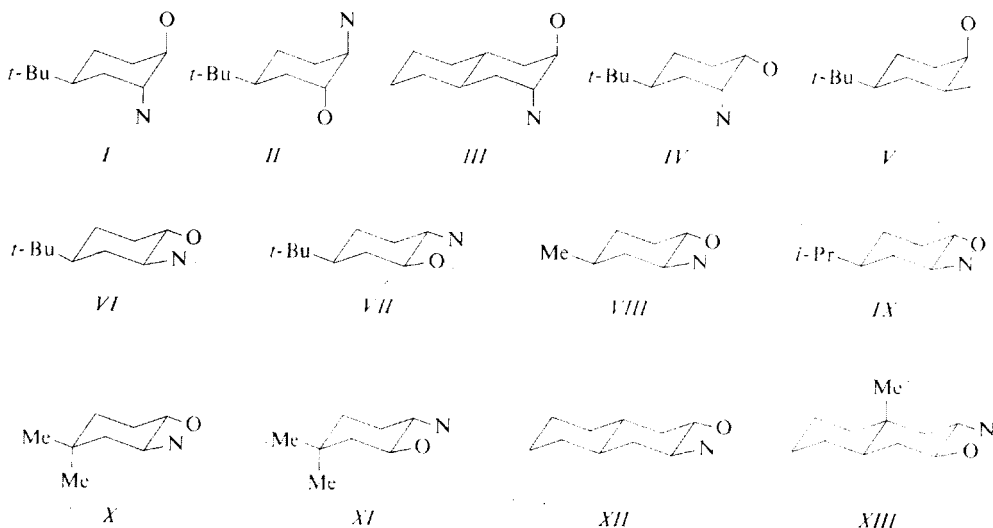
SCHEME 1

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reacting groups (regarded as the best for the intramolecular S_N2 reaction) is already preformed in the ground state (Scheme 1, *A*), in *VId* the molecule must react *via* an energetically much less advantageous boat transition state (Scheme 1, *B*) and therefore the reaction rate of this isomer is lower³.

However, a closer analysis of models suggests that there might be an alternative transition state through which *VId* (and in principle other biased derivatives with equatorial functional groups) could react: the (flattened) chair with both functional groups in quasi-equatorial positions (Scheme 1, *C*).* This alternative was first suggested by the late Professor S. Winstein.

It is, of course, hardly possible to obtain information about the exact geometry of the transition state, but nevertheless some insight into this question might be obtained by kinetic measurement of a greater number of variously substituted cyclohexane derivatives and an analysis of the possible trends. In this paper we investigate a series of "diequatorial" derivatives *VI–XIII* which we believe to be conformationally homogeneous in the ground state. Also the "diaxial" (*I–III*) and "cis" (*IV*



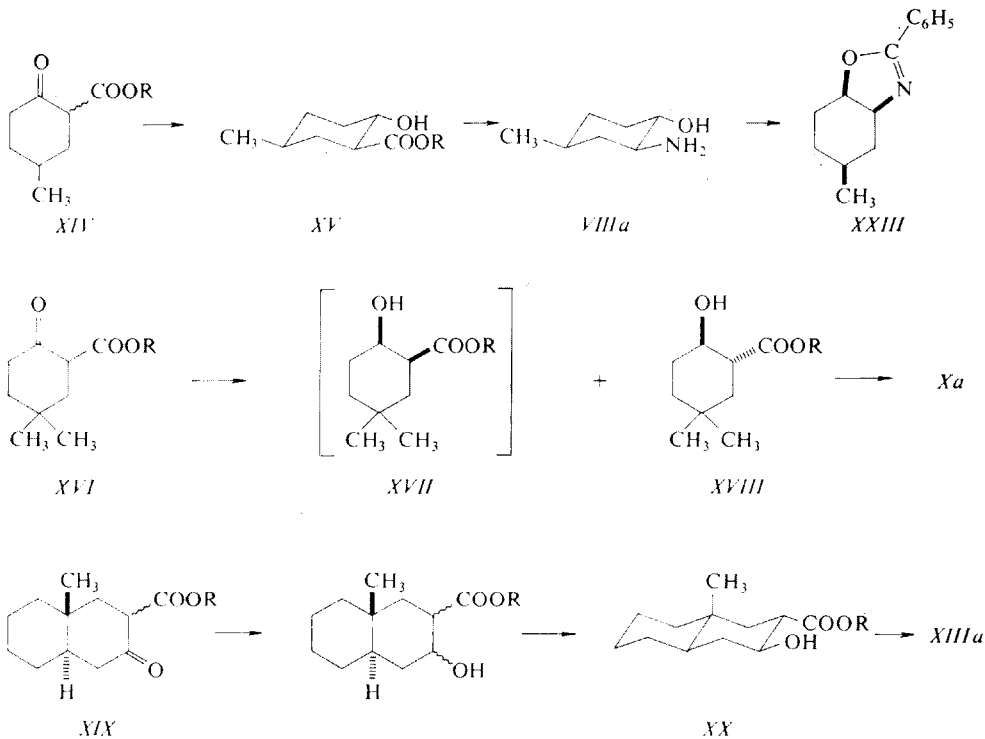
a; O = OH, N = NH₂ *b*; O = OH, N = NHCOC₆H₅ *c*; O = OH, N = NHCOC₆H₅
(NO₂)-*p* *d*; O = OMe, N = NHCOC₆H₅ *e*; O = OMe, N = NHCOC₆H₄(NO₂)-*p*

