837. *Cyclic Keto-amines. Part II.* The Preparation and Spectroscopic Characteristics of Substituted* 1 : 2 : 3 : 4-*Tetrahydro*-4-*oxoquinolines.*

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

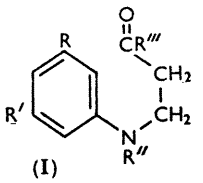
A number of new substituted 1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines has been prepared; the standard cyclisation procedures are found to be more widely applicable than hitherto reported. The infrared and ultraviolet spectra of these compounds are discussed in relation to their structures.

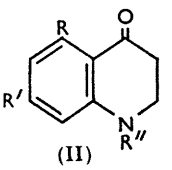
THE synthesis of 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (II; R = R′ = R″ = H) and certain simple derivatives was first described by Clemo and Perkin;[1] β-(toluene-*p*-sulphonanilido)-propionic acids of type (I; R″ = SO_2·C_6H_4Me, R‴ = OH) were either converted into their acid chlorides and cyclised by phosphorus oxychloride, or were cyclised directly with phosphoric anhydride, and hydrolytic removal of the protecting toluene-*p*-sulphonyl group then gave the parent keto-amines. This route has been followed by other workers[2,3] and gives good yields of various *Bz*-substituted 1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines. A second route involves the monocyclisation of various *NN*-biscyanoethyl derivatives of

* Ittyerah and Mann, *J.*, 1956, 3179, is to be regarded as Part I of this series.

[1] Clemo and Perkin, *J.*, (*a*) 1924, **125**, 1608; (*b*) 1925, **127**, 2297.
[2] Johnson, Woroch, and Buell, *J. Amer. Chem. Soc.*, 1949, **71**, 1901.
[3] Elderfield, Gensler, Bembry, Kremer, Brody, Hageman, and Head, *ibid.*, 1946, **68**, 1259; Elderfield and Maggiolo, *ibid.*, 1949, **71**, 1906.

aromatic amines to give quinolines of type (II; R″ = $[CH_2]_2$·CO_2H or $[CH_2]_2$·CN),[4,5] which in boiling hydrochloric acid lose the 2-carboxyethyl group to form the corresponding quinolines (II; R″ = H).[4] Another cyclisation route has been used by Bekhli,[6] who converted the acid (III) into the quinoline (II; R = H, R′ = Cl, R″ = Ac) by the action of acetic anhydride and potassium acetate.


(I)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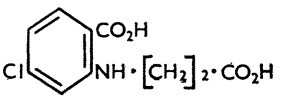

(III)

As a preliminary to work designed to lead to analogous systems containing a seven-membered keto-amine ring (see following paper), the synthesis of new ketones of type (II) containing the activating methoxyl group, and the influence of the acyl group R″ on the course of the cyclisation were investigated.

Methyl β-arylaminopropionates were readily obtained by addition of methyl acrylate to aromatic primary amines in the presence of acetic acid,[2] and then converted by the usual steps into the *N*-acylated amino-acids (I; R″ = SO_2Ph, SO_2·C_6H_4Me, Bz, or Ac, R‴ = OH) suitable for cyclisation.

We find, not unexpectedly, that the Friedel–Crafts procedure converts the benzenesulphonyl compound (I; R = R′ = H, R″ = SO_2Ph, R‴ = OH) into the 1-benzenesulphonyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (II; R = R′ = H, R″ = SO_2Ph) in good yield, similar to that obtained for the toluene-*p*-sulphonyl analogue (II; R = R′ = H, R″ = SO_2·C_6H_4Me).

Previous workers [3] had stressed that the presence of the *N*-toluene-*p*-sulphonyl group in acids of type (I) was apparently essential for cyclisation. We have therefore briefly examined the behaviour of the acids (I; R = R′ = H, R″ = Ac or Bz, R‴ = OH) under similar conditions.

β-*N*-Acetanilidopropionic acid (I; R = R′ = H, R″ = Ac, R‴ = OH) was converted by thionyl chloride into the acid chloride, but attempted cyclisation of the latter under various conditions gave intractable tars, having an almost negligible ketonic content. On the other hand, the acid chloride of the analogous *N*-benzoyl-acid, when treated with aluminium chloride, gave two distinct types of ketone according to the solvent employed. When dissolved in benzene at room temperature, it reacted with the solvent to form the β-substituted propiophenone (I; R = R′ = H, R″ = Bz, R‴ = Ph) in good yield: the constitution of this compound was confirmed by its infrared spectrum, which showed strong sharp bands at 1675 (conjugated C:O) and at 1629 cm.$^{-1}$ (tertiary amide). In boiling chlorobenzene, the ketone (I; R = R′ = H, R″ = Bz, R‴ = C_6H_4Cl) was similarly obtained.

