Preparation and Cyclisation of Some 3-Aza-1,5-diketones

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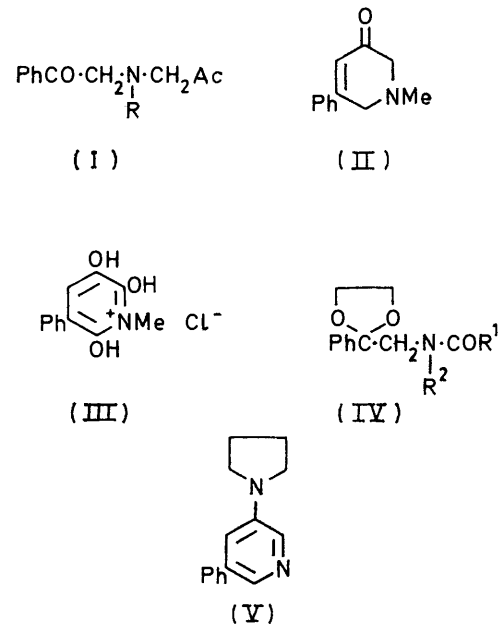
The *N*-methyl, *N*-acetyl, and *N*-methoxycarbonyl derivatives of 2-(acetonylamino)acetophenone (I; R = H) have been prepared and conditions for their internal cyclisation studied. 2-(*N*-Acetonylbenzylamino)- and 2-(*N*-acetonylbenzamido)-3,4-dihydronaphthalen-1(2*H*)-ones (VII; R = CH_2Ph or Bz) have also been synthesised, and cyclised to tricyclic unsaturated ketones. The use of magnesium methyl carbonate appears to be of particular value in such condensations.

THE present investigations were undertaken as model experiments for the construction of ring D in a projected synthesis of lysergic acid. The reaction of phenacyl bromide with (*N*-benzylmethylamino)acetone in ether yielded a gummy quaternary salt which on catalytic hydrogenation over palladised charcoal gave the hydrochloride salt of 2-(*N*-acetonylmethylamino)acetophenone (I; R = Me). Cyclisation of this base proceeded with remarkable ease in that treatment in aqueous solution with excess of 2N-sodium hydroxide for a few minutes sufficed to give 1,6-dihydro-1-methyl-5-phenyl-3(2*H*)-pyridone (II) in 60% yield. Similar cyclisations have been reported in the case of more complex molecules,[1,2] but only under more severe conditions.

However, when potassium t-butoxide was used for cyclisation, the main product (*ca.* 50% yield) was a crystalline hydrated salt which lost water of crystallisation on heating at 100°. From its mode of formation and analytical data, and despite the absence of OH bands in its i.r. spectrum, we believe this substance to be a trihydroxy-1-methyl-5-phenylpyridinium chloride (*e.g.* (III)].

Preparations of the unmethylated diketone (; R = H) and its *N*-acetyl derivative proved more difficult but were eventually achieved from sodio-2-acetamidoacetophenone ethylene acetal (IV; R^1 = Me, R^2 = Na). Condensation with prop-2-ynyl bromide yielded the *N*-prop-2-ynyl derivative, which, without purification, was treated with 2N-hydrochloric acid at 65° in the presence of mercury(II) sulphate. Both hydration of the triple bond and removal of the acetyl grouping occurred, to give the basic diketone (I; R = H); at a later date we were able to prepare the *N*-methoxycarbonyl derivative (I; R = CO_2Me) by a similar series of reactions without loss of the acyl group. Alternatively, reaction with β-ethoxyallyl chloride furnished a crude tertiary amide with structure (IV; R^1 = Me, R^2 = CH=CMe·OEt), presumably as the result of an allylic rearrangement; this product on careful hydrolysis gave the *N*-acetyl diketone (I; R = Ac).

Cyclisation of this *N*-acetyl diketone proceeded again under remarkably mild alkaline conditions at 2° in



aqueous solution to give a crystalline compound which on the evidence from potentiometric titration data and i.r. and u.v. spectra is formulated as 3-hydroxy-5-phenylpyridine; this compound presumably arose as the result of removal of the acetyl grouping followed by aerial oxidation of a dihydropyridone precursor.

