The Conversion of Phenols to Primary and Secondary Aromatic Amines *via* a Smiles Rearrangement

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The conversion of phenols to 2-aryloxy-2-methylpropanamides (**1**) and the Smiles rearrangement of these to *N*-aryl-2-hydroxy-2-methyl propanamides are described; hydrolysis of the latter compounds yields anilines. The scope and limitations of reaction are discussed. Routes, some involving α-lactams, from phenols to *N*-substituted derivatives of (**1**) have been developed. Under the conditions of the Smiles rearrangement these secondary 2-methylpropanamides can form *directly* anilides, *N*-alkylanilines, or benzoxazinones.

There are few general methods for the direct conversion of phenols to anilines. Transformations involving 4-chloro-2-phenylquinazoline[1–5] are limited to substrates resistant to high temperatures and basic conditions, while a more versatile route[6] *via* diethyl phosphate esters of phenols requires the use of toxic diethyl chlorophosphate and of potassium in liquid ammonia. The well known Bucherer reaction is restricted to naphthalenes and related heterocycles.

It has, however, been reported[7] that 2-aryloxy-2-methylpropanamides (**1**), on treatment with base, undergo a Smiles rearrangement to give *N*-aryl-2-hydroxy-2-methylpropanamides (**2**) which, after acid or base hydrolysis yield anilines (Scheme 1). For ethers (**1**) in which the aryl moiety contains

$$\underset{(1)}{ArOC(Me_2)CONH_2} \longrightarrow \underset{(2)}{ArNHCOC(Me_2)OH} \longrightarrow ArNH_2$$

Scheme 1.

electron-withdrawing subtituents, the rearrangement can be effected by sodium hydride in *N*,*N*-dimethylformamide (DMF), but for electron-donating substituents reactions have to be carried out in hexamethylphosphoric triamide (HMPA). This promising solution to the problem of phenol–aniline conversion appears to have been neglected, and we here report a study into the scope and limitations of the reaction. In the previous investigation[7] phenols were converted to ethers (**1**) *via* aryloxy-2-methylpropanoic acids prepared by reaction of the phenol with acetone, alkali, and chloroform. This, in our experience,[8] is an erratic procedure, and a simpler route to (**1**) was devised in which the sodium salt of the phenol was treated in dioxane with 2-bromo-2-methylpropanamide (**3**), readily obtained from commercially available 2-bromoisobutyryl bromide (2-bromo-7-methylpropanoyl bromide).

$$ArONa + \underset{(3)}{BrC(Me_2)CONH_2} \longrightarrow (1)$$

By this method were prepared in moderate to good yields (Table 1) the 2-methylpropanamides (**1a**)–(**1r**). As expected, there are steric constraints to this reaction, ethers (**1**) not being formed from 2,6-dimethyl-, -di-t-butyl-, or -diphenyl-phenols. The bromoamide (**3**) also did not react with the anions of 4-hydroxybenzaldehyde, methyl salicylate, methyl 4-hydroxybenzoate, or umbelliferone. In all these anions the negative charge is in conjugation with a carbonyl group, reducing the nucleophilicity of the intermediate, but the sodium salts of methyl 3-hydroxybenzoate and of dihydroumbelliferone, in which this conjugation is absent, reacted readily to give amides (**1k**) and (**1r**) respectively. A serious drawback to the original method was the use of the carcinogenic HMPA as a solvent for unreactive substrates. *N*,*N*′-Dimethyl-*N*,*N*′-propyleneurea [DMPU; 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one] has been advocated[9] as a non-toxic replacement for HMPA, and in initial experiments it was established that 2-methyl-2-phenoxypropanamide (**1a**) on treatment with sodium hydride in a 10% solution of DMPU in DMF rearranged smoothly and in high yield at 100 °C to *N*-phenyl-2-hydroxypropanamide (**2a**). These conditions were used in all subsequent rearrangement studies.

