Formation of 2,3-Dihydro-4(1*H*)-quinolones and Related Compounds *via* Fries-type Acid-catalysed Rearrangement of 1-Arylazetidin-2-ones

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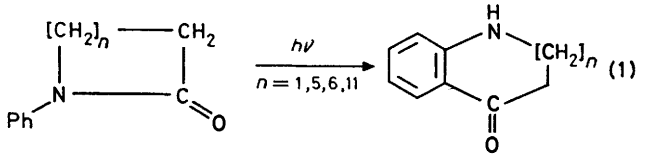
A variety of 1-arylazetidin-2-ones were treated with trifluoroacetic acid under reflux, methanesulphonic acid at 100 °C, or conc. sulphuric acid to give the corresponding 2,3-dihydro-4(1*H*)-quinolones *via* acyl migration and N–CO fission. In the case of 1-(3-substituted phenyl)azetidin-2-ones, two positional isomeric products, 5- and 7-substituted 2,3-dihydro-4(1*H*)-quinolones were obtained. 4-Methyl-, 4-ethoxycarbonyl-, and 4-piperidin-2-yl-1-arylazetidin-2-ones and their analogues were also converted into the corresponding 2-substituted 2,3-dihydro-4(1*H*)-quinolones under acidic conditions. The 3-substituted 1-phenylazetidin-2-ones (36) and (37) were converted into the furo[3,2-*c*]quinoline systems (38) and (40), respectively, by application of this method.

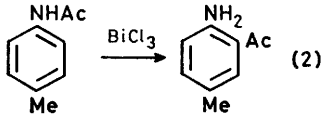
MANY *N*-substituted anilides are known to rearrange to *ortho*- or *para*-substituted aniline derivatives with Lewis acids,[1] and several types of *N*-phenyl-lactam are converted into the corresponding *ortho*-migrated products



(1)

under the conditions of the photo-Fries rearrangement, initiated by cleavage of the N–CO bond [equation (1)].[2] Recently, a new high-yield migration of the acyl group in various anilides to give *o*-acylanilines using bismuth chloride as catalyst has been reported [equation (2)].[3] However, there has been no survey of intramolecular acyl migration in 1-arylazetidin-2-ones with Lewis acids except for our initial study,[4] even though it is well known that the amide bond of azetidin-2-ones is easily cleaved with nucleophiles such as amines and alcohols. We have investigated the Fries-type acid-catalysed rearrangement of various 1-arylazetidin-2-ones in acidic solution giving 2,3-dihydro-4(1*H*)-quinolones, and report the results here.

Preparation of 1-*Arylazetidin*-2-*ones.*—Various monocyclic 1-arylazetidin-2-ones were synthesised to examine the intramolecular rearrangement of the acyl group *via* cleavage of the N–CO bond (see later). The 1-arylazetidin-2-ones (2a—i) were prepared by cyclisation of the ethyl β-anilinopropionates (1a—i), obtained by Michael addition of ethyl acrylate to the corresponding aniline derivatives [5] with ethylmagnesium bromide, as reported by Holley.[6] The 3-hydroxyphenyl compound (2j) was obtained by reductive debenzylation of (2i) in the presence of 10% palladium on charcoal. Cyclisation of the butyrate (3), obtained by Michael addition of ethyl crotonate to *p*-anisidine, afforded the 4-methoxyphenyl compound (6). Reductive amination of ethyl benzoylacetate with *p*-anisidine in the presence of 10% palladium on charcoal and sodium borohydride afforded compound



(2)

(4), cyclisation of which with ethylmagnesium bromide gave the azetidinone (7). Similarly, the pyridyl derivative (8) was also prepared *via* (5) starting from ethyl 2-pyridylcarbonyl acetate instead of ethyl benzoylacetate.

TABLE 1

Microanalysis or mass spectrum (M^+) of the ethyl β-anilinopropionates (1), (3), and (12)

Compound	M.p./°C (b.p./°C; *P*/Torr)	Found (%) C	H	N	Analyses of mass spectra (M^+) Formula	Required (%) C	H	N
(1c)	110—112 [a] (153; 3)	50.05	5.75	5.35	$C_{11}H_{15}Cl_2NO_2$	50.0	5.7	5.55
(1d) [b]		$M^+ + 2$, 273, M^+, 271			$C_{11}H_{14}BrNO_2$	$M^+ + 2$, 273, M^+, 271		
(1e)	106—108 [c] (123; 3)	62.35	7.9	22.0	$C_{10}H_{15}N_3O$	62.15	7.8	21.75
(1h) [b]		M^+, 236			$C_{13}H_{20}N_2O_2$	M^+, 236		
(1i)	104—105 [c]	67.3	6.75	15.0	$C_{16}H_{19}N_3O_2$	67.35	6.7	14.75
(3)	125—127 [c] (150; 3)	59.15	7.7	18.8	$C_{11}H_{17}N_3O_2$	59.15	7.6	18.95
(12)	151—153 [a]	64.4	6.5	5.0	$C_{15}H_{18}ClNO_2$	64.4	6.55	5.05

[a] Crystallised as the hydrochloride (from MeOH–Et_2O). [b] Not crystallised. [c] Crystallised as the hydrazide (from MeOH–Et_2O).