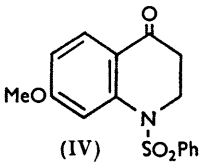
The chloride, when treated however with aluminium chloride in carbon disulphide at room temperature, underwent cyclisation to form 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (II; R = R′ = H, R″ = Bz), identical with that which Clemo and Perkin [1] obtained by benzoylation of the parent oxoquinoline (II; R = R′ = R″ = H). The infrared spectrum of this compound showed bands at 1682 (conjugated cyclic C:O) and at 1642 cm.$^{-1}$ (tertiary amide).

These results show that the presence of the *N*-benzoyl group in chlorides of the acids of type (I) deactivates the benzene ring for cyclisation purposes to a much greater extent

[4] Braunholtz and Mann, *J.*, 1952, 3046.
[5] *Idem*, *J.*, 1954, 651; Johnson and DeAcetis, *J. Amer. Chem. Soc.*, 1953, **75**, 2766.
[6] Bekhli, *Doklady Akad. Nauk S.S.S.R.*, 1955, **101**, 679; *Chem. Abs.*, 1956, **50**, 3441.

than does the *N*-arylsulphonyl group, and subsequently promotes direct reaction with an aromatic solvent.

In order to promote the desired cyclisation by activation of the benzene ring, we have prepared from *m*-anisidine the acids (I; R = H, R′ = OMe, R″ = SO_2Ph and $SO_2{\cdot}C_6H_4Me$, R‴ = OH). The chloride of the first acid in benzene solution gave solely the quinolone (IV), but that of the second gave two isomeric quinolones, (V), m. p. 104—105°, and (VI), m. p. 114°, in almost equal quantities.



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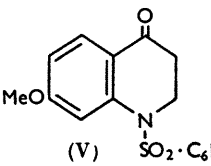
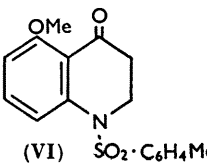


(V)



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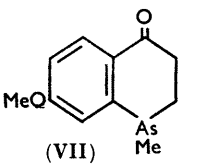


(VII)

It is noteworthy that, from similar cyclisations, 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1-methyl-4-oxoarsinoline [7] (VII) and the quinolone [2] (II; R = H, R′ = Cl, R″ = $SO_2{\cdot}C_6H_4Me$) have been isolated without accompanying isomers, whereas the acid (I; R = H, R′ = Me, R″ = $SO_2{\cdot}C_6H_4Me$, R‴ = OH) gave rise to both the quinolones (II; R = H, R′ = Me, R″ = $SO_2{\cdot}C_6H_4Me$) and (II; R = Me, R′ = H, R″ = $\cdot SO_2{\cdot}C_6H_4Me$), the former being isolated in much greater yield than the latter.[1b]

Spectroscopic evidence described below provides support for the allocation of structures (IV), (V), and (VI).

(*a*) The infrared spectra, in the region 880—690 cm.$^{-1}$, of the quinolones (IV), (V), and (VI), and of certain related compounds, are summarised in Table 1. The band systems of the quinolone (IV) and its *Bz*-unsubstituted analogue (II; R = R′ = H, R″ = SO_2Ph) in the region 690—790 cm.$^{-1}$ correspond very closely in both position and relative intensities; it is therefore possible, without detailed assignment of these bands, to correlate the additional absorption at 863 cm.$^{-1}$ in the spectrum of (IV) with a 1 : 2 : 4-pattern of nuclear substitution, for which a " normal " range of 860—800 cm.$^{-1}$ has been suggested.[8]

In the infrared spectra of the isomers (V) and (VI), absorption bands at 822 and 817 cm.$^{-1}$ respectively may be assigned to the toluene-*p*-sulphonyl group by comparison with that of the quinolone (II; R = R′ = H, R″ = $SO_2{\cdot}C_6H_4Me$), in which the corresponding absorption is at 817 cm.$^{-1}$. The proposed structure (V) for the less soluble isomer is

TABLE 1. *Infrared spectra of the tetrahydro-4-oxoquinolines in the region* 880—690 *cm.*$^{-1}$ *in Nujol mull.**