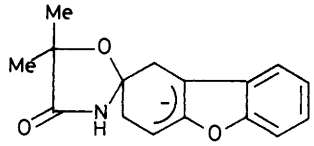
Generally, the rearrangement of aryloxyisobutyramides to anilides proceeded smoothly in satisfactory (60–98%) yields (see Table 1). However, from the reaction of the dihydroumbelliferone derivative (**1r**) with sodium hydride in DMF–DMPU a complex mixture was obtained. This is possibly due to abstraction of benzylic protons from (**1r**), or to attack by nucleophiles on the lactone carbonyl; the lower susceptibility of the aromatic ester (**1k**) to such side reactions might account

Table 1. Yields for the conversions:
$ArOH \longrightarrow \underset{(1)\text{ or }(15c,d)}{ArOC(Me_2)CONH_2} \longrightarrow \underset{(2)\text{ or }(15e,f)}{ArNHCOC(Me_2)OH}$

Ar	Compound	% Yield	Compound	% Yield
Ph	(**1a**)	67	(**2a**)	80
4-ClC_6H_4	(**1b**)	75	(**2b**)	98
4-$MeOC_6H_4$	(**1c**)	85	(**2c**)	68
4-PhC_6H_4	(**1d**)	98	(**2d**)	87
4-MeC_6H_4	(**1e**)	82	(**2e**)	72
2-$MeOC_6H_4$	(**1f**)	49	(**2f**)	31
2-FC_6H_4	(**1g**)	75	(**2g**)	62
2-ClC_6H_4	(**1h**)	69	(**2h**)	54
2-BrC_6H_4	(**1i**)	40	(**2i**)	96
2-IC_6H_4	(**1j**)	48	(**2j**)	87
3-$MeO_2CC_6H_4$	(**1k**)	63	(**2k**)	62
2-PhC_6H_4	(**1l**)	77	(**2l**)	45
1-Naphthyl	(**1m**)	98	(**2m**)	81
2-Naphthyl	(**1n**)	92	(**2n**)	93
5,6,7,8-Tetrahydro-2-naphthyl	(**1o**)	83	(**2o**)	81
8-Quinolyl	(**1p**)	31	(**2p**)	60
2-Dibenzofuryl	(**1q**)	45	(**2q**)	21
Dihydroumbelliferyl[a]	(**1r**)	51	(**2r**)	0
	(**15c**)	77	(**15e**)	94
	(**15d**)	88	(**15f**)	87

[a] Dihydroumbelliferyl = 3,4-dihydro-2-oxo-2*H*-1-benzopyran-7-yl.

for its successful conversion to (**2k**). Rearrangement of the dibenzofuran derivative (**1q**) proceeded extremely slowly and in poor (21%) yield. This may be attributed to steric strain in the Meisenheimer intermediate (**4**) and molecular modelling

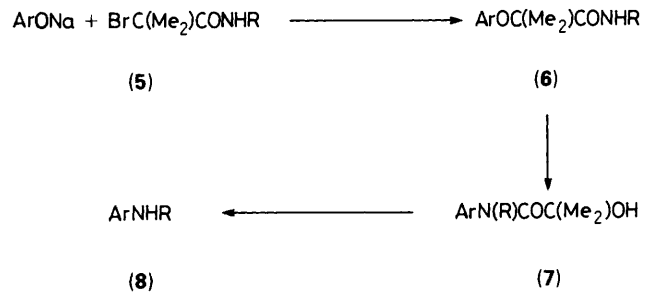


(**4**)

calculations tend to support this explanation; from an AMPAC computation the heat of formation of (**4**) was higher (3.7 kJ mol^{-1}) than that of the corresponding structure without the carbon–carbon aryl bond.