In another approach, reaction of the *N*-acetyl diketone with pyrrolidine was found to proceed slowly at 80° with elimination of water and acetic acid to give a mixture from which 3-phenyl-5-pyrrolidin-1-ylpyridine (V) could

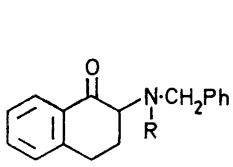
[1] E. C. Kornfeld, E. S. Fornefeld, G. B. Kline, M. J. Mann, D. E. Morrison, R. G. Jones, and R. B. Woodward, *J. Amer. Chem. Soc.*, 1956, **78**, 3087.

[2] J. Cymerman Craig, D. M. Temple, and B. Moore, *Austral. J. Chem.*, 1961, **14**, 84.

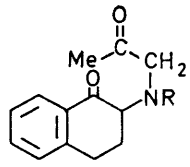
be isolated in reasonable yield. Attempts to cyclise the *N*-methoxycarbonyl derivative were unsuccessful.

Despite little encouragement from these experiments on the cyclisation of *N*-acyl 1,5-diketones we next studied the corresponding 1-tetralone derivatives. Initial attempts to apply methods of synthesis used for the open-chain analogues proved unsuccessful, but 2-benzylamino-1-tetralone (VI; R = H), readily prepared by reductive condensation of 2-hydroxyiminotetralone and benzaldehyde in the presence of hydrogen and palladised charcoal, was sufficiently stable as its free base to permit direct alkylation. Thus, with prop-2-ynyl bromide in the presence of sodium hydrogen carbonate, it furnished the *N*-prop-2-ynyl derivative (VI; R = CH_2–C≡CH), which was readily hydrated by treatment with aqueous sulphuric–acetic acids and mercury(II) sulphate at room temperature to give the required diketone (VI; R = CH_2Ac); if the reaction mixture was heated, however, cleavage occurred with the formation in quantity of benzylaminoacetone, isolated as its hydrochloride. This unexpected reaction deserves further investigation.

Later it was found that the *N*-benzyl diketone (VI; R = CH_2Ac) could be obtained in one stage by direct alkylation with chloracetone. Catalytic debenzylation of compound (VI; R = CH_2Ac) furnished the corresponding secondary base (VII; R = H), which was converted into its *N*-benzoyl derivative (VII; R = Bz) in the usual manner. Attempts to cyclise this *N*-benzoyl diketone with alkali, potassium-t-butoxide, or sodium methoxide were unsuccessful, but ring closure was achieved, albeit in low yield, by the Stork technique [3]

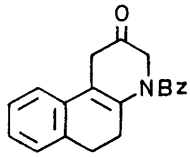


(VI)



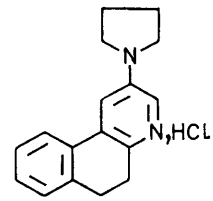
(VII)

(reaction with pyrrolidine followed by hydrolysis of the resulting enamine). The neutral product was a yellow crystalline ketone which on account of its strong i.r. absorption at 1730 cm^{-1} must be the βγ- (VIII) rather than the required αβ-unsaturated tricyclic ketone.

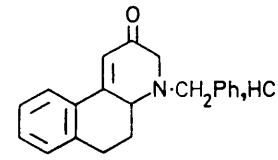


(VIII)

Extraction of the product at the crude enamine stage with 2N-hydrochloric acid furnished an almost equal amount of a yellow crystalline salt (IX), formed presumably as the result of *N*-debenzoylation and subsequent oxidative dehydrogenation.