SCHEME 2

* As we have already mentioned⁴, the boat and the chair transition states (Scheme 1, *B* and *1 C*, respectively) should be separated by an energetic maximum, corresponding to a form in which the part of the ring in question is planar.

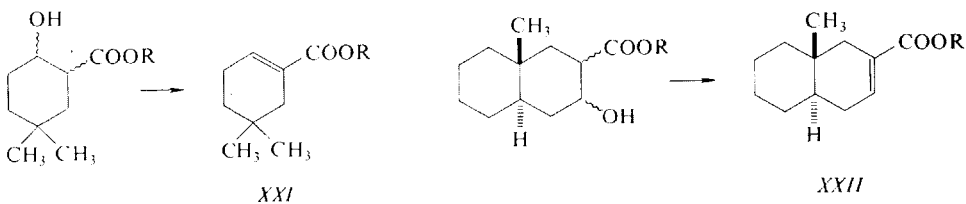
and *V*) isomers, which were measured for comparison, are assumed to exist exclusively in one conformation (which is shown in Scheme 2).

Most of the parent amino alcohols have already been described⁵⁻⁸. The new compounds *VIIIa*, *Xa* and *XIIIa* were prepared by Curtius degradation of the hydroxy



a; R = H, *b*; R = CH₃

SCHEME 3



a; R = H, *b*; R = CH₃

SCHEME 4

acids *XVa*, *XVIIIa* and *XXa* which in turn were synthesized by reduction of the corresponding keto acid (*XIVa* and *XIXa*)⁹ or keto ester¹⁰ (*XIVb*) followed by epimerisation (Scheme 3). The alkaline epimerisation (0.1–0.2M sodium alkoxide) of the hydroxy esters, arising from *XVIa* and *XIXa*, was accompanied by formation of small amounts of conjugated unsaturated esters *XXIb* and *XXIIb* (Scheme 4).

The configuration of the new amino alcohols *VIIIa*, *Xa* and *XIIIa* follows from the equilibration of the starting hydroxy esters and from the IR-spectroscopic study (in the 3 μ region) of the intramolecular hydrogen bond in the hydroxy esters as well as in the amino alcohols. The shape of the hydroxyl bands in the spectrum of *XVb*, *XVIIIb* and *XXb* was characteristic for the hydroxy esters with both the functional groups in the equatorial position¹¹. The bonded hydroxyl band in the spectra of the amino alcohols was located in all amino alcohols at 3530 cm^{-1} which is also in accord with the spectral parameters of diequatorial 2-aminocyclohexanols¹² ($\Delta\nu_{\text{OH}} \sim 90$ to 100 cm^{-1}).

RESULTS AND DISCUSSION

Comparison of Reaction Rates

The reaction rates of the investigated compounds calculated for 60°C are listed in Table I. Let us first compare the rates of the position isomeric "diaxial" derivatives *Id* and *IId*. This comparison should show how a substituent at $\text{C}_{(4)}$ affects the reaction rate in a chair transition state. As is evident from models, an intramolecular $\text{S}_{\text{N}}2$ reaction on $\text{C}_{(1)}$ (which carries the methanesulphonyloxy group) requires a widening of the bond angle $\text{C}_{(6)}-\text{C}_{(1)}-\text{C}_{(2)}$ and therefore a flattening of this part of the ring.

The reaction rates of *Id* and *IId* are practically identical; also the rate of the "diaxial" *trans*-decalin derivative *IIId* is only somewhat smaller* than that of the monocyclic compounds (about 2/3 of the rate of *VIIId*), which is in accord with the generally lower reactivity of the *trans*-decalin system in nucleophilic reactions (*e.g.* the rate of ethanolysis of 2-toluenesulphonyloxy-*trans*-decalin is also about 2/3 of the rate of *trans*-4-*tert*-butylcyclohexyl toluenesulphonate).