The naphthyl compounds (13) and (14) were prepared by the cyclisation of the corresponding naphthylaminopropionates (11) and (12), respectively. The properties and analytical data of the anilinopropionates and the aryl-azetidinones are listed in Tables 1 and 2. Catalytic

hydrogenation of (8) over Adams catalyst gave compound (9). Treatment of (9) with trifluoroacetic anhydride yielded the trifluoroacetamide (10). The hydrazine derivative (17) was prepared from the acid chloride

TABLE 2

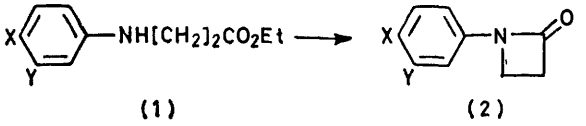
1-Arylazetidin-2-ones

Compound	Yield (%)	M.p. [a]/ °C	m/e (M^+)	δ ($CDCl_3$), 3-H and 4-H; J in Hz	Found (%) C	H	N	Analyses Formula	Required (%) C	H	N
(2b)	45	97—98	177	2.98 (2 H, t, J 4), 3.50 (2 H, t, J 4)	67.6	6.2	7.95	$C_{10}H_{11}NO_2$	67.8	6.25	7.9
(2c)	35	111—112	181 [b]	3.12 (2 H, t, J 4), 3.60 (2 H, t, J 4)	59.45	4.6	7.4	C_9H_8ClNO	59.5	4.45	7.7
(2d)	30	102—104	225 [c]	2.93—3.12 (2 H, m), 3.43—3.62 (2 H, m)	47.9	3.8	6.05	C_9H_8BrNO	47.8	3.55	6.2
(2e)	40	75—78	161	2.90—3.05 (2 H, m), 3.45—3.58 (2 H, m)	74.45	6.95	8.45	$C_{10}H_{11}NO$	74.5	6.9	8.7
(2f)	45	67—69	177	3.01 (2 H, m), 3.53 (2 H, m)	67.75	6.3	7.75	$C_{10}H_{11}NO_2$	67.8	6 25	7 9
(2g)	35	56—58	181 [b]	3.05 (2 H, m), 3.54 (2 H, m)	59.8	4.5	7.65	C_9H_8ClNO	59.5	4.45	7.7
(2h)	35	117—118	190	2.95 (2 H, t, J 4), 3.48 (2 H, t, J 4)	69.4	7.5	14.7	$C_{11}H_{14}N_2O$	69.45	7.4	14.4
(2i)	40	98—99	253	3.07 (2 H, t, J 4.5), 3.57 (2 H, t, J 4.5)	76.1	5.95	5.25	$C_{18}H_{15}NO_2$	75.85	5.95	5.55
(6)	60	97—99	191	2.56 (1 H, dd, J 2, 15 Hz), 3.17 (1 H, dd, J 5, 15), 4.03 (1 H, m)	69.2	6.9	7.1	$C_{11}H_{13}NO_2$	69.1	6.85	7.35
(7)	60	94—96	253	2.83 (1 H, dd, J 2.5, 15), 3.48 (1 H, dd, J 5, 15), 4.90 (1 H, dd, J 2.5, 5)	75.9	5.95	5.7	$C_{16}H_{15}NO_2$	75.85	5.95	5.55
(8)	50	111—113	254	2.96 (1 H, dd, J 3, 15), 3.53 (1 H, dd, J 5.5, 15), 5.06 (1 H, dd, J 3, 5.5)	70.95	5.6	11.15	$C_{15}H_{14}N_2O_2$	70.85	5.55	11.0
(13)	25	Oil	197	2.98—3.13 (2 H, m), 3.63—3.78 (2 H, m)							
(14)	30	131—133	197	3.13 (2 H, t, J 4), 3.59 (2 H, t, J 4)	78.95	5.7	6.9	$C_{13}H_{11}NO$	79.15	5.6	7.1

[a] All compounds were recrystallised from benzene–hexane except (13). [b] $M^+ + 2$ at m/e 183. [c] $M^+ + 2$ at m/e 227.

(15),[7] obtained from the ester (16) [7] by reaction with *NN*-dimethylhydrazine.