(II; R = R′ = H, R″ = $SO_2{\cdot}C_6H_4Me$) ...	834 (m)	817 (m)	779 (s)	735 (s)	687 (s)
(II; R = R′ = H, R″ = SO_2Ph)	835 (m)	787 (s)	767 (m)	738 (m)	694 (m)
(IV)	863 (m)	784 (s)	765 (m)	728 (s)	695 (m)
(V)	875 (m)	822 (m)	777 (s)	710 (m)	690 (s)
(VI)	850 (m)	817 (s)	790 (m)	698 (s)	

* m and s indicate medium and strong bands respectively.

supported by an absorption band at 875 cm.$^{-1}$, close to that characterising the 1 : 2 : 4-trisubstituted system of the quinolone (IV); absorption at 790 cm.$^{-1}$ in the spectrum of the more soluble quinolone (VI) corresponds to the 1 : 2 : 3-trisubstituted aromatic nucleus.

(*b*) Decisive interpretation of the infrared spectra of the quinolones (V) and (VI) in the 880—790 cm.$^{-1}$ region is, however, complicated by the polar groups present. Confirmation of the structural assignments has therefore been sought from ultraviolet absorption studies designed to detect interaction between the carbonyl group (or a derivative of this group) and a methoxyl group *ortho* to it. Table 2 shows that, although the spectra of

[7] Mann and Wilkinson, *J.*, 1957, 3336.
[8] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1956 pp. 54 ff.

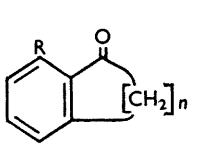
quinolones of type (II) are considerably modified by the introduction of a methoxyl group, they do not afford evidence for such steric effects; similar insensitivity to *ortho*-substitution has also been discovered in the case of certain cyclanones [9] (*e.g.*, VIII; $n = 3$), although the ultraviolet spectra of *ortho*-substituted acetophenones are appreciably modified.

TABLE 2. *Ultraviolet absorption spectra of the tetrahydro-4-oxoquinolines and their derivatives in ethanol* (ε *in parentheses*).

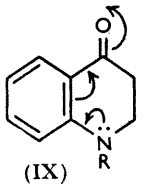
Compound	$\lambda_{max.}$	$\lambda_{min.}$	$\lambda_{infl.}$
(II; R = R′ = H, R″ = SO_2Ph)	319 (2,700)	285—286 (840)	236—240 (15,500)
	219—220 (20,600)		256—260 (9,990)
(IV)	281 (13,900)	277—278 (13,800)	
	275 (13,900)	270 (12,600)	
	252—253 (18,000)	233—235 (13,000)	
	217—218 (17,300)		
(V)	277 (14,620)	270—271 (13,740)	
	254 (19,710)	238—239 (11,070)	
	225 (19,470)		
(VI) *	278, 255, 225	268, 240	
2 : 4-Dinitrophenylhydrazone of (V) ...	392 (33,600)	324 (5,800)	302—294 (10,980)
	218—219 (37,300)		256—246 (25,550)
2 : 4-Dinitrophenylhydrazone of (VI)...	392 (29,700)	325 (4,740)	304—284 (10,900)
	218 (32,000)	210—209 (29,700)	258—250 (21,500)

* Owing to the very small quantity of material available, the ε values are not accurately comparable with those in other spectra, and are omitted.

When however the ketones (V) and (VI) are converted into their 2 : 4-dinitrophenylhydrazones, appreciable differences in ε values become apparent; the allotted structures are thereby supported, since the derivative with the less intense absorption maxima will be the one in which a weak *ortho*-effect causes partial steric inhibition of resonance.



(VIII)



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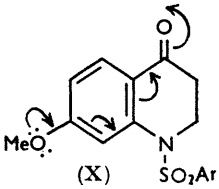


(X)

In earlier papers [10] concerning cyclic keto-amines of type (II) or of analogous structure, we have correlated the colour (and fluorescence) of their solutions with nitrogen–carbonyl interaction as shown in (IX). The more precise spectroscopic evidence now given in the Figure demonstrates the predicted hypsochromic shift of the long-wavelength absorption maximum when electron-release by nitrogen is reduced by the substituent R. It is noteworthy that the highest-wavelength absorption maximum of the arsinolone (VII), in which arsenic–carbonyl interaction is probably negligible, occurs at 281 mμ (ε 14,000),[7] that of α-tetralone (VIII; R = H, $n = 3$) being at 248 mμ (ε 12,200).[11]

