2,3-Dihydroquinolin-4(1*H*)-ones. Part I. Halogen-substituted 2,3-Dihydroquinolin-4(1*H*)-ones and their 1-(2-Acylethyl) Derivatives

By **G. Bradley** and **Jim Clark,*** Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT
W. Kernick, Department of Chemistry, Flintshire College of Technology, Connah's Quay, Flintshire

Synthesis of five 6- or 8-halogen-substituted 2,3-dihydroquinolin-4(1*H*)-ones and their 1-acetyl derivatives are described. The 6-substituted compounds reacted with suitable Mannich bases to yield 1-(2-arenoylethyl) derivatives but 8-substituted compounds were unchanged under the same conditions. ^{1}H N.m.r. and u.v. spectra of some of the compounds are recorded.

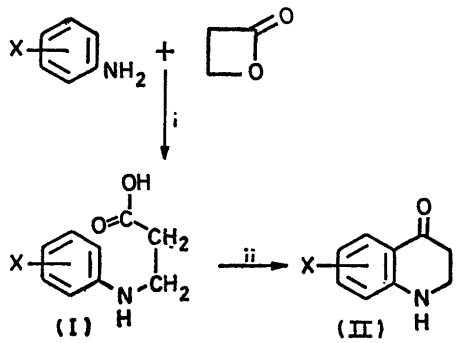
SEVERAL derivatives of 2,3-dihydroquinolin-4-one have been shown to possess analgesic activity,[1] and Mannich bases derived from this system have been described as having central nervous system depressant, antipyretic, and anti-inflammatory activity.[2] We now describe the synthesis of halogenated derivatives (II; X = Hal) of 2,3-dihydroquinolin-4-one, some of which have been converted into corresponding 1-(2-acylethyl) compounds (V).

The route used to prepare 6- and 8-halogen-substituted tetrahydro-oxoquinolines (II) involved the reaction of a 2- or 4-substituted aniline with β-propiolactone in refluxing acetonitrile [1] to give a 3-(substituted anilino)propionic acid (I) (Table 1) which was cyclised in polyphosphoric acid (Scheme). The temperature of cyclisation (Table 2) was more critical than is apparent from the literature,[1,3,4] control to within ±5° of the optimum being desirable to avoid formation of tarry by-products.

3-(4-Fluoroanilino)propionic acid (I; X = 4-F) was also cyclised as its readily crystallised *p*-tolylsulphonyl derivative in polyphosphoric acid under the conditions described by Collins [5] for the corresponding anilino-compound. The tosyl group was removed during

[1] M. S. Atwal, L. Bauer, S. N. Dixit, J. E. Gearien, and R. W. Morris, *J. Medicin. Chem.*, 1965, **8**, 566.
[2] J. W. Bolger, U.S.P. 3,287,450/1966.
[3] J. Koo, *J. Org. Chem.*, 1961, **26**, 2440.
[4] J. Koo, *J. Org. Chem.*, 1963, **28**, 1134.
[5] R. F. Collins, *J. Chem. Soc.*, 1960, 2053.

cyclisation to give the quinolone (II; X = 6-F). *N*-(4-Fluorophenyl)-3-hydroxypropionamide (III) and



SCHEME Reagents: i, MeCN (reflux); ii, polyphosphoric acid

3,3′-(4-chlorophenylimino)dipropionic acid (IV) were by-products isolated during preparations of the corresponding anilinopropionic acids (I; X = 4-F or 4-Cl).

crystallisation, from the aqueous solution resulting from the acid hydrolysis of the Girard P derivatives, into 2,3-dihydroquinolin-4(1*H*)-one (II; X = H) and 2,3-dihydro-6-iodoquinolin-4(1*H*)-one (II; X = 6-I). The latter was presumably formed by iodination of the former by iodine produced by deiodination of the iodoanilinopropionic acid (I; X = 2-I) or the 8-iodoquinoline (II; X = 8-I). Iodination of the quinolinone (II; X = H) with iodine monochloride gave the 6-iodo-derivative (II; X = 6-I), identical with the specimen already described. The position of substitution was established by ^{1}H n.m.r. spectrometry (Table 3). The oxoquinolines were characterised as 1-acetyl derivatives (Table 6).