In striking contrast to the sluggish reaction of (**1q**), the Smiles rearrangement of the related amide (**1l**) which lacks a constraining furan ring proceeded rapidly in neat DMF, perhaps another example of the steric acceleration of Smiles rearrangement noted previously by Bunnett and Okamoto.[10]

Conversion of Phenols to N-*Substituted Anilides.*—A recent paper[11] emphasises the problems of preparing *N*-alkylanilines, and the prospect of preparing such compounds from phenol precursors by an extension of the above methodology is appealing. The obvious route is shown in Scheme 2, but

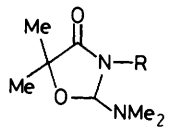


Scheme 2.

unexpected difficulties were encountered in the preparation of (**6b**)–(**6f**) (Table 2) by the reaction of appropriate phenols and bromoamides (**5b**)–(**5f**) with sodium hydride in dioxane. Product yields were low, and reaction was incomplete even after prolonged periods. It was initially suspected that this might be due to the low solubility of some of the sodium phenolates in dioxane, but substitution of this solvent by tetrahydrofuran, diglyme, or even DMPU gave no improvement.

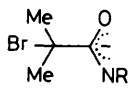
From the reaction of the *N*-phenylbromisobutyramides (**5i**) and (**5j**) with sodium phenolate in DMF, the sole products isolated were the oxazolidinones (**9**). Such compounds have been described by D'Angeli and co-workers,[12] and are thought to arise from addition of ions (**10**) or derived aziridinones (**11**) to DMF; this led us to suspect that formation of (**11**) might be a competing process in Scheme 2. Aziridinones are reported[13–15] to undergo cleavage of the acyl–nitrogen bond exclusively upon treatment with ionic, aprotic nucleophiles (salts) and predominant cleavage of the alkyl–nitrogen bond by non-ionic, protic nucleophiles. Although such a simple explanation of selectivity in ring-opening reactions of aziridinones has been recently challenged,[16] it was decided to determine whether phenoxyisobutyramides (**6**) might be more efficiently obtained by the reaction of phenols on preformed α-lactams.

Treatment of bromoamides (**5f**) and (**5g**) with sodium hydride in THF gave stable α-lactams (**11a**) and (**11b**) respectively, which reacted with phenol to form phenoxyamides (**6i**) and (**6j**). In an extension of this method, sodium hydride

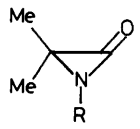


(**9**)

a; R = Ph
b; R = 4-$MeOC_6H_4$

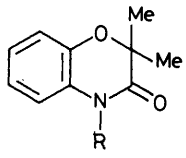


(**10**)



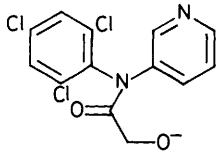
(**11**)

a; R = 1-adamantyl
b; R = Bu^t

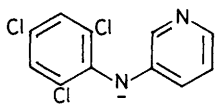


(**12**)

a; R = Me
b; R = 1-adamantyl



(**13**)



(**14**)

was added to THF solutions of bromoamides (**5**) at −20 to −40 °C, the formation of the α-lactam being followed by TLC and IR spectroscopy; subsequent addition of the appropriate phenol gave amides (**6**) in good to high yields. Phenols with bulky substituents in the 2- and 6-position gave no product with α-lactams, but 2,6-dimethylphenol formed (**6l**).

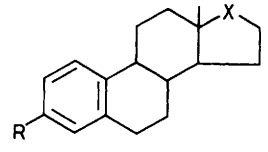
The preparation of an aziridinone from *N*-neopentyliso-butyramide (**5a**) presented unexpected difficulties, as the compound was totally inert towards sodium hydride. Significantly the amide (**5a**) reacted virtually quantitatively with sodium phenoxide in dioxane to afford (**6a**), which again suggests that α-lactam formation is a complication of Scheme 2. A third route to amides (**6**) is an extension of the previously described[7] synthesis of primary isobutyramides in which phenols are converted to intermediate aryloxyisobutyric acids; by this method were obtained (**6p**) and (**6q**).