(IX)



(X)

At that time it occurred to us that further activation of the terminal methyl grouping in compound (VII; R = Bz) was required in order to achieve a more ready cyclisation. Several unsuccessful attempts were made in this direction and it was not until much later that we considered the possibility of using magnesium methyl carbonate (MMC) [4] for this purpose. Stiles [5] had shown that this reagent carboxylates methyl ketones to give the corresponding β-keto-acids, and in the case of compound (VII; R = Bz) the resulting β-keto-acid would be expected to condense readily with the hydroaromatic ketone with subsequent loss of carbon dioxide. In the event, treatment of the *N*-benzoyl diketone with an excess of MMC produced a 50% yield of a tricyclic ketone, which, however, was again the βγ-unsaturated ketone (VIII). A similar reaction with the corresponding *N*-benzyl diketone (VII; *R* = CH_2Ph) gave, in low yield, the required αβ-unsaturated tricyclic ketone (X) recognised by its expected [2] i.r. spectrum ($\nu_{max.}$ 1660 cm^{-1}).

EXPERIMENTAL

I.r. spectra of solids were determined for Nujol mulls and those of oils for liquid films. Potentiometric titrations were performed for solutions in aqueous ethanol (1 : 1).

2-(N-*Acetonylmethylamino*)*acetophenone* (I; R = Me).—Solutions of phenacyl bromide (19·9 g) in anhydrous ether (100 ml) and *N*-benzylmethylaminoacetone [6] (19·5 g) in ether (100 ml) were mixed and left at room temperature for 4 days; a semi-crystalline gum formed. The supernatant liquid was removed by decantation and the residue was washed with fresh ether and dried *in vacuo*. The crude quaternary salt (25 g) was then hydrogenated in ethanol (200 ml) over 10% palladised charcoal (2 g) at room temperature and pressure (uptake 1745 ml in 1·25 h). Removal of catalyst and evaporation furnished the *base hydrobromide* (12·8 g) as needles (from propan-2-ol–ether), m.p. 143—144° (Found: C, 50·9; H, 5·1; N, 4·9. $C_{12}H_{16}BrNO_2$ requires C, 50·4; H, 5·6; N, 4·9%).

1,6-*Dihydro*-1-*methyl*-5-*phenyl*-3(2H)-*pyridone Hydrochloride* (II).—2N-Sodium hydroxide (90 ml) was added during 2 min to a solution of the preceding hydrobromide (20·7 g) in water (100 ml) with stirring at 2°. Stirring was continued for a further 1 min; the oil which had separated was isolated with ether, dissolved in ethanol, and treated with ethereal hydrogen chloride. The *pyridone hydrochloride* (9·5 g) which separated crystallised from ethanol

[3] G. Stork, A. Brizzolara, H. K. Landesman, J. Szmuszkovicz, and R. Terrel, *J. Amer. Chem. Soc.*, 1963, **85**, 207.

[4] H. L. Finkbeiner and M. Stiles, *J. Amer. Chem. Soc.*, 1963, **85**, 616.

[5] M. Stiles, *J. Amer. Chem. Soc.*, 1959, **81**, 2598.

[6] J. W. Magee and H. R. Henze, *J. Amer. Chem. Soc.*, 1940, **62**, 910.

(96%) in pale yellow needles, m.p. 174—176°, $\lambda_{max.}$ (EtOH) 207 (ε 9340), 227 (9450), and 284 (18,000), $\lambda_{max.}$ (EtOH–NaOH) 247 (16,000) and 340 (6380) nm, $\nu_{max.}$ 2932, 2354, 1671, 1603, and 1568 cm^{-1} (Found: C, 64·7; H, 6·1; Cl, 15·8; N, 6·2. $C_{12}H_{14}ClNO$ requires C, 64·4; H, 6·3; Cl, 15·9; N, 6·3%).

Cyclisation of 2-(N-*Acetonylmethylamino*)*acetophenone with Potassium t-Butoxide.*—A solution of potassium t-butoxide in t-butyl alcohol (0·7M; 30 ml) was added to the base hydrobromide (2·9 g) in methanol (70 ml) with stirring at 5°. The mixture was then stirred at room temperature for 2 h and 3N-methanolic hydrogen chloride (10 ml) was added. Potassium chloride was filtered off and the filtrate was evaporated to dryness *in vacuo* to give a trihydroxy-1-methyl-5-phenylpyridinium chloride monohydrate (1·5 g) as rhombs (from propan-2-ol–ether), m.p. *ca.* 120° which resolidified and then melted at 215—218° (decomp.), $\nu_{max.}$ 3200br, 1605, 1525, and 1460 cm^{-1}, pK_a 4·91 (Found: C, 53·0; H, 5·4; Cl, 12·9; N, 5·3%; equiv., 273. Calc. for $C_{12}H_{12}ClNO_3,H_2O$: C, 53·1; H, 5·2; Cl, 13·1; N, 5·3%; equiv., 272).