The corresponding carbonyl absorption frequencies in the infrared spectra of the quinolones are summarised in Table 3. If the carbonyl band at 1681 $cm.^{-1}$ for α-tetralone [12] (liquid) (VIII; R = H, $n = 3$) is taken as a standard, nitrogen–carbonyl interaction in the quinolones (II; R = R′ = H, R″ = Me or Ph) leads to a " frequency " decrease of 4 $cm.^{-1}$; when this interaction is suppressed by acylation of the amine group, the resulting keto-amines show carbonyl absorption at higher frequencies, close to the normal α-tetralone value. When, however, the methoxyl group is introduced into these acylated quinolones

[9] Hedden and Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 3744.
[10] *E.g.*, Braunholtz and Mann, *J.*, 1953, 1817.
[11] Schubert and Sweeney, *J. Amer. Chem. Soc.*, 1955, **77**, 2297.
[12] *Idem, ibid.*, p. 4172.

(as in IV, V, and VI), its interaction with the carbonyl group (see X) now reduces the carbonyl absorption to almost the same value as that produced by the amine–carbonyl interaction in the quinolones (II; R = R′ = H, R″ = Me or Ph). The appreciable variation (6 cm.$^{-1}$) between the (C:O) bands for the isomeric toluene-*p*-sulphonyl ketones

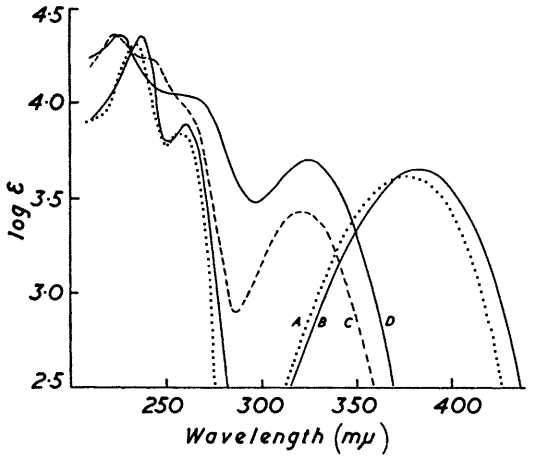
TABLE 3. *Infrared spectra of the tetrahydro-4-oxoquinolines* (II) *in the region* 1650—1700 *cm.*$^{-1}$ (*in Nujol except as stated*).

R	R′	R″	ν_{CO} (cm.$^{-1}$)	R	R′	R″	ν_{CO} (cm.$^{-1}$)
H	H	Ph	1677	H	H	$SO_2{\cdot}C_6H_4Me$	1685
*H	H	Me	1677	H	OMe	SO_2Ph	1675
H	H	Bz	1682	H	OMe	$SO_2{\cdot}C_6H_4Me$	1676
H	H	SO_2Ph	1683	OMe	H	$SO_2{\cdot}C_6H_4Me$	1670

* Liquid film.

(V) and (VI) has apparently the same structural significance as the difference in the ν_{CO} values of *o*-methoxyacetophenone (1649 cm.$^{-1}$, liquid) and *p*-methoxyacetophenone (1657 cm.$^{-1}$, liquid).[13]

The spectroscopic results discussed above provide clear evidence for partial nitrogen–carbonyl interaction of the amide type, but this is not sufficiently powerful to destroy the normal ketonic and (where applicable) basic reactivities of such systems. It is to be



Ultraviolet spectra, in ethanol, of (*A*) 1 : 2 : 3 : 4-*tetrahydro-4-oxoquinoline,* (*B*) 1 : 2 : 3 : 4-*tetrahydro-1-methyl-4-oxoquinoline,* (*C*) 1 : 2 : 3 : 4-*tetrahydro-4-oxo-1-toluene-*p*-sulphonylquinoline, and* (*D*) 1-*benzoyl*-1 : 2 : 3 : 4-*tetrahydro-4-oxoquinoline.*

expected, moreover, that any steric factor reducing coplanarity of the carbonyl and amino-groups and the aromatic ring system should enhance these normal properties; this factor is of importance in the study of analogous seven-membered ring systems described elsewhere [14] (see also following paper).