This similarity of the reaction rates indicates that in the chair form of the cyclohexane ring an introduction of a substituent at $\text{C}_{(4)}$ or $\text{C}_{(3)}$ (or an anellation of another six-membered ring) has no great effect on the rate of the cyclisation. In other words,

* The reaction rates of the decalin derivatives *IIId* and *XIIId* in the same medium have already been measured by Wylde and Atard¹³. The reaction rate of *IIId*, found by these authors, is about 2/3 of the value obtained by ourselves, the thermodynamic values being the same; on the other hand, the rates found for *XIIId* are not very different from our values but the thermodynamic parameters do differ ($\Delta H^\ddagger = 26.2 \text{ kcal mol}^{-1}$ vs 23.8 kcal mol^{-1} and $\Delta S^\ddagger = -1.6 \text{ e.u.}$ vs -7.5 e.u.).

a flattening at $C_{(1)}$ does not affect markedly the other part of the ring. (This fact is not altogether new; other evidence is also available, see ref.^{14,15}.) If this is so, then any greater change in reaction rate caused by substitution at $C_{(3)}$ or $C_{(4)}$ should indicate that the transition state probably deviates substantially from the "normal" chair form.

TABLE I

First Order Rate Constants, k , of the Reaction of the N-Acyl-O-Methanesulphonyl Derivatives of the Amino Alcohols *Ia*—*XIIIa* at 60°C in Ethanol, Values of the Thermodynamic Parameters, and Values of k_H/k_{NO_2}

Compound	$10^5 \cdot k$ s^{-1}	ΔH^\ddagger kcal/mol	ΔS^\ddagger e.u.	k_H/k_{NO_2}
<i>Id</i>	628	22.3	-2.0	3.8
<i>Ie</i>	165	22.3	-1.5	
<i>IId</i>	631	22.2	-2.0	3.7
<i>Ile</i>	169	22.8	-3.0	
<i>IIId</i>	459	22.5	-2.0	3.9
<i>IIle</i>	118	22.4	-5.0	
<i>IVd</i>	0.296	27.1	-2.5	1.7
<i>IVe</i>	0.178	26.8	-4.5	
<i>Vd</i>	0.0687	27.4	-4.5	1.3
<i>Ve</i>	0.0515	26.1	-9.0	
<i>VIId</i>	7.62	25.2	-2.0	4.3
<i>VIle</i>	1.79	26.0	-2.5	
<i>VIIId</i>	6.54	24.6	-4.0	3.9
<i>VIIle</i>	1.67	—	—	
<i>VIIIId</i>	5.92	24.7	-4.0	3.9
<i>VIIIle</i>	1.52	—	—	
<i>IXd</i>	6.12	25.2	-2.5	—
<i>Xd</i>	13.2	24.7	-2.0	4.6
<i>Xe</i>	2.91	25.0	-4.0	
<i>XId</i>	4.79	24.9	-3.5	4.4
<i>XIle</i>	1.08	26.3	-2.5	
<i>XIIId</i>	4.17	23.8	-7.5	3.8
<i>XIIle</i>	1.09	25.4	-5.0	
<i>XIIIId</i>	9.63	22.2	-10.5	4.0
<i>XIIIle</i>	2.42	24.0	-7.5	

As seen from Table I, the reaction rates of the "diequatorial" compounds *VId* to *XIIId* differ only very little, the whole range corresponding only to a factor of about 3. The two geminally disubstituted compounds *Xd* and *XId* represent the fastest and the slowest monocyclic derivatives. The decalin derivative *XIIId* reacts somewhat more slowly than the monocyclic derivatives *VId*–*IXd* (about 2/3 of the rate of *VIIId*), this difference being very probably again due to the lower reactivity of the bicyclic system.

However, when an axial methyl is introduced into the 9 position of the decalin system — as in *XIIId* — the reaction rate is doubled: the situation is analogous to the case of the compound *VIIId* where introduction of another methyl into the position 4 (compound *Xd*) also doubles the reaction rate.

The small differences in the reaction rates of the whole "diequatorial" series indicate that the energy of the transition state does not depend very much on the size of the equatorial substituents on the far side of the ring unless in all compounds various factors happen to cancel each other, which would be very improbable. This fact can hardly be explained by the concept of a "boat" transition state, since in the boat form different steric requirements of various substituents in *VId*–*XId* would lead to very different energetic content of the transition state and this would manifest itself in different reaction rates of the compounds studied.

On the other hand, steric requirements of a "flattened diequatorial chair" transition state are in accord with the mentioned similarity of the rates, and also with the enhanced rates of *Xd* and *XIIId*. We may assume that in these compounds the axial methyl exerts pressure on the axial hydrogen attached to the carbon, carrying the benzamido group, and thus actually flattens the ring in the direction required for the reaction.* Therefore we consider it to be probable that "diequatorial" benzamido methanesulphonates which cannot react *via* "diaxial" chair transition state (Scheme 1) might react *via* the "flattened chair" transition state rather than *via* the originally assumed¹ boat.