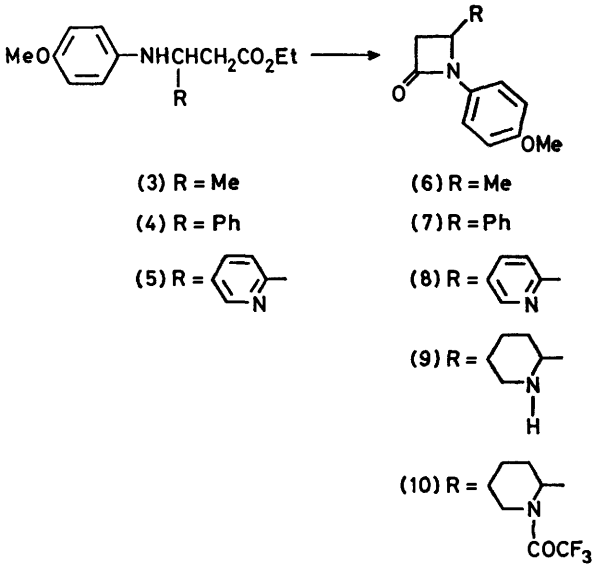
Fries-type Acid-catalysed Rearrangement of 1-Aryl-2-azetidinones.—We first examined the migration of the



(1) (2)

	X	Y		X	Y
a;	H	H	f;	H	OMe
b;	OMe	H	g;	H	Cl
c;	Cl	H	h;	H	NMe_2
d;	Br	H	i;	H	OCH_2Ph
e;	H	Me	j;	H	OH

carbonyl group in various acidic solutions to determine the optimum conditions giving 2,3-dihydro-4(1*H*)-quinolones. Treatment of (2b) with trifluoroacetic acid under reflux for 1 h gave 2,3-dihydro-6-methoxy-4(1*H*)-quinolone (18b) [8] in 95% yield. Use of concentrated sulphuric acid, methanesulphonic acid, trifluoromethanesulphonic acid, and boron trifluoride–diethyl ether at 100 °C led to different yields of (18b), as shown in the Table 3. Acetic acid and formic acid were not effective for cleavage of the amide bond of (2b), which remained unchanged. Thus, trifluoroacetic acid or methanesulphonic acid were most suitable for migration of the carbonyl group. The reactions of (2a), (2c), and (2d) with trifluoroacetic acid to give the corresponding 2,3-dihydro-4(1*H*)-quinolones (18a),[8] (18c),[9] and (18d), respectively, were also examined (Table 3). The formation of (18a—d) seems to depend on the electronic effect of the substituent on the benzene ring, electron-donating groups leading to increased yields. Similar reactions of (2b) were also carried out in the presence of

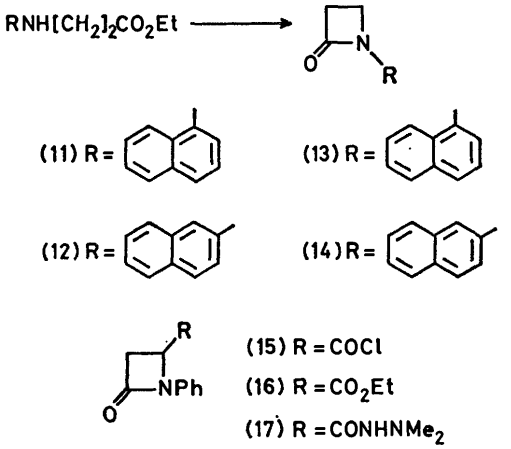


(3) R = Me
(4) R = Ph
(5) R =

(6) R = Me
(7) R = Ph
(8) R =
(9) R =
(10) R =

nucleophilic aromatic compounds such as phenol or anisole in order to examine whether or not intermolecular acyl migration to these aromatic compounds might occur. However, intermolecular acylated products were not obtained and the reaction resulted in the formation of only (18b). This indicates that this acyl migration occurs in a different manner from the general nucleophilic cleavage of the amide bond of azetidin-2-ones.[10]

This acyl migration was applied to the synthesis of the benzoquinolones (19)[11] and (20).[12] Treatment of (13)



with trifluoroacetic acid for 2 h under reflux led to smooth acyl migration at the β-position to give (19) in 50% yield, and (20) was obtained in 85% yield from (14) under the same conditions.

It was of interest to examine whether the acyl rearrangement occurred at the *para*- or *ortho*-position with respect to the substituent on the benzene ring for the 1-(3-substituted phenyl)azetidin-2-ones. Treatment of (2e) with trifluoroacetic acid for 1 h under reflux gave the 7-methylquinolone (21a) (35%)[4] and the 5-methyl isomer (22a) (35%).[4] Similarly, (2f) gave (21b)[13] (40%) and the 5-methoxy-isomer (22b)[4] (20%); (2g) also afforded two products (21c) (25%) and (22c)[14] (8%) in much lower yields. However, (2j) afforded only the 5-hydroxyquinolone (22d), in 73% yield, and the 7-hydroxy-isomer (21d) was not observed. In the case of (2h), trifluoroacetic acid was not effective for migration

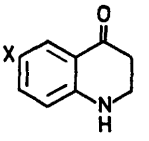
TABLE 3

Formation of 2,3-dihydro-4(1*H*)-quinolones (18a—d) from (2a—d)

