A Reinvestigation of the Pictet–Gams Isoquinoline Synthesis. Part 1. The Consequences of Oxazoline rather than Isoquinoline Formation

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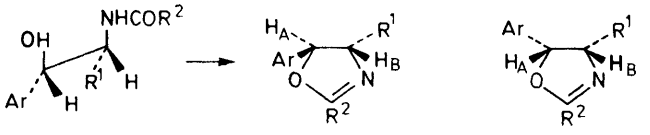
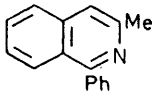
Cyclisation of various 2-acylamino-1-arylalkan-1-ols under typical Pictet–Gams conditions yields Δ^2-oxazolines and not isoquinolines as previously reported. Compounds originally formulated as isoquinolines and isoquinoline hydrochlorides are shown to be derivatives of 2-amino-1-phenylalkan-1-ols, and to have arisen through ring-cleavage of the Δ^2-oxazolines during the isolation procedure. Their mode of formation is fully explained.

ONE of the most widely-used isoquinoline syntheses is the Pictet–Gams modification of the Bischler–Napieralski reaction. In a typical Pictet–Gams synthesis, cyclisation of *erythro*-2-benzamido-1-phenylpropan-1-ol (1a) was expected to yield 3-methyl-1-phenylisoquinoline (4), but it was shown [1] that instead, the product was the



(1) (2) (3)

a; Ar = Ph, R^1 = Me, R^2 = Ph
b; Ar = Ph, R^1 = Me, R^2 = *m* − C_6H_4Me
c; Ar = Ph, R^1 = Me, R^2 = *p*-C_6H_4Me
d; Ar = Ph, R^1 = Me R^2 = *p*-C_6H_4OMe
e; Ar = Ph, R^1 = Me, R^2 = 3,4-$C_6H_3(OMe)_2$
f; Ar = Ph, R^1 = R^2 = Me
g; Ar = Ph, R^1 = Me, R^2 = Et
h; Ar = Ph, R^1 = Me, R^2 = Pr^n
i; Ar = Ph, R^1 = Me, R^2 = CH_2Ph
j; Ar = Ph, R^1 = Et, R^2 = Ph
k; Ar = Ph, R^1 = Pr^n, R^2 = Ph
l; Ar = Ph, R^1 = Bu^n, R^2 = Ph
m; Ar = Ph, R^1 = R^2 = Ph
n; Ar = α-Naph, R^1 = Me, R^2 = Ph



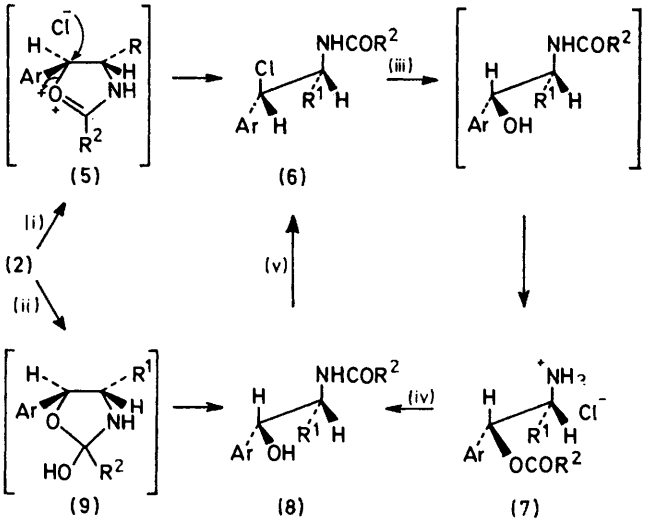
(4)

threo-isomer (8a) of the original *erythro*-amide (1a). This confusion arose because cyclisation of *erythro*-2-benzamido-1-phenylpropan-1-ol gave mainly *trans*- and *cis*-4-methyl-2,5-diphenyl-Δ^2-oxazoline (2a and 3a) which was converted by a multi-stage process into the *threo*-amide during isolation of the anticipated isoquinoline *via* its hydrochloride salt. It was also shown [2] that under the more forcing conditions of phosphorus pentaoxide in refluxing decalin, 4-methyl-2,5-diphenyl-Δ^2-oxazoline could be converted into 3-methyl-1-phenylisoquinoline, as could *erythro*-2-benzamido-1-phenylpropan-1-ol. When the latter reaction was interrupted, the oxazoline could be isolated, and this led to the suggestion that in this and other [2] Pictet–Gams cyclisations, oxazolines were intermediates.