Alkylation of 2,3-dihydroquinolin-4-ones under conventional conditions of alkyl halide and base proceeds with difficulty.[1,5] However the 6-substituted quinolinones (II) reacted readily with Mannich bases ($ArCO{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_2$), derived from aryl ketones to yield 1-(2-arenoylethyl) derivatives (V) (Table 4). In

TABLE 1

3-Anilinopropionic acids (I)

X	Crude yield (%)	M.p. (°C)	Recryst. solvent	Found (%) C	H	N	X	Required (%) C	H	N	X
2-F	49 *	100·5—101·5	EtOAc–LP	58·7	5·5	7·7	10·0	59·0	5·5	7·7	10·4
2-Br	64	152·5—153	MeCN	44·2	4·5	5·7	32·9	44·3	4·1	5·7	32·7
2-I	66	156—157	MeCN	37·4	3·2	5·1	44·2	37·1	3·5	4·8	43·6
4-F	89	77·5—78·5 †	C_6H_6–LP	58·8	5·8	7·6	9·9	59·0	5·5	7·6	10·4

LP = Light petroleum (b.p. 60—80°).

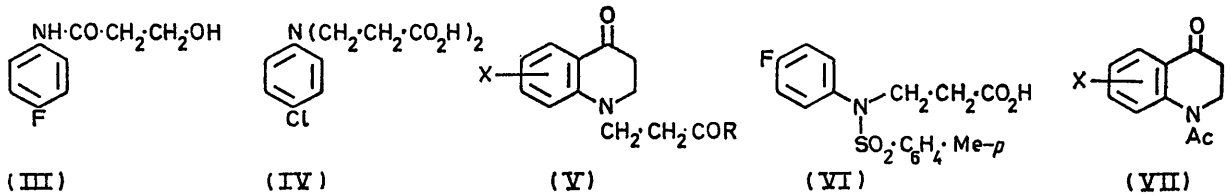
* Once crystallised. † Purified by column chromatography on silica gel and recrystallised twice from benzene–light petroleum (b.p. 60—80°).

TABLE 2

Halogen-substituted 2,3-dihydroquinolin-4(1*H*)-ones (II)

X	Reaction temp.	Reaction time (min)	Crude (yield %)	M.p. (°C)	$\lambda_{max.}$ (MeOH) nm (log ε)	Found (%) C	H	N	X	Required (%) C	H	N	X
6-F	120 ± 5°	60	31 [a]	72—73 [b]	234(4·19), 257(3·78), 391(3·64)	65·1	4·9	8·7	11·5	65·4	4·9	8·5	11·5
6-I			90 [c]	152—153	238·5(4·43), 265(3·48), 390(3·53)	39·4	3·0	4·8		39·6	2·95	5·0	
8-F	130 ± 5	30	100	128—129 [d]	230·5(4·29), 251·5(3·79), 372(3·57)	65·3	4·9	8·4	11·7	65·4	4·9	8·5	11·5
8-Br	125 ± 1	80	100	50—56 [e]	235·5, 257infl, 377								

[a] Prepared from crude 3-(4-fluoroanilino)propionic acid (I; X = 4-F). [b] Sublimed at 60° and 0·1 mmHg. [c] Crude yield from iodoination of 2,3-dihydroquinolin-4(1*H*)-one with iodine monochloride. [d] Recrystallised from benzene. [e] This compound was not obtained analytically pure and was characterised as its 1-acetyl derivative (Table 6).



All attempts to cyclise the 2-iodoanilinopropionic acid (I; X = 2-I) in polyphosphoric acid resulted in loss of elemental iodine and production of little ketonic material. Attempted cyclisations in poly(ethyl phosphate) [6] gave similar results. The ketonic material from one reaction in polyphosphoric acid was separated, by fractional

the case of 8-substituted quinolinones (II) no reaction with Mannich bases occurred and the latter decomposed to give complex products while the quinolines were recovered unchanged. Failure of these reactions was attributed to steric hindrance by the 8-substituent.

[6] K. Langheld, *Ber.*, 1910, **43**, 1857.