Lactam	Acid	Product	% Yield
(2a)	CF_3CO_2H	(18a)	80 [a]
(2b)	CF_3CO_2H	(18b)	95 [a]
(2b)	Conc. H_2SO_4	(18b)	50 [a]
(2b)	$MeSO_3H$	(18b)	60 [a]
(2b)	CF_3SO_3H	(18b)	40 [a]
(2b)	BF_3–Et_2O	(18b)	15 [a]
(2c)	CF_3CO_2H	(18c)	30 [b]
(2d)	CF_3CO_2H	(18d)	30 [b]

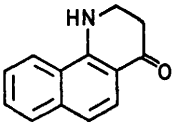
[a] 1 h reaction at 100 °C. [b] 1.5 h reaction at 100 °C.

of carbonyl group and the reaction resulted in the formation of only resin. Treatment of (2h) with methanesulphonic acid at 100 °C gave the 7-dimethylaminoquinolone (21e) in 15% yield and the 5-dimethylamino-derivative (22e) was not formed. The 5-substituted dihydroquinolones were easily distinguished from the 7-

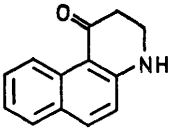


(18)

a; X = H c; X = Cl
b; X = OMe d; X = Br



(19)



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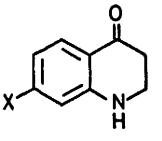

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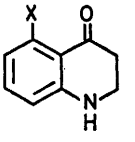
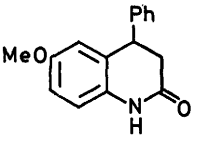


(22)

X X
a; Me d; OH
b; OMe e; NMe_2
c; Cl



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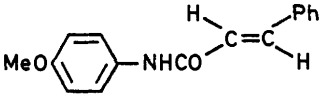

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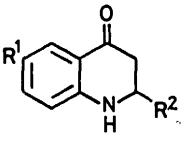
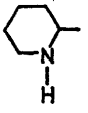
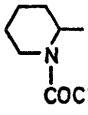
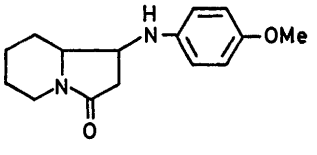


(25) R^1 = OMe, R^2 = Me
(26) R^1 = H, R^2 = CO_2Et
(27) R^1 = H, R^2 = $CONHNMe_2$
(28) R^1 = OMe, R^2 =



(29) R^1 = OMe, R^2 =





(30)

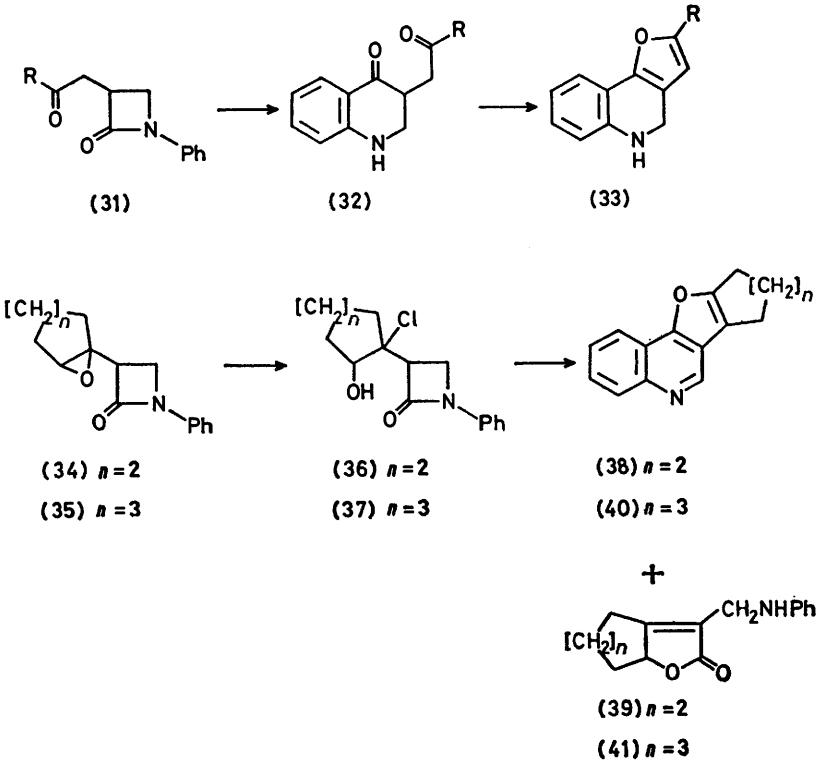
substituted isomers by the observation of characteristic signals at δ *ca.* 7.7—7.73 due to 5-H in the ^{1}H n.m.r. spectra of the 7-substituted compounds. The isomers obtained from (2e—g) were easily separated by column chromatography on silica gel with benzene–chloroform as eluant.