Since the cyclisation conditions originally used by Whaley and Hartung [3] in their abortive attempt to convert the *erythro*-amide (1a) into the isoquinoline (4) are typical [4] of those employed by these and other authors [5] for Pictet–Gams cyclisations, it is clearly of interest to re-examine the products from related cyclisations. This paper represents a reinvestigation of the work of Whaley and Hartung and examines other related cyclisations in the light of the earlier observations on the cyclisation of 2-benzamido-1-phenylpropan-1-ol.

RESULTS AND DISCUSSION

Amides (1b—n) were synthesised and then cyclised in various conditions, similar to those employed by Whaley and Hartung. Using a work-up procedure which avoided isolation of the basic product *via* its hydrochloride, the main products, (see Table 1) were *trans-cis*-Δ^2-oxazoline mixtures [(2) and (3)], although in some cases [*e.g.* the products from (1i) and (1j)] the oxazolines were contaminated by considerable amounts of the *threo*-isomers of the starting *erythro*-amides. Isoquinolines were never formed in greater than trace amounts



(5) (6) (2) (9) (8) (7)

a; Ar = Ph, R^1 = Me, R^2 = Ph
b; Ar = Ph, R^1 = R^2 = Me
c; Ar = Ph, R^1 = Me, R^2 = Pr^n
d; Ar = Ph, R^1 = Me, R^2 = CH_2Ph
e; Ar = Ph, R^1 = Et, R^2 = Ph
f; Ar = Ph, R^1 = Pr^n, R^2 = Ph
g; Ar = Ph, R^1 = Bu^n, R^2 = Ph
h; Ar = α-Naph, R^1 = Me, R^2 = Ph
i; Ar = Ph, R^1 = R^2 = Ph

SCHEME (*i*) H^+; (*ii*) H_2O; (*iii*) H_2O–HCl; (*iv*) $NaHCO_3$; (*v*) HCl

and usually could not be detected amongst the products. The products were then subjected to the reactions

originally used by Whaley and Hartung during their attempts to isolate the so-called isoquinolines *via* their hydrochloride salts. Thus, each product was treated with dry hydrogen chloride gas, and the resulting suspected isoquinoline hydrochlorides of Whaley and Hartung (see Table 3). Treatment of the amine hydrochlorides with aqueous sodium hydrogencarbonate then afforded *threo*-2-acylamino-1-arylalkan-1-ols (8),

TABLE 1

Cyclisation of *erythro*-2-acylamino-1-arylalkan-1-ols (1)