EXPERIMENTAL

Addition of Methyl Acrylate to Aromatic Primary Amines. Methyl β-Anilinopropionate (I; R = R′ = R″ = H, R‴ = OMe).—This ester was prepared essentially by the method of Johnson *et al.*[2] A mixture of aniline (100 c.c.), methyl acrylate (110 c.c., 1·25 mols.), and acetic acid (10 c.c.) was heated under reflux for 8 hr., and then distilled under reduced pressuer, giving the fractions, (*a*) b. p. 60—125°/2 mm. (3 g.), (*b*) b. p. 132°/2·5 mm. (140 g.), and (*c*) b. p. 160—170°/3 mm. (*ca.* 10 g.), and a residue of undistillable polymer. Fraction (*b*) crystallised

[13] Hergert and Kurth, *ibid.*, 1953, **75**, 1622.
[14] Braunholtz and Mann, *Chem. and Ind.*, 1957, 266

readily, giving methyl β-anilinopropionate, m. p. 38° (75% yield), sufficiently pure for subsequent work.

Methyl β-m-*methoxyphenylpropionate*. A mixture of *m*-anisidine (25 g.), methyl acrylate (18 g., 1 mol.), and acetic acid (5 c.c.), when heated under reflux for 12 hr. gave on distillation solely the *ester*, b. p. 165—167°/1 mm. (31 g., 75%) (Found: N, 6·8. $C_{11}H_{15}O_3N$ requires N, 6·7%). This ester gave no precipitate with methanolic picric acid.

N-*Acyl*-β-*arylaminopropionic Acids*.—N-*Acetyl*-β-*anilinopropionic acid* (I; R = R′ = H, R″ = Ac, R‴ = OH). Attempts to acetylate the methyl ester (I; R = R′ = R″ = H, R‴ = OMe) by acetic acid–acetic anhydride under reflux were unsatisfactory. A solution of the ester (17·9 g.) in dry benzene (50 c.c.) was therefore treated (in alternate portions, with shaking) with acetyl chloride (7·9 g.) and pyridine (7·9 g.). After 30 min., the mixture was shaken with water and aqueous sodium carbonate. The benzene layer on evaporation left a pale straw-coloured mobile syrup, which was dissolved in methanol (150 c.c.) and 10% aqueous potassium hydroxide (50 c.c.) and set aside at room temperature for 20 hr. The solution was acidified and evaporated under reduced pressure; the residual syrup slowly crystallised when triturated with water, affording the *acid*, m. p. 108° from water (10 g., 50%) (Found: C, 64·1; H, 6·3; N, 6·6. $C_{11}H_{13}O_3N$ requires C, 63·8; H, 6·3; N, 6·8%).

N-*Benzoyl*-β-*anilinopropionic acid*. The methyl ester (I; R = R′ = R″ = H, R‴ = OMe) (17·9 g.) was shaken with benzoyl chloride (14 g., 1 mol.) and 10% aqueous sodium hydroxide (100 c.c.) for 1 hr., the temperature being allowed to rise to 50°. The mixture when acidified deposited an oil which ultimately crystallised, and was partially purified by reprecipitation from aqueous sodium carbonate solution. Recrystallisation from benzene gave the *acid*, m. p. 84—87° (20 g., 74%) (Found: C, 71·5; H, 5·6; N, 5·2. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6; N, 5·2%).

Repetition of this experiment at 15—20° gave a granular solid before acidification; this was collected, and addition of hydrochloric acid to the filtrate precipitated the acid (I; R = R′ = H, R″ = Bz, R‴ = OH) (9 g.), as before. The granular solid was the *methyl ester* (I; R = R′ = H, R″ = Bz, R‴ = OMe), m. p. 77·5—78·5° after crystallisation from aqueous methanol (13 g.) (Found: C, 72·3; H, 6·3; N, 5·0. $C_{17}H_{17}O_3N$ requires C, 72·3; H, 6·05; N, 4·95%).

N-*Benzenesulphonyl*-β-*anilinopropionic acid*. The ester (17·9 g.) was shaken with benzenesulphonyl chloride (17·7 g., 1 mol.) and 10% aqueous sodium hydroxide (100 c.c.). Acidification gave a heavy syrup which was separated, washed with water, and then dissolved in methanol (150 c.c.) containing 10% aqueous potassium hydroxide (50 c.c.) and set aside for 16 hr. to complete the hydrolysis. Acidification then afforded the *acid*, m. p. 115° (from benzene–*cyclo*hexane) (10 g., 33%) (Found: C, 59·1; H, 4·5; N, 4·55. $C_{15}H_{15}O_4NS$ requires C, 59·0; H, 4·9; N, 4·6%).