TABLE 3

^{1}H N.m.r. spectra (60 MHz; τ values) of 2,3-dihydroquinolin-4(1*H*)-ones (II) [a] (*J* in Hz)

X	1-H	2-H	3-H	5-H	6-H	7-H	8-H
H	5·45br	6·45 (t, $J_{2,3}$ 7)	7·35 (t, $J_{2,3}$ 7)	2·17 (m)	3·30 (2H, m)		2·75 (m)
6-F	5·40br	6·42 (t, $J_{2,3}$ 7)	7·32 (t, $J_{2,3}$ 7)	2·50 (dd,[b] $J_{5,7}$ 3, J_{HF} 9)	2·92 (m)		3·32 (dd, $J_{7,8}$ 9, J_{HF} 4·3)
6-Cl	5·12br	6·43br (t, $J_{2,3}$ 7) [c]	7·35 (t, $J_{2,3}$ 7)	2·27 (d, $J_{5,7}$ 2·7)	2·71 (dd, $J_{5,7}$ 2·7, $J_{7,8}$ 8·8)		3·37 (d, $J_{7,8}$ 8·8)
6-I	5·60br	6·36br (t, $J_{2,3}$ 7·2) [c]	7·30 (t, $J_{2,3}$ 7·2)	1·79 (d, $J_{5,7}$ 2)	2·40 (dd,[b] $J_{5,7}$ 2, $J_{7,8}$ 8·5)		3·44 (d, $J_{7,8}$ 8·5)
8-F	5·20br	6·35 (dt,[d] $J_{1,2}$ 2, $J_{2,3}$ 7·2) [c]	7·28 (t, $J_{2,3}$ 7)	2·35br (d, $J_{5,6}$ 8) [f]	3·38 (dt, $J_{5,6}$ = $J_{6,7}$ = 8 J_{HF} 5)	2·88 (m)	
8-Cl	4·9br	6·34br (t, $J_{2,3}$ 7) [c]	7·32 (t, $J_{2,3}$ 7)	2·21 (dd, $J_{5,6}$ 8, $J_{5,7}$ 1·5)	3·37 (t, $J_{5,6}$ = $J_{6,7}$ = 8)	2·62 (dd, $J_{5,7}$ 1·5, $J_{6,7}$ 8)	
8-Br	4·9br	6·35 (dt, $J_{1,2}$ 2, $J_{2,3}$ 7) [c]	7·31 (t, $J_{2,3}$ 7)	2·17 (dd, $J_{5,6}$ 8, $J_{5,7}$ 1·5)	3·41 (t, $J_{5,6}$ = $J_{6,7}$ = 8)	2·45 (dd, $J_{5,7}$ 1·5, $J_{6,7}$ 8)	

[a] Determined on Varian A60A equipment at 37°. Compounds were in [^{2}H]chloroform solution with tetramethylsilane (TMS) as internal standard; in all spectra the width at half-height ($W_{\frac{1}{2}}$) of the TMS resonance was approximately 1 Hz. [b] dd = Two doublets. [c] Broadening ($W_{\frac{1}{2}}$ *ca.* 3 Hz) due to coupling with the 1-proton, reduced on deuteriation to *ca.* 1·5 Hz. [d] dt = Two triplets. [e] Coupling with 1-proton no longer resolved after deuteriation. [f] Coupling with 8-F not resolved.

TABLE 4

1-(2-Acylethyl)-2,3-dihydroquinolin-4(1*H*)-ones (V)