On heating at 100° and 1 mmHg for 4 h, the anhydrous salt was formed, m.p. 216—218° (decomp.), $\nu_{max.}$ 1600, 1525, and 1460 cm^{-1} (Found: C, 56·7; H, 4·9; Cl, 13·9; N, 5·7. Calc. for $C_{12}H_{12}ClNO_3$: C, 56·8; H, 4·8; Cl, 14·0; N, 5·5%).

2-*Acetamidomethyl*-2-*phenyl*-1,3-*dioxolan* (IV; R^1 = Me, R^2 = H).—A mixture of 2-acetamidoacetophenone [7] (32 g), ethylene glycol (25 ml), toluene-*p*-sulphonic acid (400 mg), and benzene (250 ml) was refluxed in an apparatus fitted with a water separator for 60 h. More toluene-*p*-sulphonic acid (1 g) was then added and refluxing was continued for a further 12 h; the reaction was then complete (i.r.). The cooled mixture was treated with anhydrous potassium carbonate and distilled, yielding the *dioxolan* (31 g, 75%) as an oil, b.p. 156—159° at 0·6 mmHg, which slowly crystallised (Found: C, 65·5; H, 6·2; N, 6·2. $C_{12}H_{15}NO_3$ requires C, 65·1; H, 6·8; N, 6·3%).

2-(*Acetonylamino*)*acetophenone* (I; R = H).—(*a*) The foregoing dioxolan (4·42 g) was added to a suspension of sodium hydride (50% oil dispersion; 1·01 g) in dimethylformamide (25 ml) under nitrogen and the mixture was heated at 60° for 15 min, gas evolution had then ceased. The solution was cooled to 25° and freshly distilled prop-2-ynyl bromide (2·4 g) was added in one portion; an exothermic reaction set in. The mixture was left overnight and poured into water, and the product was isolated with benzene as a viscous oil (4·6 g), $\nu_{max.}$ 3350 cm^{-1} (C≡C).

The latter was heated under reflux with a mixture of 2N-hydrochloric acid (50 ml), methanol (100 ml), and mercury(II) sulphate (100 mg) for 4 h. The resulting solution was treated with charcoal and evaporated to small bulk; the *base hydrochloride* (1·84 g) separated as plates, m.p. 195—196°, $\nu_{max.}$ 1718 (aliphatic C=O) and 1690 (aromatic C=O) cm^{-1}, pK_a 6·02 (Found: C, 58·3; H, 6·6; Cl, 15·8; N, 6·5%; equiv. 232. $C_{11}H_{14}ClNO_2$ requires C, 58·0; H, 6·1; Cl, 15·6; N, 6·1%; equiv., 228).

(*b*) β-Ethoxyallyl chloride (60 g) [8] was added to a solution of sodio-2-acetamidoacetophenone (24 g; prepared as before) in dimethylformamide (150 ml) under nitrogen and the mixture was heated at 60° overnight. The product, isolated as in (*a*), was an oil (no i.r. absorption at 980 cm^{-1} indicating absence of CH_2=C<), which was dissolved in aqueous ethanol (50%; 300 ml). Amberlite 120 (H^+) ion-exchange resin (10 g) was added and the mixture was then heated with stirring under reflux for 30 h. Filtration, evaporation of the filtrate to dryness *in vacuo*, and trituration with ether yielded 2-(N-*acetonylacetamido*)*acetophenone* (I; R = Ac) (9·3 g) as needles, m.p. 95—96°, $\nu_{max.}$ 1716 and 1683 (C=O), and 1640 (CO·N<) cm^{-1} (Found: C, 66·8; H, 6·5; N, 6·0. $C_{13}H_{15}NO_3$ requires C, 66·9; H, 6·5; N, 6·0%).