N-Toluene-*p*-sulphonyl-β-anilinopropionic acid was prepared in 80% yield from the ester by the method of Johnson *et al.*,[2] and had m. p. 144—146° after crystallisation from benzene.

N-*Benzenesulphonyl*-β-m-*methoxyphenylpropionic acid*. The ester (I; R = R″ = H, R′ = R‴ = OMe) (10 g.) was treated with benzenesulphonyl chloride (10 g.) precisely as the ester (I; R = R′ = R″ = H, R‴ = OMe). The solution of the oil in alkali–methanol was acidified after 20 hr.; the precipitated viscous syrup solidified after trituration with water, methanol, and benzene. Recrystallisation from benzene gave the *acid*, m. p. 118° (10 g., 30%) (Found: C, 57·1; H, 5·0; N, 4·3. $C_{16}H_{17}O_5NS$ requires C, 57·3; H, 5·1; N, 4·2%).

N-*Toluene*-p-*sulphonyl*-β-m-*methoxyphenylpropionic acid* (I; R = H, R′ = OMe, R″ = $SO_2{\cdot}C_6H_4Me$, R‴ = OH) similarly prepared, formed needles, m. p. 112—113°, from benzene–*cyclo*hexane (Found: C, 58·6; H, 5·3; N, 3·8. $C_{17}H_{19}O_5NS$ requires C, 58·4; H, 5·5; N, 4·0%): 30% yield.

Characterisation of Acid Chlorides.—In the case of the acids (I; R = R′ = H, R″ = Ac or Bz, R‴ = OH) where subsequent cyclisation might be difficult, evidence was required that the intermediate acid chloride was formed in high yield. A solution of each acid (1 g.) in benzene (10 c.c.) containing thionyl chloride (1 c.c.) was heated under reflux for 30 min. Volatile constituents were removed first by heat under reduced pressure, and then by several co-distillations with small quantities of benzene. A benzene solution of the residual syrup, when treated with *p*-toluidine (1 g.), deposited *p*-toluidine hydrochloride almost quantitatively. The filtrate from the first acid gave a viscous syrup: that from the second acid readily afforded N-*benzoyl*-β-*anilinopropiono*-p-*toluidide* (I; R = R′ = H, R″ = Bz, R‴ = $NH{\cdot}C_6H_4Me$),

m. p. 134—135° (from ethanol) (1·2 g., 90%) (Found: C, 77·3; H, 6·2; N, 7·7. $C_{23}H_{22}O_2N_2$ requires C, 77·1; H, 6·2; N, 7·8%).

Friedel–Crafts Condensations of Acid Chlorides.—The acid (unless otherwise stated) was converted into the chloride by the above method.

(i) N-*Acetyl*-β-*anilinopropionic acid.* Attempts to cyclise the chloride were inconclusive. A benzene solution when treated with a small excess of aluminium chloride at room temperature darkened and yielded only a trace of ketonic material.

(ii) N-*Benzoyl*-β-*anilinopropionic acid.* (*a*) The acid (5 g.) was converted into the chloride which was treated in benzene at 0° with powdered aluminium chloride (5 g.); there was considerable evolution of hydrogen chloride. The mixture was set aside at room temperature for 20 hr., then poured into a slight excess of cold 10% aqueous sodium hydroxide. Benzene-extraction yielded a dark gum, which when recrystallised from ethanol afforded β-N-*benzanilidopropiophenone* (I; R = R′ = H, R″ = Bz, R‴ = Ph), needles, m. p. 132° (4 g., 65%) (Found: C, 80·1; H, 5·9; N, 4·5%; *M*, in boiling acetone, 362, 353. $C_{22}H_{19}O_2N$ requires C, 80·1; H, 5·8; N, 4·25%; *M*, 329). This ketone readily gave the *phenylhydrazone*, pale cream prisms, m. p. 166—167° (from ethanol) (Found: C, 79·9; H, 6·2; N, 10·0. $C_{28}H_{25}ON_3$ requires C, 80·2; H, 6·0; N, 10·0%). The 2 : 4-*dinitrophenylhydrazone* formed orange platelets, m. p. 205°, too insoluble for recrystallisation from the usual solvents (Found: N, 14·2. $C_{28}H_{23}O_5N_5$ requires N, 13·8%).