X	R	Reaction time (h)	Yield (%) *	M.p. (°C)	Recryst. solvent	$\lambda_{max.}$ (MeOH)/nm (log ε)	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
H	Ph	20	55	84—86	MeOH	240·5(4·47), 261infl (4·02), 385(3·70)	77·2	6·0	4·9		77·4	6·1	5·0	
H	4-FC_6H_4	20	64	111—112	IPA †	241(4·47), 261infl (4·06), 385(3·72)	72·8	5·4	4·9		72·7	5·4	4·7	
H	4-PhC_6H_4	16	53	101·5—105·5	IPA	239·5(4·39), 272·5(4·38), 282·5(4·37), 385(3·70)	81·0	5·9	3·8		81·1	6·0	3·9	
H	4-MeO·C_6H_4	40	61	127·5—129·5	IPA	240(4·39), 269·5(4·36), 387(3·72)	73·9	6·3	4·5		73·8	6·2	4·5	
H	4-NO_2·C_6H_4	8	76 ‡	147—150	IPA–$CHCl_3$ then BunOH	240(4·43), 264(4·35), 385(3·72)	66·7	5·0	8·6		66·7	5·0	8·6	
H	2-C_4H_3S	21	64	95·5—97	IPA	240(4·40), 262(4·22), 284infl (3·92), 385(3·70)	67·3	5·4	5·0		67·3	5·3	4·9	
Cl	Ph	16½	68	97—98	IPA	240·5(4·51), 271(4·10), 399(3·65)	68·8	5·1	4·7	11·5	68·9	5·1	4·5	11·3
Cl	4-FC_6H_4	8	71	132—133	IPA	242(4·50), 270·5(4·13), 400(3·66)	64·9	4·5	4·3	10·6	65·2	4·6	4·2	10·7
Cl	4-PhC_6H_4	5½	61	111·5—112·5	IPA–$CHCl_3$	239·5(4·41), 274·5(4·50), 398(3·69)	74·0	5·0	3·4	9·6	73·9	5·2	3·6	9·1
Cl	4-MeO·C_6H_4	11½	80	110·5—111·5	IPA	240(4·39), 272(4·44), 397(3·67)	66·7	5·1	3·9	10·4	66·4	5·3	4·1	10·3
Cl	4-NO_2·C_6H_4	1	88 ‡	148—151·5	MeOH–$CHCl_3$	240·5(4·43), 268·5(4·37), 396(3·66)	60·3	4·1	7·6	10·0	60·25	4·2	7·8	9·9
Cl	2-C_4H_3S	5½	75	132—132·5	IPA	240·5(4·41), 266·5(4·26), 396(3·65)	60·4	4·3	4·4	11·0	60·1	4·4	4·4	11·1
Cl	Me	24	58 §	83—83·5	¶	239(4·41), 270(4·04), 346(3·08), 397(3·60)	61·8	5·6	5·7		62·0	5·6	5·55	

* Of once-recrystallised product. † IPA = Propan-2-ol. ‡ These two compounds precipitated from the reaction mixtures and were filtered off and dried. The yield of crude compound is recorded. § From but-3-en-2-one. ¶ IPA then light petroleum (b.p. 60—80°)–benzene–ethyl acetate.

TABLE 5

^{1}H N.m.r. spectra (60 MHz; τ values; *J* in Hz) of 1-(2-acylethyl)-2,3-dihydroquinolin-4(1*H*)-ones in [^{2}H]chloroform at 37° (standard Me_4Si)

X	R	Aromatic protons	2-H	3-H	1-H	2-H	Others
H	Ph	1·85—3·45 (9H, m)	6·40 (t, *J* 7·0)	7·37 (t, *J* 7·0)	6·12 (t, *J* 6·5)	6·70 (t, *J* 6·5)	
H	4-FC_6H_4	1·83—3·45 (8H, m)	6·40 (t, *J* 7·0)	7·36 (t, *J* 7·0)	6·12 (t, *J* 6·5)	6·72 (t, *J* 6·5)	
H	4-PhC_6H_4	1·85—3·45 (13H, m)	6·42 (t, *J* 7·0)	7·36 (t, *J* 7·0)	6·12 (t, *J* 6·5)	6·70 (t, *J* 6·5)	
H	4-MeO·C_6H_4	1·95—3·45 (8H, m)	6·42 (t, *J* 7·0)	7·37 (t, *J* 7·0)	6·17 (t, *J* 7·0) *	6·77 (t, *J* 7·0)	6·17 (3H, s, OMe)
H	4-NO_2·C_6H_4 ‡	1·54—3·45 (8H, m)	†	7·39 (t, *J* 7·0)	†	†	
H	2-C_4H_3S	1·95—3·45 (7H, m)	6·42 (t, *J* 7·0)	7·38 (t, *J* 7·0)	6·14 (t, *J* 6·5)	6·78 (t, *J* 6·5)	
Cl	Ph	1·90—3·40 (8H, m)	6·42 (t, *J* 7·0)	7·40 (t, *J* 7·0)	6·17 (t, *J* 6·5)	6·72 (t, *J* 6·5)	
Cl	4-FC_6H_4	1·83—3·40 (7H, m)	6·39 (t, *J* 7·0)	7·36 (t, *J* 7·0)	6·13 (t, *J* 6·5)	6·72 (t, *J* 6·5)	
Cl	4-PhC_6H_4	1·85—3·40 (12H, m)	6·41 (t, *J* 7·0)	7·38 (t, *J* 7·0)	6·15 (t, *J* 6·5)	6·72 (t, *J* 6·5)	
Cl	4-MeO·C_6H_4	1·90—3·40 (7H, m)	6·41 (t, *J* 7·0)	7·38 (t, *J* 7·0)	6·16 (t, *J* 7·0) *	6·78 (t, *J* 7·0)	6·15 (3H, s, OMe)
Cl	4-NO_2·C_6H_4 ‡	1·50—3·17 (7H, m)	†	7·37 (t, *J* 7·0)	†	†	
Cl	2-C_4H_3S	2·10—3·40 (6H, m)	6·40 (t, *J* 7·0)	7·38 (t, *J* 7·0)	6·15 (t, *J* 6·5)	6·78 (t, *J* 6·5)	
Cl	Me	2·00—3·40 (3H, m)	Resonances overlap to give τ 6·1—6·6 (4H, m, H-2 and H-1) and 7·0—7·5 (4H, m, H-3 and H-2′)				7·79 (3H, s, OAc)