The isomerization of 1,4-diarylazetidin-2-ones giving 4-aryl-3,4-dihydro-2(1*H*)-quinolones by use of acids such as sulphuric acid or polyphosphoric acid was first reported by Gambaryan [15] and the results were extended by Bird [16] and Suschitzky.[17] We also examined a similar reaction by treatment of (7) with trifluoroacetic acid for 6 h under reflux to give the quinolone (23) accompanied by the amide (24) through fission of the 1—4 bond without cleavage of the amide bond as expected. In contrast, (6) afforded only the quinolone (25) in 95% yield under similar conditions.

This significant difference in the reactivity of 1-arylazetidin-2-ones caused by different substituents at the 4-position led us to examine the same reaction with (16) and (17). However, treatment of (16) with concentrated sulphuric acid at room temperature afforded the quinolone (26) and (17) was also converted into (27) on treatment with methanesulphonic acid at 100 °C.

The amide bond of azetidin-2-ones is well known to be easily cleaved by nucleophiles such as amine and alcohol derivatives.[10] Thus, (9) produced the indolizine derivative (30) on treatment with sodium ethoxide.[18] However, treatment of (9) with methanesulphonic acid yielded the quinolone (28) in 30% yield and (30) was not obtained under these acidic conditions. Protection of the amino-group as the trifluoracetamide did not improve the yield of the product, and significant differences were not observed in the yields of the corresponding products (28) and (29) from (9) and (10), respectively.

Finally, we attempted to synthesise furo[3,2-*c*]-quinoline derivatives by this acyl migration, since the acid-catalysed rearrangement of 1-aryl-3-(β-oxoalkyl)-azetidin-2-ones (31) or their equivalents might give the



furo[3,2-*c*]quinolines (33) *via* the quinolones (32). In view of this, the cyclohexyl-azetidinone (36), easily obtained from the epoxide (34),[19] was treated with methanesulphonic acid in benzene under reflux for 1.5 h to give the desired tetrahydrobenzofuro[3,2-*c*]quinoline (38) accompanied by the alternative product, the butenolide (39),[19] as expected, which were easily separated by column chromatography on silica gel. Assignment of structure (38) was based on its molecular formula, $C_{15}H_{13}NO$ (mass spectrum and microanalysis), and its ^{1}H and ^{13}C n.m.r. spectra which showed the presence of the quinoline skeleton (see Experimental section). Aromatisation of a 1,2-dihydroquinoline type intermediate can be accounted for by aerial oxidation.

Similarly, the cycloheptyl compound (37), obtained from the epoxide (35),[19] was also treated with methanesulphonic acid to give the furo[3,2-*c*]quinoline derivative (40) accompanied by the butenolide (41).[19]

The intramolecular acyl migration of 1-arylazetidin-2-ones is thus applicable to the synthesis of quinoline derivatives.

EXPERIMENTAL

^{1}H N.m.r. spectra were measured with a Varian T-60 spectrometer, and ^{13}C n.m.r. spectra with a JEOL FX-100 spectrometer operating at 25.0 MHz. Mass spectra were measured with a Hitachi RMU-7L instrument.

General Procedure for the Preparation of Ethyl β-Anilinopropionates.—A mixture of the appropriate aniline derivative (0.5 mol), ethanol (500 ml), concentrated hydrochloric acid (48 ml), and ethyl acrylate (55 g, 0.55 mol) [ethyl crotonate (73 g, 0.55 mol) for the preparation of (3)] was heated under reflux for 48 h. Solvent was then evaporated off and the residue made basic with 28% aqueous ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was purified by distillation *in vacuo* or column chromatography on silica gel to give the product in 70—80% yield in each case. Analytical data for compounds which had not been reported previously are in Table 1.

Ethyl β-(4-Methoxyanilino)-β-phenylpropionate (4).—A mixture of ethyl benzoylacetate (25 g, 0.13 mol), *p*-anisidine (16 g, 0.13 mole), and benzene (200 ml) was refluxed in the presence of a catalytic amount of toluene-*p*-sulphonic acid for 12 h. The solvent was evaporated off and a solution of the residue in ethanol (200 ml) catalytically hydrogenated under hydrogen at atmospheric pressure in the presence of sodium borohydride (5 g, 0.15 mol) and 10% palladium on charcoal (10 g). The catalyst was filtered off and the filtrate evaporated. The residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. Chromatography of the residue on silica gel with benzene as eluant followed by removal of solvent afforded the *ester* (4) (23.5 g, 70%), m.p. 52.5—54 °C (from benzene–hexane) (Found: C, 72.05; H, 6.95; N, 4.85. $C_{18}H_{21}NO_3$ requires C, 72.2; H, 7.05; N, 4.7%).

Ethyl β-(4-Methoxyanilino)-β-(2-pyridyl)propionate (5).—The reaction of ethyl 2-pyridylcarbonylacetate (25 g, 0.13 mol) and *p*-anisidine (15.9 g, 0.13 mol) by the procedure in the foregoing preparation gave the *ester* (5) (25.5 g, 65%), m.p. 72—74 °C (from MeOH–Et_2O) (Found: C, 67.95; H, 6.7; N, 9.45. $C_{17}H_{20}N_2O_3$ requires C, 68.0; H, 6.7; N, 9.35%), M^+, *m/e* 300.