(*b*) In a modified experiment, the acid (2 g.) was converted into the acid chloride, which was then dissolved in chlorobenzene (15 c.c.); powdered aluminium chloride (2 g.) was added; the mixture was heated at 130—140° for 5 min. and then worked up. The syrupy residue from the benzene extract, when crystallised from a small quantity of warm ethanol, gave 2-N-*benzanilidoethyl* p-*chlorophenyl ketone* (I; R = R′ = H, R″ = Bz, R‴ = C_6H_4Cl), m. p. 113° (from ethanol) (1 g., 37%) (Found: C, 72·6; H, 5·35; N, 3·8. $C_{22}H_{18}O_2NCl$ requires C, 72·6; H, 5·0; N, 3·85%). The ketone gave a strong positive Beilstein test for halogen. It formed an insoluble 2 : 4-*dinitrophenylhydrazone*, orange platelets, m. p. 181° (Found: N, 12·9. $C_{28}H_{22}O_5N_5Cl$ requires N, 12·9%).

(*c*) The acid (2 g.) was converted into the chloride, which was treated in carbon disulphide (15 c.c.) with powdered aluminium chloride (2 g.); after 20 hr. at room temperature, the mixture was hydrolysed and extracted with benzene in the usual way. The residue when recrystallised from ethanol gave 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (II; R = R′ = H, R″ = Bz), m. p. 118° (lit.,[1a] 122°) (0·4 g., 21%) (Found: C, 76·6; H, 5·5; N, 5·9. Calc. for $C_{16}H_{13}O_2N$: C, 76·5; H, 5·2; N, 5·6%). The oxoquinolone gave a scarlet 2 : 4-*dinitrophenylhydrazone*, m. p. 254—255° (insertion at 250°) (Found: N, 15·9. $C_{22}H_{17}O_5N_5$ requires N, 16·2%).

An authentic sample of the oxoquinoline (II; R = R′ = H, R″ = Bz), prepared by the benzoylation of 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline, had m. p. and mixed m. p. 119—120°.

(iii) N-*Benzenesulphonyl*-β-*anilinopropionic acid.* (*a*) The acid chloride was prepared from the acid (I; R = R′ = H, R″ = SO_2Ph, R‴ = OH) (2 g.), and dissolved in benzene to which powdered aluminium chloride (2 g.) was added; the mixture was set aside at room temperature for 15 hr. Alkaline hydrolysis followed by benzene extraction ultimately afforded 1-*benzenesulphonyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxoquinoline*, m. p. 130° (from ethanol) (0·6 g., 32%) (Found: C, 63·0; H, 4·6; N, 4·9. $C_{15}H_{13}O_3NS$ requires C, 62·7; H, 4·6; N, 4·9%).

(*b*) The acid (4·8 g.) in benzene (25 c.c.) was heated under reflux for 30 min. with phosphorus pentachloride (3·2 g.); the mixture was then cooled to 0°, and stannic chloride (2·7 c.c.) in benzene (5 c.c.) was added. After 24 hr., the mixture was worked up and gave the above ketone (1·6 g., 35%), m. p. and mixed m. p. 130°. The 2 : 4-*dinitrophenylhydrazone* formed red-orange platelets, m. p. 218° (Found: N, 15·3. $C_{21}H_{17}O_6N_5S$ requires N, 15·0%).

The ketone (II; R = R′ = H, R″ = SO_2Ph) was hydrolysed to 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline in good yield by the method of Johnson *et al.*[2]

(iv) N-*Toluene*-p-*sulphonyl*-β-*anilinopropionic acid.* This acid afforded the 4-oxo-1-toluene-*p*-sulphonylquinoline (II; R = R′ = H, R″ = $SO_2{\cdot}C_6H_4Me$) by the following procedures.[1,2] The use of thionyl chloride in benzene, followed by aluminium chloride in the same solvent, gave yields from 35—50%, not consistently dependent upon the order of mixing of the cyclisation components or the nature (acid or alkaline) of the hydrolysis. A higher yield (*ca.* 70%) was achieved with the use of phosphorus pentachloride in benzene, followed by stannic chloride. Polyphosphoric acid (160°, 20 min.) was unsatisfactory, and gave only traces of an unidentified ketone.

The purified ketone had m. p. 141—142° (lit.,[1,2] 141—142°), pale cream crystals from ethanol (Found: N, 4·7. Calc. for $C_{16}H_{15}O_3NS$: N, 4·7%). It readily formed a highly crystalline *phenylhydrazone*, cream platelets, m. p. 232° (decomp.) (from dioxan) (Found: C, 67·8; H, 5·4; N, 10·8. $C_{22}H_{21}O_2N_3S$ requires C, 67·5; H, 5·4; N, 10·7%), and an orange 2 : 4-*dinitrophenylhydrazone*, m. p. 204—205° (Found: N, 14·7. $C_{22}H_{19}O_6N_5S$ requires N, 14·6%).