Predictably the rearrangement of (**6**) to (**7**) is strongly influenced by steric factors (see Table 2). Treatment of the *N*-arylamides (**6b**) and (**6p**) with sodium hydride in DMF–DMPU gave the anilides (**7a**) and (**7b**) but the amides (**6i**)–(**6l**), all with bulky substituents, were recovered unchanged. The failure of the amide (**6a**) to react may be due to resistance to proton abstraction rather than to steric crowding during rearrangement. Although 2-halogenophenoxybutyramides (**1g**)–(**1j**) had rearranged to the expected anilides, it was expected that in the *N*-substituted amides such as (**6h**), the greater steric restraints to formation of a spiro-Meisenheimer intermediate might lead to alternative attack at the halogenated position of the aromatic ring, yielding benzoxazinones (**12**). Indeed, treatment in DMF–DMPU with sodium hydride of the amides (**6m**) and (**6n**) gave (**12a**), while the amide (**6o**) afforded (**12b**), the reactions being almost quantitative. This novel preparation of (**12**) compares favourably in ease and yield with methods previously reported.[17]

Table 2. Products from the rearrangement of (6).

(5) RNHCOCMe$_2$Br	R	Ar	(6) RNHCOCMe$_2$OAr	Product from (6) + NaH–DMPU–DMF (% yield) (7) Anilide	(8) Aniline	(12) Benzoxazinone
(5a)	$CH_2Bu^t_3$	Ph	(6a)	—	—	—
(5b)	3,5-$(CF_3)_2C_6H_3$	4-PHC_6H_4	(6b)	(7a) (56)	—	—
(5c)	Me	4-ClC_6H_4	(6c)	—	(8a) (96)	—
(5d)	CH_2Ph	4-ClC_6H_4	(6d)	—	(8b) (55)	—
(5c)	Me	4-PhC_6H_4	(6e)	—	(8c) (91)	—
(5d)	CH_2Ph	4-PhC_6H_4	(6f)	—	(8d) (88)	—
(5c)	Me	Ph	(6g)	—	(8e) (55)	—
(5e)	Et	Ph	(6h)	—	(8f) (46)	—
(5f)	1-Adamantyl	Ph	(6i)	—	—	—
(5g)	Bu^t	Ph	(6j)	—	—	—
(5h)	C_6H_{11}	Ph	(6k)	—	—	—
(5c)	Me	2,6-$Me_2C_6H_3$	(6l)	—	—	—
(5c)	Me	2-ClC_6H_4	(6m)	—	—	(12a) (98)
(5c)	Me	2-IC_6H_4	(6n)	—	—	(12a) (98)
(5f)	1-Adamantyl	2-FC_6H_4	(6o)	—	—	(12b) (98)
(5i)	Ph	Ph	(6p)	(7b) (31)	—	—
(5d)	CH_2Ph	Ph	(6q)	—	(8g) (94)	—
(5j)	4-$MeOC_6H_4$	—	—	—	—	—

The most interesting results come from the rearrangements of the *N*-alkyl-amides (**6c**)–(**6h**), and (**6q**). The products obtained in 46–98% yield were not the anilides (**7**), but the corresponding *N*-alkyl-anilines (**8**). This is an unexpected finding, as anilides (**7**) are usually cleaved only by heating with moderate alkali or strong acids. It has recently been reported[18] that the Smiles rearrangement of 3-(2,4,6-trichlorophenoxyacetamido)pyridine to (**13**) is followed by alkaline hydrolysis to the resonance-stabilised anion (**14**). However, in our study, it is the aromatic anilides (**7a**) and (**7b**) which are isolated uncleaved. Whatever the mechanism, this serendipitous reaction provides under moderately mild conditions a smooth transformation of phenols to *N*-alkylanilines. Since the alkyl group may be benzyl, it also allows access by standard deblocking procedures to primary arylamines. A limited investigation into the application to more complex molecules of the phenol–aniline conversion has been carried out. Both estrone (**15a**) and estradiol (**15b**) were transformed *via* aryloxyamides (**15c**) and



(**15**)

a, R = OH, X = CO; **b**, R = OH, X = CHOH; **c**, R = $OCMe_2CONH_2$, X = CO; **d**, R = $OCMe_2CONH_2$, X = CHOH; **e**, R = $NHCOCMe_2OH$, X = CO; **f**, R = $NHCOCMe_2OH$, X = CHOH; **g**, R = $OCMe_2CONHMe$, X = CHOH; **h**, R = NHMe, X = CHOH.