General Procedure for the Preparation of 1-Arylazetidin-2-ones.—A solution of ethylmagnesium bromide (3 mol l^{-1}) in ether (20 ml) was added to a solution of the appropriate ethyl β-anilinopropionate (0.04 mol) in dry tetrahydrofuran (250 ml) at room temperature. For (2h), ethylmagnesium bromide was added while the mixture was cooled in ice. The mixture was stirred for 14 h, evaporated, and the residue diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel with benzene as eluant (see Table 1).

1-(4-Methoxyphenyl)-4-piperidin-2-ylazetidin-2-one (9).—A solution of (8) (2 g, 7.87 mmol) in ethanol–acetic acid (150 ml; 1 : 1) was stirred under hydrogen at atmospheric pressure in the presence of platinum catalyst (0.5 g) until the theoretical amount of hydrogen (524 ml) had been absorbed. After removal of the catalyst and evaporation the residue was recrystallised from benzene–hexane to give the *azetidinone* (9) (1.74 g, 85%), m.p. 107—108 °C (Found: C, 69.5; H, 7.8; N, 10.75. $C_{15}H_{20}N_2O_2$ requires C, 69.2; H, 7.75; N, 10.8%); δ ($CDCl_3$) 3.76 (3 H, s), 3.90 (1 H, m, 4-H), 6.82 (2 H, d, *J* 9 Hz), and 7.35 (2 H, d, *J* 9 Hz); M^+, *m/e* 260.

1-(4-Methoxyphenyl)-4-(N-trifluoroacetylpiperidin-2-yl)-azetidin-2-one (10).—A mixture of (9) (600 mg, 2.3 mmol), trifluoroacetic anhydride (1.2 g, 5.7 mmol), and pyridine (5 ml) was stirred at room temperature for 2 h. After dilution with water, the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was recrystallised from benzene–hexane to give the *trifluoroacetyl compound* (10) (740 mg, 90%), m.p. 136—137 °C (Found: C, 57.35; H, 5.4; N, 7.9. $C_{17}H_{19}F_3N_2O_3$ requires C, 57.3; H, 5.35; N, 7.85); M^+, *m/e* 356; δ ($CDCl_3$) 3.78 (3 H, s), 4.52—4.80 (3 H, m), 6.83 (2 H, d, *J* 9 Hz), and 7.19 (2 H, d, *J* 9 Hz).

4-(NN-Dimethylhydrazinocarbonyl)-1-phenylazetidin-2-one (17).—A mixture of (15) (800 mg, 3.82 mmol), *NN*-dimethylhydrazine (600 mg, 10 mmol), triethylamine (0.7 ml), and dry benzene (30 ml) was stirred at room temperature for 3 h. After evaporation the residue was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave the *hydrazine* (17) (712 mg, 80%), m.p. 197—198 °C (from MeOH–Et_2O) (Found: C, 61.75; H, 6.5; N, 17.95. $C_{12}H_{13}N_3O_2$ requires C, 61.8; H, 6.45; N, 18.0%).

General Procedure for the Fries-type Rearrangement of 1-Arylazetidin-2-ones.—A mixture of the 1-arylazetidin-2-one (200—500 mg, 1.5—3.0 mmol) and trifluoroacetic acid (5—10 ml) was heated under reflux for 1—1.5 h. The cooled mixture was diluted with water, made basic with 28% aqueous ammonia, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the almost pure 2,3-dihydro-4(1*H*)-quinolones in the case of (18a—d), (19), (20), (22d), (25), and (29). In the reaction of (2e—g), the products were easily separated by column chromatography on silica gel (3—4 g). Elution with benzene afforded (21a—c) and elution with chloroform or chloroform–methanol (98 : 2) yielded (22a—c). M.p.s and analytical data are as follows (18a), m.p. 42—44 °C (lit.,[9] 44.5 °C); (18b), m.p. 111—113 °C (lit.,[9] 114.5 °C); (18c), m.p. 126—126.5 °C (lit.,[8] 126 °C); (18d), m.p. 110—111 °C (from MeOH–Et_2O) (Found: C, 47.9; H, 3.45; N, 6.25. C_9H_8BrNO requires C, 47.8; H, 3.55; N, 6.2%); (19), m.p. 158—160 °C (from MeOH–Et_2O) (Found: 79.25; H, 5.05; N, 6.95. $C_{13}H_{11}NO$ requires C, 79.15; H, 5.15; N, 6.9%); (20), m.p. 140—141 °C (from MeOH–Et_2O) (Found: C, 78.9; H, 5.2; N, 6.9%); (21a), m.p. 93—95 °C (from MeOH–Et_2O) (Found: C, 74.55; H, 6.85; N, 8.5. $C_{10}H_{11}NO$ requires C, 74.5; H, 6.9; N, 8.7%); (22a), m.p. 97—98 °C (from MeOH–Et_2O) (Found: C, 74.35; H, 6.9; N, 8.45%); (21b), m.p. 138—139 °C (lit.,[13] 137 °C); (22b), m.p. 183—184 °C (from MeOH–Et_2O) (Found: C, 67.6; H, 6.25; N, 7.7. $C_{10}H_{11}NO_2$ requires C, 67.8; H, 6.25; N, 7.9%); (21c), m.p. 128—130 °C (from MeOH–Et_2O) (Found: C, 59.3; H, 4.45; N, 7.45. C_9H_8ClNO requires C, 59.5; H, 4.45; N, 7.7%); (22c), m.p. 122—123 °C (from MeOH–Et_2O) (Found: C, 59.35; H, 4.4; N, 7.5%); (22d), m.p. 105—106 °C (from MeOH–Et_2O) (Found: C, 66.1; H, 5.5; N, 8.5. $C_9H_9NO_2$ requires C, 66.25; H, 5.55; N, 8.6%); (25), m.p. 139—140 °C (from C_6H_6–Et_2O) (Found: C, 69.3; H, 6.95; N, 7.3. $C_{11}H_{19}NO_2$ requires C, 69.1; H, 6.85; N, 7.35%); (29), m.p. 173—174 °C (from MeOH–Et_2O) (Found: C, 57.45; H, 5.45; N, 7.75. $C_{17}H_{19}F_3N_2O_3$ requires C, 57.3; H, 5.35; N, 7.9%).