(v) N-*Benzenesulphonyl*-β-m-*methoxyphenylpropionic acid*. The acid (6·7 g.) was converted into the chloride by phosphorus pentachloride (4·2 g.) in benzene (40 c.c.), followed by stannic chloride (3·5 c.c.) at 0°; the mixture was set aside at room temperature for 15 hr., and when then worked up gave 1-*benzenesulphonyl*-1 : 2 : 3 : 4-*tetrahydro*-7-*methoxy*-4-*oxoquinoline* (IV), m. p. 138—139° (from ethanol) (3 g., 47%) (Found: C, 60·9; H, 5·05; N, 4·7. $C_{16}H_{15}O_4NS$ requires C, 60·6; H, 4·8; N, 4·4%). A lower yield (40%) was obtained by the thionyl chloride–aluminium chloride–benzene method. The mother-liquors were examined without success for the presence of the possible 5-methoxy-isomer. The ketone gave an insoluble deep orange 2 : 4-*dinitrophenylhydrazone*, m. p. 201° (Found: N, 14·2. $C_{22}H_{19}O_7N_5S$ requires N, 14·1%).

To obtain 1 : 2 : 3 : 4-tetrahydro-7-methoxy-4-oxoquinoline (II; R = R″ = H, R′ = OMe), a solution of the ketone (II; R = H, R′ = OMe, R″ = SO_2Ph) (2 g.) in acetic acid (2 c.c.), water (0·5 c.c.), and concentrated hydrochloric acid (2 c.c.) was boiled under reflux for 3 hr., then poured into water (25 c.c.) and extracted with ether. Evaporation of the extract gave a residue, which on fractional recrystallisation from ethanol yielded the unchanged ketone (0·2 g., 10%) and the required 4-oxoquinoline, m. p. 135—137°, depressed to 108—120° on admixture with unchanged ketone. The aqueous solution from the ether extraction was brought to pH 7 by the addition of powdered sodium carbonate, and a second ether-extraction gave a second crop of the 4-*oxoquinoline*; the combined crops (0·65 g., 63%), when recrystallised from ethanol, formed pale yellow prisms, m. p. 139° (Found: C, 66·6; H, 5·7; N, 8·1; OMe, 17·8. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2; N, 7·9; OMe, 17·5%). The pale yellow ethanolic solution has a blue fluorescence. The ketone gave a deep purple 2 : 4-*dinitrophenylhydrazone*, m. p. 274° (Found: N, 20·4. $C_{16}H_{15}O_5N_5$ requires N, 19·7%).

(vi) N-*Toluene*-p-*sulphonyl*-β-m-*methoxyphenylpropionic acid*. The acid (4 g.) was converted into its chloride by treatment with phosphorus pentachloride (2·6 g.) in benzene (25 c.c.) under reflux (30 min.), and cyclisation was effected with stannic chloride (2·1 c.c.) as before. The dark brown-yellow mixture, with a red oily lower layer, was poured into dilute aqueous sodium hydroxide and extracted with benzene. Evaporation of the extract afforded a dark brown syrup, which on fractional crystallisation from ethanol gave first 1 : 2 : 3 : 4-*tetrahydro*-7-*methoxy*-4-*oxo*-1-*toluene*-p-*sulphonylquinoline* (V) (0·75 g., 20%), m. p. 94—98°, increased to 104—105° by recrystallisation from ethanol (Found: C, 61·6; H, 5·5; N, 4·5. $C_{17}H_{17}O_4NS$ requires C, 61·6; H, 5·2; N, 4·25%). It gave a deep orange 2 : 4-*dinitrophenylhydrazone*, melting to a glass at 182—184°, then remelting at 212° (Found: N, 13·8. $C_{23}H_{21}O_7N_5S$ requires N, 13·7%).

The second ketonic fraction, from the ethanolic mother-liquors, furnished the 5-*methoxy*-isomer (VI) (0·75 g., 20%), m. p. 114° after recrystallisation from ethanol (Found: C, 61·9; H, 5·2; N, 4·5%). The 2 : 4-*dinitrophenylhydrazone* formed vermilion platelets, m. p. 202° (Found: N, 14·0%). A mixture of the isomeric ketones (V) and (VI) had m. p. 109—112°.

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