The Values of $k_{\text{H}}/k_{\text{NO}_2}$

In some of our previous papers^{16,17} we have used the ratio of the rate constants of benzamido and *p*-nitrobenzamido methanesulphonates (k_{H} and k_{NO_2} , respectively) in order to assess the extent of the neighbouring group participation and hence, indirectly, to obtain information about the geometry of the transition state. For the "cis"-isomers *IVd* and *Vd* which are known to afford exclusively products of solvolysis³, the value of $k_{\text{H}}/k_{\text{NO}_2}$ is 1.7 and 1.3, respectively. Thus, the $k_{\text{H}}/k_{\text{NO}_2}$ value of about 1.5 may be considered as to be due to the inductive contribution. The values for the

* The fact that *trans*-4-*tert*-butyl-2-dimethylaminocyclohexanol and similar compounds seem to prefer substantial flattening of the chair form to an alternative boat conformation¹⁴, supports also the concept of a flattened diequatorial chair transition state.

diaxial as well as diequatorial isomers *VI–XIII* range from 3.7 to 4.6. Provided we accept the simple interpretation of the values of k_H/k_{NO_2} given previously, we have to conclude that the extent of participation in both types of *trans* isomers is very similar, a feature by no means predictable from simple model considerations.

EXPERIMENTAL

Kinetic Measurements

The kinetic procedure employed was essentially that reported by Winstein and Boschan¹, modified in detail as described in our previous papers^{2,3}. The experimental first order rate constants obtained are listed in Table II.

Compounds

The following methanesulphonyl derivatives have already been described (pertinent references in parentheses): *Id*, *IVd*, *Vd* (ref.³), *IIIId*, *XIIId* (ref.¹³; in this citation no m.p. and analysis are given for *IIIId*), *VIId* (ref.⁵), *VIIId* (ref.⁶), *XIId* (ref.⁷). Physical properties, yields and analytical values of N-acyl and N-acyl-O-methanesulphonyl derivatives of the amino alcohols *Ia–XIIIa* are listed in Table III and IV, respectively.

5,5-Dimethyl-*trans*-2-hydroxycyclohexanecarboxylic Acid (*XVIIIa*)

Hydrogenation of methyl 5,5-dimethyl-2-oxocyclohexane-1-carboxylate¹⁰ *XVIb* (29.5 g) in methanol (60 ml) over Adams catalyst (1.0 g) afforded a mixture of epimeric hydroxy esters (*XVII*: *XVIII* 3 : 2), b.p. 108°C/10 Torr. The mixture (29.5 g) was refluxed with 1% methanolic sodium methoxide (100 ml) for 2 hours, neutralised with methanolic hydrogen chloride and isolated in the usual manner. The product was chromatographed on neutral alumina (grade III). Elution with benzene afforded as the first fraction 4.3 g of *XXIb*, b.p. 114–115°C/35 Torr, n_D^{20} 1.4675. IR-spectrum (CCl₄): 1725 cm⁻¹ (CO conj.) 1660 cm⁻¹ (C=C conj.). For C₁₀H₁₆O₂ (168.2) calculated: 71.40% C, 9.59% H; found: 71.23% C, 9.34% H. Alkaline saponification of this ester afforded the acid *XXIa*, m.p. 61–62°C (aqueous methanol). For C₉H₁₄O₂ (154.2) calculated: 70.10% C, 9.15% H; found 69.87% C, 8.81% H. The second benzene fraction consisted of *XVIIb*, b.p. 105°C/10 Torr (2.5 g). IR-spectrum (CCl₄, 5 · 10⁻³M) cm⁻¹: 3625 (sh), 3545 (s). For C₁₀H₁₈O₃ (186.2) calculated: 64.49% C, 9.74% H; found: 64.21% C, 9.72% H. Saponification of the ester afforded the *cis*-acid *XVIIa*, m.p. 140–142°C. For C₉H₁₆O₃ (172.2) calculated: 62.76% C, 9.36% H; found: 62.98% C, 9.25% H. The ethereal fractions contained mainly *XVIIIb*. The fractions containing the *cis*-ester *XVIIb* were evaporated and again isomerized and chromatographed. The fractions rich in the desired *trans*-ester *XVIIIb* were combined, (14.5 g), dissolved in ethanol (30 ml) and refluxed with 30% aqueous NaOH (30 ml) for 1/2 hour. The ethanol was distilled off, the separated sodium salt filtered off, dissolved in warm water and acidified with dilute hydrochloric acid, affording *XVIIIa* which on crystallisation from ethyl acetate melted at 114–115°C, yield 8.0 g (59.6%). For C₉H₁₆O₃ (172.2) calculated: 62.76% C, 9.36% H; found: 62.89% C, 9.27% H. Methyl ester *XVIIIb*, m.p. 42–43°C (pentane). IR-spectrum (CCl₄, 5 · 10⁻³M) cm⁻¹: 3615 (sh), 3595 (s), 3560 (sh). For C₁₀H₁₈O₃ (186.2) calculated: 64.49% C, 9.74% H; found: 64.45% C, 9.80% H.