(**15d**) to anilides (**15e**) and (**15f**). Estradiol also reacted with *N*-methylisobutyramide (**5c**) to give (**15g**) which again rearranged in good yield to the aniline (**15h**). Estrone, by the α-lactam method, can be converted to the amide (**15i**), but this gave complex mixtures on attempted rearrangement.

Experimental

IR spectra were recorded using a Perkin-Elmer 683 grating spectrophotometer. ^{1}H NMR spectroscopy was performed using a Hitchi–Perkin-Elmer R24B 60 MHz spectrometer with tetramethylsilane as the internal standard. ^{13}C NMR spectra were recorded on a JEOL JNM FX60Q 60 MHz Fourier transform spectrometer. Elemental analyses were determined by the analytical sections of either ICI Pharmaceuticals Division or Nottingham University. M.p.s were measured using open capilliaries in a Gallenkamp apparatus and are not corrected. THF was dried over calcium hydride, and other solvents using 5 Å molecular sieves. Light petroleum has b.p. 60–80 °C unless otherwise stated.

2-Bromo-2-methylpropanamide (**3**).—To a vigorously stirred solution of 2-bromo-2-methylpropanoyl bromide (11 ml) in light petroleum (250 ml) at 0 °C was added in portions aqueous ammonia (*d* 0.88; 40 ml). Stirring was continued for a further 30 min, and the resulting precipitate collected and washed using water to give the bromoamide, m.p. 147–148 °C (from chloroform–light petroleum) (lit.,[19] 147–148 °C).

General Preparation of Aryloxyamides (**1**), (**15c**), *and* (**15d**).—The appropriate phenol (2 g) was stirred in dry dioxane (20 ml) with sodium hydride (1.1 mol equiv.) for 1 h. 2-Bromo-2-methylpropanamide (1.0 mol equiv.) was added and the reaction mixture was heated at 100 °C for 4 h. After cooling, the precipitated sodium bromide was filtered off, the filtrate evaporated under reduced pressure, and the residual solid triturated with dilute base and recrystallised from toluene to give compounds (**1**), (**15c**), and (**15d**). Analytical data are in Table 3.

Smiles Rearrangement of Aryloxyamides (**1**).—To a solution of the aryloxyamide (1 g) in dry DMPU (1 ml) and dry DMF (10 ml) was added sodium hydride (1.1 mol equiv.) and the mixture was heated on a steam-bath for 1 h. The solution was poured into water (400 ml) and extracted with ethyl acetate (400 ml); the organic layer was washed with water (3 × 500 ml), dried ($MgSO_4$), and evaporated. The residue was purified by distillation or by crystallisation from cyclohexane or toluene to give compounds (**2**), (**15e**), or (**15f**). Analytical data are in Table 3.

Table 3. Analytical data for compounds (1), (2), and (15).