7-Dimethylamino-2,3-dihydro-4(1H)-quinolone (21e).—A mixture of (2h) (500 mg, 2.63 mmol) and methanesulphonic acid (5 ml) was heated at 100 °C for 1 h. The mixture was diluted with water, made basic with 28% aqueous ammonia,

and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated, and the residue was recrystallised from methanol–ether to give the *dihydroquinolone* (21e) (75 mg, 15%), m.p. 163.5—164.5 °C (Found: C, 69.65; H, 7.6; N, 15.0. $C_{11}H_{14}N_2O$ requires C, 69.45; H, 7.4; N, 14.75%); M^+, *m/e* 190; δ ($CDCl_3$) 5.72 (1 H, d, *J* 2 Hz), 6.16 (1 H, dd, *J* 2 and 9 Hz), and 7.73 (1 H, d, *J* 9 Hz).

2-*Ethoxycarbonyl*-2,3-*dihydro*-4(1H)-*quinolone* (26).—A mixture of (16) (500 mg, 2.28 mmol) and conc. sulphuric acid (5 ml) was stirred at room temperature for 3 h. The mixture was poured into ice–water, made basic with 28% aqueous ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the *ester* (26) (135 mg, 12%), m.p. 77.5—79 °C (from MeOH–Et_2O) (Found: C, 65.65; H, 5.95; N, 6.15. $C_{12}H_{13}NO_3$ requires C, 65.75; H, 6.0; N, 6.4%); M^+, *m/e* 219.

2-(NN-*Dimethylhydrazinocarbonyl*)-2,3-*dihydro*-4(1H)-*quinolone* (27).—A mixture of (17) (500 mg, 2.15 mmol) and methanesulphonic acid (5 ml) was heated at 100 °C for 1.5 h. The mixture was diluted with water, made basic with 28% aqueous ammonia, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield the *hydrazine* (27) (300 mg, 60%), m.p. 150—151 °C (from MeOH–Et_2O) (Found: C, 61.65; H, 6.55; N, 18.05. $C_{12}H_{15}N_3O_2$ requires C, 61.8; H, 6.5; N, 18%); M^+, *m/e* 233; δ ($CDCl_3$) 2.58 (2 H, m), 7.10 (1 H, m), and 7.63—7.87 (1 H, m).

2,3-*Dihydro*-7-*methoxy*-2-*piperidin*-2-*yl*-4(1H)-*quinolone* (28).—A mixture of (9) (500 mg, 1.92 mmol) and methanesulphonic acid (5 ml) was heated at 100 °C for 1.5 h and worked up as above to yield the *piperidine* (28) (150 mg, 15%), m.p. 151—151.5 °C (from MeOH–Et_2O) (Found: C, 69.0; H, 7.7; N, 10.55. $C_{15}H_{20}N_2O_2$ requires C, 69.2; H, 7.75; N, 10.75%); M^+, *m/e* 260; δ ($CDCl_3$) 6.60 (1 H, d, *J* 9 Hz), 6.91 (1 H, dd, *J* 2.5, 9 Hz), and 7.20 (1 H, d, *J* 2.5 Hz).