TABLE II

First Order Rate Constants, k , for the Reaction of the Methanesulphonyl Derivatives I–XIII in the Presence of Potassium Acetate in Anhydrous Ethanol

Compound	k, s^{-1} (temperature, °C)			
<i>Ie</i>	$1.17 \cdot 10^{-5}$ (19.95)	$1.62 \cdot 10^{-4}$ (39.85)	$5.24 \cdot 10^{-4}$ (49.80)	$1.65 \cdot 10^{-3}$ (60.00)
<i>IId</i>	$5.83 \cdot 10^{-5}$ (19.95)	$2.00 \cdot 10^{-4}$ (29.90)	$6.86 \cdot 10^{-4}$ (39.85)	
<i>IIf</i>	$1.33 \cdot 10^{-5}$ (19.95)	$5.05 \cdot 10^{-5}$ (29.90)	$1.74 \cdot 10^{-4}$ (39.85)	$5.42 \cdot 10^{-4}$ (49.80)
<i>IIId</i>	$3.93 \cdot 10^{-5}$ (20.01)	$1.43 \cdot 10^{-4}$ (29.95)	$4.91 \cdot 10^{-4}$ (39.90)	
<i>IIIf</i>	$3.79 \cdot 10^{-5}$ (29.95)	$1.28 \cdot 10^{-4}$ (39.90)	$4.00 \cdot 10^{-4}$ (49.92)	
<i>IVe</i>	$5.93 \cdot 10^{-6}$ (70.01)	$1.85 \cdot 10^{-5}$ (80.00)	$5.54 \cdot 10^{-5}$ (90.03)	
<i>Vd</i>	$7.59 \cdot 10^{-6}$ (80.00)	$2.19 \cdot 10^{-5}$ (90.03)	$6.30 \cdot 10^{-5}$ (99.95)	$1.53 \cdot 10^{-4}$ (110)
<i>Ve</i>	$5.09 \cdot 10^{-6}$ (80.00)	$1.47 \cdot 10^{-5}$ (90.03)	$4.03 \cdot 10^{-5}$ (99.95)	$1.00 \cdot 10^{-4}$ (110)
<i>VIe</i>	$1.73 \cdot 10^{-5}$ (59.80)	$5.63 \cdot 10^{-5}$ (69.75)	$1.72 \cdot 10^{-4}$ (79.85)	
<i>VIIId</i>	$1.98 \cdot 10^{-5}$ (49.90)	$6.54 \cdot 10^{-5}$ (60.00)	$2.03 \cdot 10^{-4}$ (70.00)	
<i>VIIIf</i>	$1.67 \cdot 10^{-5}$ (60.00)			
<i>VIIIId</i>	$1.77 \cdot 10^{-5}$ (50.00)	$5.92 \cdot 10^{-5}$ (60.00)	$1.87 \cdot 10^{-4}$ (70.00)	
<i>VIIIIf</i>	$1.52 \cdot 10^{-5}$ (60.00)			
<i>IXd</i>	$1.89 \cdot 10^{-5}$ (49.92)	$6.20 \cdot 10^{-5}$ (60.02)	$1.90 \cdot 10^{-4}$ (70.01)	$5.78 \cdot 10^{-4}$ (80.00)
<i>Xd</i>	$3.93 \cdot 10^{-5}$ (49.92)	$1.32 \cdot 10^{-4}$ (60.02)	$4.00 \cdot 10^{-4}$ (70.01)	
<i>Xe</i>	$2.91 \cdot 10^{-5}$ (60.02)	$9.31 \cdot 10^{-5}$ (70.01)	$2.65 \cdot 10^{-4}$ (80.00)	

TABLE II
 (continued)

Compound	k, s^{-1} (temperature, °C)			
	<i>XId</i>	$4.79 \cdot 10^{-5}$ (60-02)	$1.46 \cdot 10^{-4}$ (70-01)	$4.27 \cdot 10^{-4}$ (80-00)
<i>XIe</i>	$1.08 \cdot 10^{-5}$ (60-02)	$3.62 \cdot 10^{-5}$ (70-01)	$1.01 \cdot 10^{-4}$ (80-00)	
<i>XIIId</i>	$4.17 \cdot 10^{-5}$ (60-02)	$1.22 \cdot 10^{-4}$ (70-01)	$3.33 \cdot 10^{-4}$ (80-00)	
<i>XIIe</i>	$1.09 \cdot 10^{-5}$ (60-02)	$3.35 \cdot 10^{-5}$ (70-01)	$1.03 \cdot 10^{-4}$ (80-00)	$2.81 \cdot 10^{-4}$ (90-03)
<i>XIIIId</i>	$9.63 \cdot 10^{-5}$ (60-02)	$2.63 \cdot 10^{-4}$ (70-01)	$6.78 \cdot 10^{-4}$ (80-00)	
<i>XIIIe</i>	$2.42 \cdot 10^{-5}$ (60-02)	$7.04 \cdot 10^{-5}$ (70-01)	$2.02 \cdot 10^{-4}$ (80-00)	$5.28 \cdot 10^{-4}$ (90-03)

trans-2-Amino-4,4-dimethylcyclohexanol (*Xa*)