Amide	Cyclising conditions [a]	Time/h	Oxazoline products	*trans* : *cis* ratio	Yield (%)	Picrate m.p.	Found (%) C	H	N	Formula	Requires (%) C	H	N	Amide (8) (%)
(1a)	*C*	2.5	(2a) + (3a)	90 : 10	80	141 [b]								
	D	3	(2a) + (3a)	80 : 20	71									
(1b)	*A*	2.5	(2b) + (3b)	90 : 10	5		80.9	6.9	5.7	$C_{17}H_{17}NO$	81.2	6.8	5.6	
	D	3	(2b) + (3b)	86 : 14	69									
(1c)	*A*	3	(2c) + (3c)	89 : 11	9	143—144	57.1	4.2	11.8	$C_{23}H_{20}N_4O_8$ [c]	57.5	4.2	11.7	
	D	3	(2c) + (3c)	89 : 11	74									
(1d)	*A*	3	(2d) + (3d)	86 : 14	66	168—169	55.7	4.1	11.2	$C_{23}H_{20}N_4O_9$ [c]	55.65	4.1	11.3	
	B	3	(2d) + (3d)	82 : 18	43									
	D	3	(2d) + (3d)	88 : 12	92									
(1e)	*A*	3	(2e) + (3e)	86 : 14	65	149—150	54.5	4.2	10.6	$C_{24}H_{22}N_4O_{10}$ [c]	54.8	4.2	10.6	
	B	3	(2e) + (3e)	82 : 18	50									
	D	3	(2e) + (3e)	87 : 13	90									
(1f)	*A*	3	(2f) + (3f)	79 : 21	26	158 [d]	50.7	4.3	14.1	$C_{17}H_{16}N_4O_8$ [c]	50.5	4.0	13.9	24
	B	3	(2f) + (3f)	88 : 12	27									
	D	3	(2f) + (3f)	70 : 30	66									
(1g)	*D*	3	(2g) + (3g)	65 : 35	70		76.4	7.9	7.4	$C_{12}H_{15}NO$	76.2	7.9	7.4	
(1h)	*C*	3.5	(2h) + (3h)	87 : 13	24		76.6	8.3	7.1	$C_{13}H_{17}NO$	76.85	8.4	6.9	16
	D	4	(2h) + (3h)	85 : 15	49									
(1i)	*C*	3	(2i)		11		81.6	7.0	5.7	$C_{17}H_{17}NO$	81.3	6.8	5.6	42
	D	6	(2i) + (3i)	58 : 42	52									45
(1j)	*C*	3	(2j) + (3j)	93 : 7	45	140	57.8	4.2	11.8	$C_{23}H_{20}N_4O_8$ [c]	57.5	4.2	11.7	64
	D	3	(2j) + (3j)	89 : 11	86									
(1k)	*B*	3	(2k)		28	158	58.2	4.7	11.4	$C_{24}H_{22}N_4O_8$ [c]	58.3	4.5	11.3	12
	C	4	(2k)		28									12
	D	3	(2k) + (3k)	88 : 12	63									
(1l)	*C*	7	(2l) + (3l)	87 : 13	13	154	59.4	4.6	11.3	$C_{25}H_{24}N_4O_8$ [c]	59.05	4.8	11.0	3
	D	7	(2l) + (3l)	74 : 26	32									
(1m)	*D*	3	(2m)		72		84.45	5.85	4.7	$C_{21}H_{17}NO$	84.3	5.7	4.7	28
(1n)	*C*	3	(2n) + (3n)	62 : 38	25		83.7	6.05	5.0	$C_{20}H_{17}NO$	83.6	6.0	4.9	25
	D	3.5	(2n) + (3n)	71 : 29	32									

[a] Cyclising conditions: *A*, phosphorus pentaoxide in refluxing toluene; *B*, phosphorus pentaoxide in refluxing xylene; *C*, phosphorus pentaoxide and phosphorus oxychloride in refluxing xylene; *D*, polyphosphoric acid at 100 °C. [b] Lit., 140—141 °C (W. N. Nagai and S. Kanao, *Annalen*, 1929, **470**, 157). [c] Analysis figures refer to Δ^2-oxazoline picrate. [d] M. Bockemühl and R. Knoll, U.S.P. 1934/1,958,529.

compound was purified by crystallisation and then basified with aqueous sodium hydrogencarbonate.