Treatment of (7) *with Trifluoroacetic Acid*.—A mixture of (7) (500 mg, 1.98 mmol) and trifluoroacetic acid (10 ml) was heated under reflux for 6 h. The mixture was diluted with water, made basic with 28% aqueous ammonia, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (3 g). Elution with trans-β-(p-*methoxyphenylcarbamoyl*)*styrene* (24) (40 mg, 8%), m.p. 140—142 °C (from benzene–hexane) (Found: C, 75.75; H, 5.65; N, 5.8. $C_{16}H_{15}NO_2$ requires C, 75.85; H, 5.95; N, 5.55%); M^+, *m/e* 253; δ ($CDCl_3$) 3.74 (3 H, s), 6.53 (1 H, d, *J* 15 Hz), 6.80 (2 H, d, *J* 9.5 Hz), 7.17—7.47 (7 H, m), and 7.69 (1 H, d, *J* 15 Hz). Elution with chloroform yielded 3,4-*dihydro*-6-*methoxy*-4-*phenyl*-2(1H)-*quinolone* (23) (150 mg, 30%), m.p. 152—153 °C (from MeOH–Et_2O) (Found: C, 75.6; H, 5.85; N, 5.35. $C_{16}H_{15}NO_2$ requires C, 75.85; H, 5.95; N, 5.55%); *m/e* 253; δ ($CDCl_3$)2.88 (2 H, d, *J* 7.5 Hz), 3.66 (3 H, s), and 4.23 (1 H, t, *J* 7.5 Hz).

3-(1-*Chloro*-2-*hydroxycyclohexyl*)-1-*phenylazetidin*-2-*one* (36).—A mixture of the epoxide (34) (1.5 g, 6.17 mmol), methanol (50 ml), and conc. hydrochloric acid (5 ml) was heated under reflux for 2 h. The solvent was evaporated off *in vacuo* and the residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was recrystallised from methanol–ether to give the *azetidinone* (36) (1.3 g, 80%), m.p. 188—190 °C (Found: C, 64.45; H, 6.5; N, 5.05. $C_{15}H_{18}ClNO_2$ requires C, 64.4; H, 6.5; N, 5.0%); *m/e* 281 ($M^+ + 2$) and 279 (M^+).

3-(1-*Chloro*-2-*hydroxycycloheptyl*)-1-*phenylazetidin*-2-*one* (37).—A mixture of the epoxide (35) (1.5 g, 5.84 mmol), methanol (50 ml), and conc. hydrochloric acid (5 ml) was heated for 1.5 h and the mixture was worked up as above to yield the *azetidinone* (37) (1.28 g, 75%), m.p. 152—154 °C (from MeOH–Et_2O) (Found: C, 65.25; H, 6.8; N, 4.6. $C_{16}H_{20}ClNO_2$ requires C, 65.4; H, 6.85; N, 4.75%); *m/e* 295 ($M^+ + 2$) and 293.

Treatment of (36) *with Methanesulphonic Acid*.—A mixture of (36) (340 mg, 1.16 mmol), benzene (14 ml), and methanesulphonic acid (3.4 ml) was refluxed for 1.5 h. After removal of solvent, the mixture was made basic with 28% aqueous ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (2 g). Elution with chloroform–benzene (1 : 1) afforded the butenolide (39) (74 mg, 25%), which was identical spectroscopically with an authentic specimen. Elution with chloroform yielded 7,8,9,10-*tetrahydrobenzofuro*[3,2-c]*quinoline* (38) (103 mg, 38%), m.p. 112—113 °C (from MeOH–Et_2O) (Found: C, 80.6; H, 5.95; N, 6.1. $C_{15}H_{13}NO$ requires C, 80.7; H, 5.85; N, 6.25%); *m/e* 223 (M^+) and 195 ($M^+ - 28$); δ ($CDCl_3$) 1.82—2.16 (4 H, m), 2.70—2.92 (4 H, m), 7.52—7.77 (2 H, m), 8.10—8.25 (2 H, m), and 9.00 (1 H, s); ^{13}C n.m.r. δ ($CDCl_3$) 20.32, 22.37, 22.66, and 23.24 (each CH_2), 119.63, 126.26, 127.23, 129.48, and 143.36 (each aromatic CH), and 112.67, 117.00, 120.80, 145.22, 154.08, and 154.32 (each aromatic C) p.p.m.

Treatment of (37) *with Methanesulphonic Acid*.—A mixture of (37) (500 mg, 1.69 mmol), benzene (20 ml) and methanesulphonic acid (4.8 ml) was refluxed for 1.5 h and the mixture was worked up as above. The residue was chromatographed on silica gel (2.5 g). Elution with chloroform–benzene (1 : 1) gave the butenolide (41) (100 mg, 23%), which was identical spectroscopically with an authentic specimen. Elution with chloroform afforded the *tetrahydrocycloheptafuroquinoline* (40) (160 mg, 40%), m.p. 110—112 °C (from benzene–hexane) (Found: C, 81.25; H, 6.30; N, 6.10; M^+, 237.114. $C_{16}H_{15}NO$ requires C, 81.0; H, 6.35; N, 5.9%; M^+, 237.115); δ ($CDCl_3$) 1.13—2.02 (6 H, m), 2.51—3.13 (4 H, m), 7.48—7.65 (2 H, m), 8.08—8.25 (2 H, m), and 8.98 (1 H, s).

[9/1569 *Received*, 3*rd October*, 1979]

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