The ester *XVIIIb* was transformed in 80% yield into its hydrazide, m.p. 158–159°C (benzene-ethanol). For $C_9H_{18}N_2O_2$ (186.2) calculated: 58.03% C, 9.74% H, 15.04% N; found: 57.91% C, 9.48% H, 15.13% N. The usual Curtius degradation *via* azide afforded the cyclic urethane, m.p. 108–111°C (ligroin) in 75% yield. For $C_9H_{15}N_2O_2$ (169.2) calculated: 63.88% C, 8.94% H, 8.28% N; found: 63.90% C, 8.72% H, 8.54% N. The desired *Xa* was obtained by the usual alkaline hydrolysis of the urethane and subsequent crystallisation from ligroin and sublimation, m.p. 78–80°C. IR-spectrum (C_2Cl_4 , $5 \cdot 10^{-5}M$): 3624 cm^{-1} (free OH), 3601 (sh), 3527 cm^{-1} (bonded OH), 3384 cm^{-1} (NH). For $C_8H_{17}NO$ (143.2) calculated: 67.09% C, 11.96% H, 9.78% N; found: 66.86% C, 11.86% H, 9.85% N.

trans-2-Hydroxy-*cis*-5-methylcyclohexanecarboxylic Acid (*XVa*)

Carboxylation of 4-methylcyclohexanone by the usual procedure using triphenylmethylpotassium in ether afforded the keto acid *XIVa*, m.p. 97–100°C (dec.) in 73% yield. (Ref.¹⁸ gives m.p. 101°C). Sodium borohydride (4.0 g) was added to a stirred and cooled (0°C) solution of *XIVa* (18.0 g) in aqueous sodium hydroxide (4.6 g in 200 ml) and the mixture was left overnight. The usual work-up procedure, followed by three crystallisations from ethyl acetate, afforded 6.1 g (33%) of the acid *XVa*, m.p. 112–113°C. (Ref.¹⁸ reports m.p. 114°C). Methyl ester *XVb* b.p. 119–120°C/11 Torr. For $C_9H_{16}O_3$ (172.2) calculated: 62.77% C, 9.36% H; found: 64.01% C, 9.77% H. IR-spectrum (CCl_4 , $5 \cdot 10^{-3}M$): 3623 (sh), 3601, 3540 (sh) cm^{-1} .

trans-2-Amino-*trans*-4-methylcyclohexanol (*VIIIa*)

The ester *XVb* was transformed into the corresponding hydrazide, m.p. 222–222.5°C (ethanol), in 62% yield. For $C_{18}H_{16}N_2O_2$ (172.2) calculated: 55.79% C, 9.36% H, 16.27% N; found:

TABLE III
Physical Properties, Yields and Analyses of N-Acyl Derivatives of the Amino Alcohols Ia—XIIIa

Compound	Yield, %	M.p., °C (solvent)	Formula (moi. wt.)	Calculated/Found		
				% C	% H	% N
N-Benzoyl derivatives						
<i>VIIIb</i>	87	172.5—173.5 (aqueous ethanol)	$C_{14}H_{19}NO_2$ (233.3)	72.07 72.06	8.21 8.19	6.00 5.81
<i>IXb</i>	85	165—166.5 (ethyl acetate)	$C_{16}H_{23}NO_2$ (261.3)	73.53 73.52	8.87 8.78	5.36 5.38
<i>Xb</i>	74	178—179 (70% ethanol)	$C_{15}H_{21}NO_2$ (247.3)	72.84 72.88	8.56 8.54	5.66 5.64
<i>XIIIb</i>	92	197—198 (70% ethanol)	$C_{18}H_{25}NO_2$ (287.4)	75.22 75.20	8.77 8.64	4.87 4.62
N- <i>p</i> -nitrobenzoyl derivatives						
<i>Ic</i>	85	155—156 (ethanol)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.38	7.55 7.38	8.74 9.05
<i>IIc</i>	91	156—157 (benzene)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.56	7.55 7.39	8.74 8.78
<i>IIIc</i>	75	192—193 (ethanol)	$C_{17}H_{22}N_2O_4$ (318.4)	64.13 64.05	6.97 7.03	8.80 8.91
<i>IVc</i>	94	204—205 (70% ethanol)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.79	7.55 7.41	8.74 8.94
<i>Vc</i>	78	194—194.5 (ethanol)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.33	7.55 7.75	8.74 8.52
<i>VIc</i>	98	174—175 (ethanol)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.43	7.55 7.47	8.74 8.98
<i>VIIc</i>	63	225—226 (ethanol)	$C_{17}H_{24}N_2O_4$ (320.4)	63.73 63.73	7.55 7.63	8.74 8.65
<i>VIIIc</i>	81	204—205 (ethanol)	$C_{14}H_{18}N_2O_4$ (278.3)	60.42 60.82	6.52 6.35	10.07 10.02
<i>Xc</i>	98	184.5—185.5 (60% ethanol)	$C_{15}H_{20}N_2O_4$ (292.3)	61.63 61.42	6.90 6.97	9.58 9.63
<i>XIc</i>	93	204.5—205.5 (60% ethanol)	$C_{15}H_{20}N_2O_4$ (292.3)	61.63 62.03	6.90 7.07	9.58 9.60
<i>XIIc</i>	60	238—240 (ethanol)	$C_{17}H_{22}N_2O_4$ (318.4)	64.13 64.21	6.97 7.17	8.80 8.71
<i>XIIIc</i>	80	205—207 (ethanol)	$C_{18}H_{24}N_2O_4$ (332.4)	65.04 65.22	7.28 7.36	9.59 9.71