It is now clear that hydrogen chloride treatment led to ring-opening of the oxazoline with formation of the suspected isoquinolines of the earlier workers (Table 4). This series of transformations is shown in the Scheme [(2)→(5) - - -➤ (8)]. The starting amides possess the *erythro*-configuration because of the mode of formation [6]

TABLE 2

erythro-2-Acylamino-1-aryl-1-chloroalkanes (6)

Compound	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Requires (%) C	H	N
(6a)	109—111 [a]	87							
(6b) [b]									
(6c)	156—158	72	64.9	7.8	5.85	$C_{13}H_{18}ClNO$	65.1	7.5	5.85
(6d) [b]	153—155	68							
(6e)	113—115	90	70.8	6.0	4.6	$C_{17}H_{18}ClNO$	70.9	6.3	4.9
(6f)	103—105	86	71.4	6.8	4.3	$C_{18}H_{20}ClNO$	71.6	6.7	4.6
(6g)	123—125	94	72.1	6.7	4.4	$C_{19}H_{22}ClNO$	72.3	7.0	4.4
(6h)	143—144	89	73.9	5.4	4.05	$C_{20}H_{18}ClNO$	74.2	5.6	4.3
(6i)	160—162	68	75.2	5.5	4.15	$C_{21}H_{18}ClNO$	75.1	5.4	4.2

[a] Lit.,[1] 112—113 °C. [b] Compounds (6b) and (6d) were isolated but were too unstable to moisture to be purified for analysis.

the *erythro*-2-acylamino-1-chloro-1-arylalkane (6). As observed earlier,[1] these compounds (Table 2) are unstable, and in the presence of traces of moisture (during attempted crystallisation) they were rapidly converted into *threo*-1-acyloxy-2-amino-1-arylalkane hydrochlorides (7), the m.p.s of which compare with those of the wrongly-of their amine precursors. The formation of *cis*- and *trans*-Δ^2-oxazolines probably indicates that two cyclisation mechanisms are operative,[7] although the isomer ratio depends on the cyclising conditions employed (see Table 1). The oxazolines were distinguished by examination of the C-5 proton in the ^1H n.m.r. spectrum of the

cis-trans ' mixture ' (Table 5). The C-5 proton of the *cis*-isomer (3) lies downfield (at *ca.* τ 4.4) from the corresponding proton of the *trans*-isomer and appears as a doublet with J *ca.* 10 Hz whereas that of the *trans*-isomer (2) appears at about τ 5.0 and has J *ca.* 8 Hz. The *cis* : *trans* ratio was established from the integration of this signal.

a further acyl migration with retention of configuration [7] giving the *threo*-2-acylamino-1-arylalkan-1-ol (8).

As mentioned earlier, varying amounts of the *threo*-amides (8) were also present at a much earlier stage of the Scheme; as contaminants of the *cis*- and *trans*-Δ^2-oxazoline products, and in certain cases, the proportion of this compound rapidly increased at the expense of

TABLE 3

threo-1-Acyloxy-2-amino-1-arylalkane hydrochlorides (7)

Compound	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Requires (%) C	H	N	Isoquinoline hydrochloride of Whaley and Hartung; m.p. (°C)
(7a)	220 *	87								229
(7b)	175	84	57.2	6.8	5.9	$C_{11}H_{16}ClNO_2$	57.5	7.0	6.1	168
(7c)	176	90	60.3	7.5	5.6	$C_{13}H_{20}ClNO_2$	60.6	7.8	5.4	165
(7d)	215	86	66.3	6.2	3.9	$C_{17}H_{20}ClNO_2$	66.1	6.4	4.8	207 (decomp.)
(7e)	215	66	66.7	6.6	4.6	$C_{17}H_{20}ClNO_2$	66.7	6.6	4.6	210
(7f)	187	72	67.1	7.3	4.5	$C_{18}H_{22}ClNO_2$	67.6	6.9	4.4	180—190
(7g)	147	68	68.3	7.5	4.4	$C_{19}H_{24}ClNO_2$	68.5	7.2	4.2	*ca.* 130
(7h)	215	86	70.5	5.7	4.4	$C_{20}H_{20}ClNO_2$	70.3	5.9	4.1	235 (decomp.)
(7i)	222	78	71.3	5.8	3.8	$C_{21}H_{20}ClNO_2$	71.3	5.7	4.0	*ca.* 185

* Lit.,[1] 220 °C.