Compound	M.p. *t*/°C	Molecular formula	Found, %			Required, %			Found, %			Compound	M.p. or b.p., *t*/°C (*p*/mmHg)
			C	H	N	C	H	N	C	H	N		
(**1d**)	183–185	$C_{16}H_{17}NO_2$	75.3	7.0	5.4	75.3	6.7	5.5	74.9	6.7	5.4	(**2d**)	167–168
(**1e**)	147–148	$C_{11}H_{15}NO_2$	68.8	8.0	7.2	68.4	7.8	7.2	68.5	8.4	6.9	(**2e**)	82–84
(**1f**)	133–134	$C_{11}H_{15}NO_3$	63.3	7.4	6.5	63.1	7.2	6.7	62.9	7.3	6.4	(**2f**)	143–144
(**1g**)	93–94	$C_{10}H_{12}FNO_2$	61.2	5.9	7.2	60.9	6.1	7.1	61.0	6.0	7.0	(**2g**)	140 (0.02)
(**1h**)	89–90	$C_{10}H_{12}ClNO_2$	56.2	5.8	6.3	56.2	5.7	6.5	56.5	5.2	6.6	(**2h**)	161 (0.6)
(**1i**)	78–80	$C_{10}H_{12}BrNO_2$	46.6	4.8	5.5	46.5	4.6	5.4	46.8	5.1	5.7	(**2i**)	150 (0.3)
(**1j**)	101–102	$C_{10}H_{12}INO_2$	39.4	4.2	4.7	39.3	3.9	4.6	39.6	4.4	4.4	(**2j**)	174 (0.2)
(**1k**)	142–143	$C_{12}H_{15}NO_4$	60.9	6.4	5.9	60.8	6.3	5.9	60.9	6.4	5.7	(**2k**)	124–125
(**1l**)	96–97	$C_{16}H_{17}NO_2$	75.0	7.0	5.5	75.3	6.7	5.5	75.5	6.8	5.5	(**2l**)	148–149
(**1m**)	119–120	$C_{14}H_{15}NO_2$	73.8	6.6	5.9	73.3	6.6	6.1	73.7	6.8	6.1	(**2m**)	161–162
(**1n**)	118–119	$C_{14}H_{15}NO_2$	73.2	6.7	6.0	73.3	6.6	6.1	73.2	6.6	6.0	(**2n**)	159–160
(**1o**)	113–114	$C_{14}H_{19}NO_2$	72.2	8.4	5.9	72.1	8.2	6.0	71.9	8.2	5.6	(**2o**)	97–98
(**1p**)	178–179	$C_{13}H_{14}N_2O_2$	67.8	6.0	12.0	67.8	6.1	12.2	68.2	6.2	11.9	(**2p**)	123–124
(**1q**)	154–155	$C_{16}H_{15}NO_3$	71.4	5.7	4.8	71.4	5.6	5.2	71.1	5.7	5.2	(**2q**)	165–166
(**1r**)	153–154	$C_{13}H_{15}NO_4$	62.3	6.1	5.8	62.6	6.1	5.6					
(**15c**)	167–168[a]	$C_{22}H_{29}NO_3$	73.9	8.2	3.6	74.3	8.2	3.9	74.0	8.1	3.2	(**15e**)	133–134[c]
(**15d**)	198–200[b]	$C_{22}H_{31}NO_3$	74.4	8.2	3.4	74.1	8.5	3.9	73.9	8.8	3.8	(**15f**)	203–204[b]

[a] From EtOH. [b] From EtOH–cyclohexane. [c] From cyclohexane–Et_2O.

Amides (**1a**)–(**1c**) and (**2a**)–(**2c**) have previously been described.[7]

In the mass spectra (EI) of new compounds, parent ions corresponded to the calculated M_r value.

Preparation of the Bromoamides (**5**).—Compounds (**5**) were synthesised by the reaction of 2-bromo-2-methylpropanoyl bromide with the appropriate amine under standard Schotten–Baumann conditions. By this method were made the known compounds (**5c**), m.p. 59–60 °C (lit.,[20] 58–60 °C); (**5d**), m.p. 71–73 °C (lit.,[21] 71 °C); (**5e**), m.p. 57–59 °C (lit.,[20] 57–58 °C); (**5f**), m.p. 77–79 °C (lit.,[20] 77 °C); (**5g**), m.p. 84–86 °C (lit.,[21] 84–86 °C); (**5h**), m.p. 107–108 °C (lit.,[22] 108–109 °C); (**5i**), m.p. 83–84 °C (lit.,[19] 83 °C), and the new *amides* (**5a**), m.p. 91–92 °C (from light petroleum) (Found: C, 45.7; H, 7.8; N, 5.9. $C_9H_{18}BrNO$ requires C, 45.7; H, 7.6; N, 5.9%); (**5b**), m.p. 122–123 °C (from cyclohexane) (Found: C, 38.5; H, 2.6; N, 3.7. $C_{12}H_{10}BrF_6NO$ requires C, 38.1; H, 2.6; N, 3.7%); (**5j**), m.p. 87–88 °C (from cyclohexane) (Found: C, 48.2; H, 5.2; N, 5.1. $C_{11}H_{14}BrNO_2$ requires C, 48.5; H, 5.1; N, 5.1%).