TABLE IV
Physical Properties, Yields and Analytical Values of N-Acyl-O-Methanesulphonyl Derivatives of the Amino Alcohols Ia—XIIIa

Compound	Yield %	M.p., °C (solvent)	Formula (mol. wt.)	Calculated/Found		
				% C	% H	% N
N-Benzoyl-O-methanesulphonyl derivatives						
<i>IId</i>	39	78—80 (light petroleum)	$C_{18}H_{27}NO_4S$ (353.5)	61.16 60.41	7.70 7.60	3.96 3.96
<i>IIId</i>	87	95—98 (light petroleum)	$C_{18}H_{25}NO_4S$ (351.4)	61.51 61.73	7.17 7.18	3.99 4.07
<i>VIIIId</i>	62	131—132 (ethyl acetate)	$C_{15}H_{21}NO_4S$ (311.4)	57.85 58.15	6.80 6.84	4.50 4.43
<i>IXd</i>	96	135—138 (light petroleum)	$C_{17}H_{25}NO_4S$ (339.4)	60.15 60.75	7.42 7.12	4.13 4.11
<i>Xd</i>	65	124—125 (ethyl acetate— —pentane)	$C_{16}H_{23}NO_4S$ (325.5)	59.05 59.11	7.12 7.13	4.30 4.17
<i>XIIIId</i>	79	134—135 (light petroleum)	$C_{19}H_{27}NO_4S$ (365.4)	62.45 58.65	7.45 7.21	— —
N- <i>p</i> -Nitrobenzoyl-O-methanesulphenyl derivatives						
<i>Ie</i>	96	108—110 (light petroleum)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 54.50	6.58 6.59	7.03 7.34
<i>IIf</i>	50	90—92 (light petroleum)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 54.44	6.58 6.62	7.03 6.66
<i>IIIe</i>	93	111—114 (ether—pentane)	$C_{18}H_{24}N_2O_6S$ (396.4)	54.53 54.53	6.10 6.19	7.07 6.83
<i>IVe</i>	86	147—148 (ethyl acetate— —ligroin)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 53.58	6.58 6.34	7.03 7.10
<i>Ve</i>	80	154—156 (ethyl acetate)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 54.21	6.58 6.73	7.03 7.09
<i>VIe</i>	95	146—147 (light petroleum)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 54.61	6.58 6.55	7.03 6.98
<i>VIIe</i>	82	143—145 (ethyl acetate— —ligroin)	$C_{18}H_{26}N_2O_6S$ (398.4)	54.26 54.14	6.58 6.85	7.08 7.05
<i>VIIIe</i>	75	144—145 (ethyl acetate— —ligroin)	$C_{15}H_{20}N_2O_6S$ (356.4)	50.55 50.66	5.66 5.70	7.86 7.65
<i>Xe</i>	97	136—138 (light petroleum)	$C_{16}H_{22}N_2O_6S$ (370.4)	51.88 52.03	5.99 5.92	7.56 7.58

TABLE IV
(continued)

Compound	Yield %	M.p., °C (solvent)	Formula (mol. wt.)	Calculated/Found		
				% C	% H	% N
<i>XIe</i>	89	155—157 (light petroleum)	C ₁₆ H ₂₂ N ₂ O ₆ S (370.4)	51.88 51.84	5.99 5.81	7.56 7.48
<i>XIle</i>	79	163—165 (ether—pentane)	C ₁₈ H ₂₄ N ₂ O ₆ S (396.4)	54.54 54.37	6.10 6.16	7.07 —
<i>XIIIe</i>	81	149—150 (ether—light petroleum)	C ₁₉ H ₂₀ N ₂ O ₆ S (410.4)	55.60 55.40	6.39 6.10	— —

55.94% C, 9.21% H, 16.31% N. Curtius degradation afforded in 89% yield the cyclic urethane, m.p. 109—109.5°C (benzene). For C₈H₁₃NO₂ (155.2) calculated: 61.91% C, 8.44% H, 9.03% N; found: 62.00% C, 8.44% H, 9.07% N. Alkaline hydrolysis of the urethane gave the desired *VIIIa*, m.p. 75.5—76°C (ligroin), in 76% yield. IR-spectrum (C₂Cl₄, 5 · 10⁻³M) cm⁻¹: 3619, 3522 (OH), 3386 (NH). For C₇H₁₅NO (129.2) calculated: 65.07% C, 11.70% H, 10.84% N; found: 64.95% C, 11.83% H, 10.89% N.