The formation of the *erythro*-2-acylamino-1-chloro-1-arylalkanes is considered to arise by attack of chloride anion on the protonated Δ^2-oxazoline during treatment of the latter with dry hydrogen chloride gas. This occurs with inversion of configuration at C-5 and hence, the *trans*-Δ^2-oxazoline (which predominates) leads to the *erythro*-chloro-compound. The *cis*-Δ^2-oxazoline is likely

oxazoline when the mixture was allowed to stand at room temperature. The *threo*-amides here are presumably formed directly from the oxazoline by hydrolytic cleavage. This would occur mainly during the aqueous work-up of the product, but can clearly continue in certain cases simply by exposure of the Δ^2-oxazoline to atmospheric moisture. The process which involves

TABLE 4

threo-2-Acylamino-1-arylalkan-1-ols (8)

Compound	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Requires (%) C	H	N
(8a)	128 [a]	58	75.3	6.8	5.3	$C_{16}H_{17}NO_2$	75.3	6.7	5.4
(8b)	99—101	40	62.6	7.8	6.55	$C_{11}H_{15}NO_2 \cdot H_2O$	62.6	8.05	6.6
(8c)	102—104	56	71.0	8.9	6.5	$C_{13}H_{19}NO_2$	70.6	6.8	6.3
(8d)	102	45 [b]	75.7	7.0	5.2	$C_{17}H_{19}NO_2$	75.8	7.1	5.2
(8e)	113	90	75.4	6.9	5.4	$C_{17}H_{19}NO_2$	75.8	7.1	5.2
(8f)	121	75	76.1	7.7	5.1	$C_{18}H_{21}NO_2$	76.2	7.5	4.9
(8g)	124	74	76.9	7.9	4.6	$C_{19}H_{23}NO_2$	76.7	7.8	4.7
(8h)	162	86	78.7	6.5	4.7	$C_{20}H_{19}NO_2$	78.7	6.3	4.6
(8i)	196—198	75	80.3	6.05	4.5	$C_{21}H_{19}NO_2$	79.9	6.0	4.4

[a] Lit.,[1] 128 °C. [b] Obtained directly from cyclisation.

to be more stable [8] to dry hydrogen chloride and will be removed from the Scheme at this stage. The chloro-amides (Table 2) could not always be obtained analytically pure because of their instability. Thus, in the presence of adventitious moisture, they were rapidly converted (usually during attempted crystallisation) into the *threo*-1-acyloxy-2-amino-1-arylalkane hydrochlorides (7). This probably occurs *via* a two-stage process involving firstly, hydrolysis with inversion of configuration to give *threo*-2-acylamino-1-arylalkan-1-ols, and secondly acyl migration of the latter which proceeds with retention of configuration.[7] The *threo*-configuration would be preserved during basification of the amine hydrochloride (7) because the resulting amine undergoes

hydration of the C=N linkage is known [8] to occur without steric charge, and the formation of *threo*-amides from the predominating *trans*-Δ^2-oxazolines [Scheme; (2)→(9)→(8)] is consistent with this. Passage of dry hydrogen chloride through a dry ethereal solution of the *threo*-amide was shown to also yield the unstable *erythro*-chloroamide [Scheme; (8)→(6)]. Thus, in the original Whaley and Hartung isolation procedure, the presence of *threo*-amide in the crude product would have been immaterial since both constituents of the Δ^2-oxazoline–*threo*-amide mixture would have given the same product, *i.e.* the *erythro*-chloroamide (6) on hydrogen chloride treatment.

Table 1 gives details of the products formed when the

cyclisations originally carried out by Whaley and Hartung were repeated under similar sets of conditions. It also includes details of cyclisations of several other *erythro*-amides under typical Pictet–Gams conditions.

The results show clearly that the conditions classically accepted to effect Pictet–Gams cyclisations to isoquinolines are unreliable. The action of phosphorus pentaoxide in refluxing toluene or xylene generally leads to oxazoline rather than isoquinoline formation, and the course of the reactions is not altered significantly when they are carried out in the presence of phosphorus oxychloride. In the above examples, isoquinolines were only formed when the cyclisations were carried out in the presence of phosphorus pentaoxide in refluxing decalin, although early results [9] show that rearranged products are frequently formed.