* Centre peak of triplet hidden by OMe signal. † Resonances overlap to give multiplet τ, 6·0—6·8. ‡ In [$^2H_6$]dimethyl sulphoxide.

TABLE 6

Halogen-substituted 1-acetyl-2,3-dihydroquinolin-4(1*H*)-ones (VII)

X	M.p. (°C)	Found (%) C	H	N	X	Required (%) C	H	N	X
6-F	144·5—146	63·2	4·8	6·7		63·8	4·9	6·8	
6-Cl	142·5—143·5	58·9	4·35	6·2	15·7	59·1	4·5	6·3	15·85
8-F	110·5—111	63·8	4·8	7·0	9·1	63·8	4·9	6·8	9·2
8-Cl	129—130	59·0	4·5	6·4	16·0	59·1	4·5	6·3	15·85
8-Br	152·5—153	49·4	3·7	5·3	29·8	49·3	3·75	5·2	29·8

Reaction of the quinolinone (II; X = 6-Cl) with a Mannich base ($MeCO{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$,HCl) [7] derived from an aliphatic ketone, gave a very low yield of alkylation product. However the desired 1-(3-oxobutyl) derivative (V; R = Me, X = 6-Cl) was obtained in higher yield by treating the quinolinone (II; X = 6-Cl) with but-3-en-2-one.

EXPERIMENTAL

3-Anilinopropionic Acids (I).—β-Propiolactone (72 g, 1 mol) was added during 0·5 h to a stirred, refluxing solution of the appropriate aniline (1 mol) in acetonitrile (500 ml). After a further 3 h at reflux the solvent was removed under reduced pressure and the residue dissolved in water (400 ml) containing sodium hydroxide (40 g). The cooled solution was repeatedly extracted with ether to remove non-acidic material and then acidified to pH 4—5 with concentrated hydrochloric acid. The crude product was filtered off, washed with water, dried, and crystallised from the appropriate solvent (Table 1).

In the case of (I; X = 4-F) a dark oil was obtained on acidification; some of this (2 g) was purified by chromatography on a column of silica gel (benzene–ether as eluant). The product (0·9 g) crystallised from benzene–light petroleum (b.p. 60—80°) to give pure *material*, m.p. 77·5—78·5°.

The following by-products were obtained from the foregoing reactions:

(a) N-(4-*Fluorophenyl*)-3-*hydroxypropionamide* (III). The crude non-acidic material from the preparation of (I; X = 4-F) deposited a solid which crystallised from benzene to yield the *hydroxypropionamide* (9%) as plates, m.p. 102—103° (Found: C, 58·9; H, 5·9; F, 10·7; N, 7·8. $C_9H_{10}FNO_2$ requires C, 59·0; H, 5·5; F, 10·4; N, 7·65%), $\nu_{max.}$ (CHBr mull) 1658 (amide I) and 1563 cm^{-1} (amide II), τ [$(CD_3)_2SO$] 0·17br (1H, s, NH), 2·17—3·15 (4H, m, aromatic), 5·35br (1H, t, *J* 4·5 Hz, OH), 6·23br (2H, q, $J_{OH,CH}$ 4·5 Hz, $J_{CH.CH}$ 6·5 Hz, $C{-}CH_2{-}O$), and 7·50 (2H, t, *J* 6·5 Hz, $CO{-}CH_2{-}C$); signals at τ 0·17 and 5·35 removed on deuteriation, when signal at 6·23 collapsed to a sharp triplet.