Cyclisation of *trans*-2-Benzamido-*trans*-4-methylcyclohexyl Methanesulphonate (*VIII*d)

A solution of *VIII*d (450 mg, 1.45 mmol) and fused potassium acetate (200 mg, 2.04 mmol) in ethanol (60 ml) was heated to 95°C for 7 hours. The separated potassium methanesulphonate was filtered off, washed with ethanol, the filtrate taken to dryness and the residue shaken between sodium carbonate solution and ether. The ethereal layer was dried and the solvent distilled off, leaving 304 mg (97.5%) of the crude oxazoline, which was converted in ether into its picrate, m.p. 188—190°C, yield 570 mg (88.5%). For C₂₀H₂₀N₄O₈ (444.4) calculated: 54.05% C, 4.54% H, 12.61% N; found: 54.25% C, 4.51% H, 12.46% N. The oxazoline *XXIII*, b.p. 120°/0.3 Torr (bath) was liberated from the picrate by lithium hydroxide solution. For C₁₄H₁₇NO (215.3) calculated: 78.10% C, 7.96% H, 6.51% N; found: 78.03% C, 7.83% H, 6.39% N.

3β-Hydroxy-9β-methyl-*trans*-decalin-2α-carboxylic Acid (*XX*a)

A solution of 3-oxo-9β-methyl-*trans*-decalin-2-carboxylic acid⁹ (*XIX*a) (35.3 g) in aqueous sodium hydroxide solution (8.5 g in 300 ml water) was reduced at 20°C with sodium borohydride (5.0 g) till the FeCl₃ test was negative. The mixture was extracted with ether, the aqueous layer was acidified with hydrochloric acid and the product taken up into a benzene-ether (1 : 2) mixture. The dried solution was taken down and the residue esterified with ethanolic hydrogen chloride, affording 26.5 g of stereoisomeric hydroxy esters, b.p. 123—130°C/0.2 Torr. The esters were dissolved in ethanolic sodium ethoxide (from 0.5 g Na in 150 ml of ethanol) and the solution heated under reflux for 4 hours. The mixture was neutralized by addition of ethanolic hydrogen chloride, isolated in the usual manner, and chromatographed on neutral alumina (activity III,

600 g). The first fraction (light petroleum) afforded on saponification crude *XXIIa* (2.8 g), m.p. 196–199°C (ref.⁹). The benzene fractions consisted mainly of the desired *trans*-hydroxy ester (16.8 g). For $C_{14}H_{24}O_3$ (240.3) calculated: 69.96% C, 10.07% H; found: 69.78% C, 10.06% H. The acid *XXa* was obtained by alkaline saponification of the ester and melted at 152–153°C (acetone–benzene). For $C_{12}H_{20}O_3$ (212.3) calculated: 67.89% C, 9.50% H; found: 67.98% C, 9.70% H. Methyl ester *XXb*, boiling at 120–125°C/0.2 Torr (bath) was prepared by treatment with diazomethane; IR-spectra (CCl_4 , $5 \cdot 10^{-3}M$) cm^{-1} : 3610 (sh), 3592 (s), 3555 (sh).

2 α -Amino-3 β -hydroxy-9 β -methyl-*trans*-decalin (*XIIIa*)

This compound was prepared by the usual Curtius degradation procedure from the ethyl ester of *XXa* from the preceding preparation. The intermediates, yields and analyses are as follows: *Hydrazide*, m.p. 209–211°C (ethanol), 92%, for $C_{12}H_{22}N_2O_2$ (226.3) calculated: 63.68% C, 9.80% H, 12.38% N; found: 63.62% C, 9.69% H, 12.70% N. Cyclic urethane, m.p. 122–124°C (benzene–ligroine), 76%. For $C_{12}H_{19}NO_2$ (209.3) calculated: 68.86% C, 9.15% H, 6.69% N; found: 69.02% C, 9.24% H, 6.67% N. Alkaline hydrolysis of the urethane afforded *XIIIa*, m.p. 108–109°C (ligroin) in 68% yield. For $C_{11}H_{21}NO$ (183.3) calculated: 72.08% C, 11.55% H, 7.64% N; found: 71.96% C, 11.52% H, 7.61% N. IR-spectrum (C_2Cl_4 , $5 \cdot 10^{-3}M$) cm^{-1} : 3622(w), 3530 (s), 3384 (w).

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