TABLE 5

Hydrogen-1 n.m.r. spectra (τ at 90 MHz; J in Hz) of *trans*- and *cis*-Δ^2-oxazolines (2) and (3)

Oxazoline	*trans*-H_A (2)	*cis*-H_A (3)	H_B (m)	Ar-H (m)	Alkyl-H
(2a) and (3a) [a]	5.00 (d, J 8)	4.35 (d, J 10)	5.88	2.65—1.84 (10 H)	8.9 (3 H, d, J 6.5)
(2b) and (3b) [b]	5.00 (d, J 8)	4.34 (d, J 10)	5.90	2.9—2.1 (9 H)	9.24 (3 H, d, J 7), 8.63 (3 H, d J 7), 7.68 (3 H, s)
(2c) and (3c) [b]	5.00 (d, J 8)	4.28 (d, J 10)	5.90	2.9—1.9 (9 H)	9.19 (3 H, d, J 7), 8.58 (3 H, d, J 7), 7.65 (3 H, s)
(2d) and (3d) [b]	5.00 (d, J 9)	5.00 (d, J 9)	5.90	3.3—2.0 (9 H)	9.2 (3 H, d, J 7), 8.6 (3 H, d, J 7) 6.3 (3 H, s)
(2e) and (3e) [b]	4.90 (d, J 9)	4.90 (d, J 9)	5.80	3.2—2.3 (8 H)	9.1 (3 H, d, J 7), 8.5 (3 H, d, J 7), 6.1 (6 H, s)
(2f) and (3f) [a]	5.08 (d, J 8)	4.31 (d, J 10)	5.92	2.75—2.52 (5 H)	8.77 (3 H, d, J 7), 8.12 (3 H, s)
(2g) and (3g) [a]	4.92 (d, J 7)	4.36 (d, J 10)	6.02	2.75—1.85 (5 H)	8.94 (6 H, m), 8.34 (2 H, q, J 7)
(2h) and (3h) [a]	5.07 (d, J 8)	4.40 (d, J 10)	5.92	2.75—2.40 (5 H)	9.33—7.50 (10 H, m)
(2i) and (3i) [a]	5.20 (d, J 8)	4.34 (d, J 10)	5.93	2.81—2.61 (10 H)	8.60 (3 H, d, J 7), 6.4 (2 H, s)
(2j) and (3j) [b]	4.92 (d, J 7)	4.36 (d, J 10)	6.02 [c]	2.75—1.85 (10 H)	8.94 (3 H, t, J 8), 8.34 (2 H, q, J 8)
(2k) and (3k) [b]	4.83 (d, J 9)	4.25 (d, J 10)	5.94	2.83—1.83 (10 H)	9.17—8.17 (7 H, m)
(2l) and (3l) [a]	4.90 (d, J 9)	4.05 (d, J 9)	5.92	2.90—1.90 (10 H)	9.20—8.25 (9 H, m)
(2m) and (3m) [a]	4.70 (d, J 9)		4.70 [d]	3.10—1.60 (15 H)	
(2n) and (3n) [b]	4.20 (d, J 7)	3.60 (d, J 9)	5.75	2.69—1.77 (12 H)	8.92 (3 H, d, J 7)

s = Singlet, d = doublet, t = triplet, q = quartet, m = multiplet centred at value shown (unless range given); J in Hz. [a] Spectrum measured in deuteriochloroform. [b] Spectrum measured in carbon tetrachloride. [c] q, J 6.5 Hz. [d] d, J 9 Hz.

EXPERIMENTAL

Hydrogen-1 n.m.r. spectra were recorded with a Varian A90 spectrometer using tetramethylsilane as internal reference. I.r. spectra were determined for Nujol mulls or liquid films on a Perkin-Elmer 257 spectrometer. Ether extracts were dried over desiccated magnesium sulphate.