N-*Substituted-2-aryloxy-2-methylpropanamides* (**6**), (**15g**), *and* (**15i**).—*Method A.* This involved heating the bromoamide (**5**) with the sodium salt of a phenol in dry dioxane, as described for the formation of (**1**).

Method B. This involved formation of an α-lactam intermediate. To the amide (**5**) (5 g) in dry THF (50 ml) at a controlled temperature (given in parentheses in Table 4) was added sodium hydride (1 mol equiv.) and the mixture was stirred. At regular intervals, aliquots were removed and examined by liquid cell IR spectroscopy and by TLC. When conversion of (**5**) to the α-lactam [ν(C=O) 1 830–1 840 cm^{-1}] was complete, the appropriate phenol (1 mol equiv.) was added, and stirring was continued for 4 h at the temperature of α-lactam formation. The solution was allowed to reach room temperature, the solvent removed, and the residue purified by crystallisation or distillation.

Method C. 2-Methyl-2-phenoxypropanoic acid was treated with thionyl chloride and amine as previously described.[7] For (**6q**) the acid in methylene chloride was condensed with benzylamine in the presence of dicyclohexylcarbodiimide.

Preparation of Oxazolidinones (**9**).—Equimolar quantities of *N*-phenyl-2-bromo-2-methylpropanamide and sodium hydride were heated in dry DMF at 100 °C for 1 h. The solvent was removed under reduced pressure, and the residue triturated with dilute sodium hydroxide and recrystallised from hexane to give the oxazolidinone (**9a**), m.p. 100–101 °C (lit.,[23] 101–102 °C). From a similar reaction with the bromoamide (**5j**) was obtained 3-(4-*methoxyphenyl*)-5,5-*dimethyl*-2-*dimethylamino oxazolidin*-4-*one* (**9b**), m.p. 89–90 °C (from hexane) (Found: C, 64.0; H, 7.7; N, 10.3. $C_{14}H_{20}N_2O_3$ requires C, 63.6; H, 7.6; N, 10.6%); ν_{max}(KBr) 1 700 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 6.8–7.4 (4 H, A_2B_2, ArH), 6.05 (1 H, s, CH), 3.8 (3 H, s, OMe), 2.4 (6 H, s, C–CH_3), and 1.5–1.6 (6 H, d, N–CH_3).

Novel Products from the Rearrangement of N-*Substituted*-2-*Aryloxy*-2-*methylpropanamides.*—The *anilide* (**7a**) had m.p. 141–142 °C (from cyclohexane) (Found: C, 61.6; H, 4.2; N, 3.0. $C_{24}H_{18}F_6NO_2$ requires C, 61.7; H, 4.0; N, 3.0%); ν_{max}(KBr) 3 260 and 1 680 cm^{-1}. The *anilide* had m.p. 102–103 °C (from cyclohexane) (Found: C, 75.6; H, 6.7; N, 5.4. $C_{16}H_{17}NO_2$ requires C, 75.3; H, 6.7; N, 5.4%); ν_{max}(KBr) 3 260 and 1 670 cm^{-1}. 3-*Desoxy*-3-*methylamino*-β-*estradiol hydrochloride* (**15h**) (60% yield) had m.p. 258–260 °C (from EtOH–H_2O) (Found: C, 70.7; H, 8.9; N, 4.2. $C_{19}H_{27}ClNO$ requires C, 71.1; H, 8.4; N, 4.4%).

All other *N*-alkylanilines obtained from the rearrangement of (**6**) had m.p. or b.p. and IR and NMR spectra in agreement with those of authentic compounds.