(b) 3,3′-(4-*Chlorophenylimino*)*dipropionic Acid* (IV).—The benzene-insoluble material from the preparation of (I; X = 4-Cl) crystallised from aqueous methanol to yield the diacid (IV) as the *monohydrate*, plates, m.p. 129—130° (lit.,[8] 133—133·5° for apparently anhydrous material) (Found: C, 49·4; H, 5·3; Cl, 12·2; N, 4·8. $C_{12}H_{14}ClNO_4,H_2O$ requires C, 49·75; H, 5·6; Cl, 12·2; N, 4·8%), τ [$(CD_3)_2SO$] 2·47br (4H, s, CO_2H and H_2O), 2·6—3·45 (4H, m, aromatic), 6·45br (4H, t, $N{-}CH_2{-}C$), and 7·60br (t overlaid by $CD_3{\cdot}SO{\cdot}CD_2H$ signal, $C{-}CH_2{-}C$).

3-(4-*Fluoro*-N-p-*tolylsulphonylanilino*)*propionic Acid* (VI).—A mixture of crude 3-(4-fluoroanilino)propionic acid (59 g), dry benzene (200 ml), dry pyridine (30 ml), and toluene-*p*-sulphonyl chloride (65 g) was heated under reflux for 3 h and allowed to cool overnight. Ether (200 ml) was added and the solution was washed repeatedly with 10% hydrochloric acid (total 750 ml). The organic phase was washed twice with water and extracted with 5% sodium hydroxide (total 600 ml). The combined extracts were poured on a mixture of ice (100 g) and concentrated hydrochloric acid (100 ml). The solid was filtered off, washed with water and reprecipitated from saturated sodium hydrogen carbonate solution (250 ml) with concentrated hydrochloric acid (25 ml). The crude p-*tolylsulphonyl derivative* (39 g), m.p. 114—120° crystallised from benzene to give material of m.p. 122—123° (Found: C, 57·0; H, 5·2; N, 4·2; S, 9·6. $C_{16}H_{16}NO_4S$ requires C, 57·0; H, 4·8; N, 4·15; S, 9·5%).

Halogen-substituted 2,3-*Dihydroquinolin*-4(1H)-*ones* (II).—(a) *By cyclisation of* 3-*anilinopropionic acids* [4] (I). Polyphosphoric acid (16·7 parts by weight) was heated to the specified reaction temperature (Table 2) and the relevant acid (I) (1 part) was added with vigorous stirring. The conditions were maintained for the specified time before the mixture was cooled and poured on to ice–water (50 parts). The quinolinone was filtered off and further material obtained by neutralisation of the filtrate to pH 9 and extraction with chloroform. The combined products were crystallised from benzene–light petroleum (b.p. 60—80°). If necessary, tarry material was removed first by passing a solution of the product in benzene through a short column of silica gel. In some cases the compounds were finally purified by sublimation at 0·1 mmHg.

As well as the new compounds listed in Table 2, the known compounds (II; X = 6-Cl) (65%), m.p. 126—126·5° lit.,[4,9] 124—126), and (II; X = 8-Cl) (65%), m.p. 75—78° (lit.,[10] 75°), were prepared in the same way.

(b) *By cyclisation of the* p-*tolylsulphonyl derivative* (VI). Polyphosphoric acid (125 g) and 3-(4-fluoro-*N*-*p*-tolylsulphonylanilino)propionic acid (14·6 g) were stirred and heated to 100° for 50 min. The cooled mixture was then poured into water (700 ml). A trace of solid was filtered off and the solution was neutralised with sodium hydroxide solution and extracted with ethyl acetate for 48 h. The residue from evaporation of the dried extract was dissolved in benzene and twice passed through a short column of silica gel. The solution was then evaporated and the residue sublimed at 60° and 0·1 mmHg to yield the yellow crystalline *quinolinone* (II; X = 6-F) (2·7 g), m.p. 71·5—73° identical with a specimen prepared as in (a).