The starting erythro-2-*acylamino*-1-*arylalkan*-1-*ols* (1) were obtained by acylation of the corresponding amines. These were prepared either by the method described by Fitton and Smalley [10] or from benzaldehyde cyanohydrin. Interaction of this with the appropriate alkyl or aryl Grignard reagent gave the α-hydroxyketone [11] which was converted into the amine by condensation with hydroxylamine followed by catalytic reduction of the resulting oxime.[12]

Cyclisations of erythro-2-*Acylamino*-1-*arylalkan*-1-*ols* (1).—These were carried out (see Table 1) using conditions *A*, *B*, *C*, or *D*, where *A* refers typically to amide (1 g) + phosphorus pentaoxide (10 g) in dry toluene (30 ml); *B* to amide (1 g) + phosphorus pentaoxide (10 g) in dry xylene (30 ml), and *C* to amide (1 g) + phosphorus pentaoxide (10 g) + phosphorus oxychloride (10 ml) in dry xylene (30 ml).

(*a*) *Isolation procedure for products from reactions using conditions* A, B, *and* C. At the end of the heating period, excess of dehydrating agent was destroyed by careful addition of ice–water, and the resulting two-phase system was separated. The organic layer was extracted three times with water, and the aqueous layer and extracts were combined, washed with ether, and then basified (with cooling) with 30% aqueous sodium hydroxide. The oil which separated was taken into ether, and after drying, the solution was evaporated to dryness. The residue gave the *trans*- and *cis*-Δ^2-oxazoline [(2) and (3)] or a mixture of (2), (3), and the *threo*-amide (8) (see Table 1).

(*b*) *Typical procedure using conditions* D. A mixture of the amide (1 g) and polyphosphoric acid (20 g) was stirred at 100 °C for 3 h, then cooled somewhat and added to ice–water (250 g). When decomposition of the complex was complete, the mixture was extracted with ether and the extracts were discarded. The aqueous phase was basified with concentrated aqueous ammonium hydroxide, then extracted with ether. Evaporation of the dried extracts gave the *trans*- and *cis*-Δ^2-oxazoline [(2) and (3)] or a mixture of (2), (3), and the *threo*-amide (see Table 1).

erythro-2-*Acylamino*-1-*aryl*-1-*chloroalkanes* (6).—(*a*) Dry hydrogen chloride gas was bubbled through a solution of the *trans*- and *cis*-Δ^2-oxazoline (2 g) in dry benzene (5 ml) for 45 min. The solution was evaporated to dryness and the residue was crystallised (usually with difficulty) from a dry mixture of isopropanol and light petroleum (b.p. 60—80 °C) to give the erythro-2-*acylamino*-1-*aryl*-1-*chloroalkane* (See Table 2).

(*b*) Dry hydrogen chloride gas was bubbled through an ethereal solution of certain *threo*-2-acylamino-1-arylalkan-1-ols for 45 min. The solution was evaporated to dryness and the residue on purification as above gave the erythro-2-*acylamino*-1-*aryl*-1-*chloroalkane* [*e.g.* (d) Table 2].

threo-1-*Acyloxy*-2-*amino*-1-*arylalkane hydrochlorides* (7).—The *erythro*-2-acylamino-1-aryl-1-chloroalkane (6) was crystallised from ethanol containing 1% water. This gave the title amine hydrochloride (7) (see Table 3).

threo-2-*Acylamino*-1-*arylalkan*-1-*ols* (8).—The *threo*-1-acyloxy-2-amino-1-arylalkane hydrochloride was thoroughly ground with an excess of saturated aqueous sodium hydrogencarbonate for 30 min. The precipitate was filtered off and gave the threo-2-*acylamino*-1-*arylalkanol* (8) see Table 4).

We thank the Inter-University Council for Higher Education Overseas for support (for F. K. O-B) and the Malaysian Government for scholarships (to A. H. b. A. H. and A. b. M. S.).

[8/478 *Received*, 15*th March*, 1978]

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