Preparation of the Benzoxazinones (**12**).—Standard treatment with sodium hydride in DMF–DMPU of the amides (**6m**) or (**6n**) gave 2,2,4-*trimethyl*-2H-1,4-*benzoxazin*-3(4H)-*one* (**12a**) (98% yield), b.p. 110 °C at 0.5 mmHg (Found: C, 69.2; H, 6.6; N, 6.8. $C_{11}H_{13}NO_2$ requires C, 69.1; H, 6.8; N, 7.2%); ν_{max}(KBr) 1 670 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 7.0 (4 H, s, Ar), 3.3 (3 H, s, CH_3–N), and 1.5 (6 H, s, CH_3–C); $\delta_C(CDCl_3)$, 23.9 (CH_3–C–), 28.6 (CH_3–N), 77.9 (*C*–Me_2), 114.1, 117.5, 122.2, 123.7 (ArC–H), 130.1 (ArC–N), 143.5 (ArC–O), and 169.0 (C=O). From the amide (**6o**) was obtained 4-*adamantyl*-2,2-*dimethyl*-2H-1,4-*benzoxazin*-3(4H)-*one* (**12b**) (98%), b.p. 180 °C at 0.2 mmHg (Found: C, 76.9; H, 8.3; N, 4.3. $C_{20}H_{25}NO_2$ requires C, 77.2, H, 8.0; N, 4.5%); ν_{max}(film) 1 680 cm^{-1}.

Table 4. *N*-Substituted-2-aryloxy-2-methylpropanamides.

Compound	Method	% Yield	M.p. or b.p. [*t*/°C (*p*/mmHg)]	Molecular formula	Found, %			Required, %		
					C	H	N	C	H	N
(6a)	A	90	86–87[a]	$C_{15}H_{23}NO_2$	72.5	9.5	5.6	72.3	9.2	5.6
(6b)	A	66	138–139[a]	$C_{24}H_{19}F_6NO_2$	61.6	4.2	2.9	61.7	4.1	3.0
(6c)	A	50	63–64[b]	$C_{11}H_{14}ClNO_2$	58.0	6.2	6.0	58.0	6.1	6.1
(6d)	A	49	38–39[b]	$C_{17}H_{18}ClNO_2$	72.9	5.8	4.2	73.3	5.9	4.6
(6e)	A	17	160–161[c]	$C_{17}H_{19}NO_2$	75.5	7.0	5.0	75.8	7.0	5.0
(6f)	A	51	106–107[a]	$C_{23}H_{23}NO_2$	80.3	6.7	4.0	80.0	6.7	4.1
(6g)	B (−40)	96	150 (0.3)	$C_{11}H_{13}NO_2$	68.3	8.3	7.2	68.4	7.8	7.2
(6h)	B (−40)	84	160 (0.2)	$C_{12}H_{17}NO_2$	69.2	8.1	6.4	69.6	8.2	6.8
(6i)	B (10)	51	80–81[b]	$C_{20}H_{28}NO_2$	76.4	8.5	3.9	76.4	8.9	4.4
(6j)	B (10)	90	150 (0.1)	$C_{14}H_{21}NO_2$	71.7	9.5	5.9	71.5	8.9	5.9
(6k)	B (−20)	55	95–96[b]	$C_{16}H_{23}NO_2$	73.9	8.6	5.3	73.6	8.8	5.4
(6l)	B (−40)	54	115–116[a]	$C_{13}H_{19}NO_2$	70.7	8.5	6.2	70.6	8.6	6.3
(6m)	B (−40)	84	135 (0.3)	$C_{11}H_{14}ClNO_2$	58.0	6.2	6.2	58.2	6.3	6.1
(6n)	B (−40)	92	180 (0.2)	$C_{11}H_{14}INO_2$	42.0	4.6	4.3	41.4	4.4	4.4
(6o)	B (10)	81	180 (0.2)	$C_{21}H_{30}NO_3$	74.0	8.0	3.6	74.1	8.4	3.9
(6p)	C	53	154 (0.3)	$C_{16}H_{17}NO_2$	75.5	6.0	5.9	75.3	6.7	5.5
(6q)	C	94	150 (0.5)	$C_{17}H_{19}NO_2$	75.6	7.6	5.7	75.8	7.2	5.3
(15g)	A	88	139–140[d]	$C_{23}H_{33}NO_3$	74.3	9.0	3.7	74.6	8.6	3.8
(15i)	B (−40)	82	95–96	$C_{23}H_{31}NO_3$	74.4	8.6	3.8	74.8	8.5	3.8

[a] From cyclohexane. [b] From hexane. [c] From EtOAc. [d] From Et_2O–cyclohexane.

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