(c) *By direct iodination of* 2,3-*dihydroquinolin*-4(1H)-*one*. A solution of 2,3-dihydroquinolin-4-one [5] (1 g) in 2N-hydrochloric acid (16 ml) was treated with a solution of iodine monochloride (1·1 g) in 2N-hydrochloric acid (0·5 ml) at 20°. The suspension was decolourised by the addition of aqueous sodium sulphite solution and the crude iodoquinoline (90%) was filtered off, washed with water, and dried. The solid was crystallised from benzene–light petroleum (b.p. 60—80°) then redissolved in benzene and passed through a short column of silica gel. The eluate was evaporated at 20° and the resulting residue sublimed at 110° and 0·1 mmHg to yield a little pure 2,3-*dihydro*-6-*iodoquinolin*-4(1H)-*one* as yellow crystals, m.p. 152—153°.

The yield of purified compound was very low because it readily decomposed on heating alone, or in solution, to give tarry products.

1-*Acetyl*-2,3-*dihydroquinolin*-4(1H)-*ones*.—Each quinolinone (II) (0·02 mol) was dissolved in dry benzene (10 ml) and anhydrous pyridine (0·04 mol), and acetyl chloride (0·04 mol) was added. The mixture was heated under reflux for 4 h, cooled, and poured into water containing sodium carbonate (4 g). The organic layer was separated

[7] A. L. Wilds, R. M. Nowak, and K. E. McCaleb, *Org. Synth.*, 1963, Coll. Vol. 4, p. 281.

[8] C. D. Hurd and S. Hayao, *J. Amer. Chem. Soc.*, 1952, **74**, 5889.

[9] R. C. Elderfield and A. Maggiolo, *J. Amer. Chem. Soc.*, 1949, **71**, 1906.

[10] R. Joly, J. Warnant, and B. Goffinet, Fr.P. 1,514,280/1968.

and the aqueous layer extracted with chloroform (4 × 25 ml). The combined organic solutions were dried ($MgSO_4$) and evaporated to yield the *acetyl derivative* (Table 6), which was crystallised from ethyl acetate–light petroleum (b.p. 60—80°).

1-(2-*Arenoylethyl*)-2,3-*dihydroquinolin*-4(1H)-*ones* (VII). —A mixture of the relevant quinolinone (II; X = H or 6-Cl) (0·04 mol), the relevant Mannich base hydrochloride (0·04 mol), ethanol (20 ml), and water (20 ml) was heated under reflux for the specified time (Table 4). [A larger volume of each solvent (50 ml) was used in condensations with $4\text{-}NO_2\cdot C_6H_4\cdot CO\cdot CH_2\cdot CH_2\cdot NMe_2$.] The cooled mixture was treated with saturated sodium chloride solution (80 ml) and then repeatedly extracted with ethyl acetate or chloroform. Evaporation of the dried extracts gave a residue which was freed from amine hydrochloride, if necessary, by dissolution in benzene and re-evaporation. Recrystallisation from a suitable solvent (Table 4) gave the pure *acylethyl compound*.

8-Fluoro-2,3-dihydroquinolin-4(1*H*)-one was recovered unchanged (96%) after treatment with 1-(4-nitrophenyl)-3-dimethylaminopropan-1-one hydrochloride in refluxing 90% ethanol for 96 h. Similarly 8-chloro-2,3-dihydroquinolin-4(1*H*)-one was unchanged by treatment with 1-phenyl-3-dimethylaminopropan-1-one hydrochloride for 163 h.

6-*Chloro*-2,3-*dihydro*-1-(3-*oxobutyl*)*quinolin*-4(1H)-*one*.— A mixture of the quinolinone (II; X = 6-Cl) (1·8 g), but-3-en-2-one (aqueous 90% solution; 0·8 g), ethanol (10 ml), and water (5 ml) was heated under reflux for 24 h. Another similar portion of but-3-en-2-one was added and heating was continued for a further 3·5 h. The solvent was removed under reduced pressure and the residue crystallised once from propan-2-ol and twice from light petroleum (b.p. 60—80°) containing a little ethyl acetate to yield the *oxobutyl derivative* as fine yellow needles (0·32 g), m.p. 83—83·5 (see Table 4).

Much of this work was carried out on the premises of Riker Laboratories (now Minnesota 3M Laboratories Ltd.). We thank the Directors for permission to publish the results, for a maintenance grant (to G. B.), and for the facilities used.

[2/633 *Received*, 20*th March*, 1972]