This amide (1·17 g) was heated with 5N-hydrochloric acid (6 ml) under reflux for 1 h. The cooled solution deposited the *base hydrochloride* as plates (930 mg), identical with the material prepared in (*a*).

3-*Hydroxy*-5-*phenylpyridine.*—2N-Sodium hydroxide (1 ml) was added to a solution of 2-(*N*-acetonylacetamido)-acetophenone (500 mg) in aqueous ethanol (50%; 4 ml); an orange colouration developed and the mixture was kept at room temperature for 5 min. A small excess of 2N-hydrochloric acid was then added, followed by saturated aqueous sodium hydrogen carbonate until the mixture was alkaline. An oil soon separated which slowly crystallised during 48 h at 2°. Filtration yielded the *pyridol* (50 mg), as cream needles (from propan-2-ol), m.p. 210—211°, $\lambda_{max.}$ (EtOH) 216 (ε 20,200), 245 (9700) and 294 (7300), $\lambda_{max.}$ (EtOH–NaOH) 230 (19,000) and 319 (4900) nm, $\nu_{max.}$ 2700—2300br cm^{-1} (zwitterion), pK_a 3·7 and 9·05 (Found: C, 76·8; H, 5·7; N, 8·1. $C_{11}H_9NO$ requires C, 77·2; H, 5·3; N, 8·2%).

3-*Phenyl*-5-*pyrrolidin*-1-*ylpyridine* (V).—A mixture of 2-(*N*-acetonylacetamido)acetophenone (2 g), pyrrolidine (2 ml), and benzene (100 ml) was refluxed in an apparatus fitted with a water separator for 16 h, during which time water (0·3 ml) was collected. The cooled mixture was then washed with water, dried, and evaporated to dryness. Crystallisation of the residue from ether furnished the *pyridine* (150 mg) as needles, m.p. 119—121°, $\nu_{max.}$ 1582 cm^{-1} (Found: C, 80·1; H, 7·2; N, 13·0. $C_{15}H_{16}N_2$ requires C, 80·3; H, 7·2; N, 12·5%).

Treatment of the ethereal mother liquors with ethereal hydrogen chloride caused deposition of the *base hydrochloride* (820 mg), as pale yellow rhombs (from propan-2-ol–ether), m.p. 230—232°, $\nu_{max.}$ 1610 cm^{-1}, $\lambda_{max.}$ (0·1N-HCl) 216 (ε 14,250), 237 (15,400), 269 (19,450), and 368 (3890) nm, pK_a 5·18 (Found: C, 69·0; H, 6·7; Cl, 13·7; N, 10·6%; equiv., 261. $C_{15}H_{17}ClN_2$ requies C, 69·1; H, 6·6; Cl, 13·6; N, 10·8%; equiv., 261).

Methyl N-*Acetonyl*-N-*phenacylcarbamate* (I; R = CO_2Me).—Methyl phenacylcarbamate was acetalised and alkylated (Na salt) with prop-2-ynyl bromide; the product was hydrated and hydrolysed as described for the corresponding *N*-acetyl derivative to give *methyl* N-(2-*phenyl*-1,3-*dioxolan*-2-*ylmethyl*)*carbamate* (IV; R^1 = OMe, R^2 = H) (96%), m.p. 66—68°, $\nu_{max.}$ 3430 (NH), 1720 (ester), and 1540 (CONH) cm^{-1} (Found: C, 61·2; H, 6·5; N, 6·1. $C_{12}H_{15}NO_4$ requires C, 60·8; H, 6·4; N, 5·9%) and *methyl* N-(2-*phenyl*-1,3-*dioxolan*-2-*ylmethyl*)-N-*prop*-2-*ynylcarbamate* (IV; R^1 = OMe, R^2 = CH_2·C≡CH) (72%), b.p. 123—124° at 0·1 mmHg, $\nu_{max.}$ 3350 (C≡C), 3000, 2930, 2105 (C≡C), and 1710 (ester) cm^{-1} (Found: C, 65·0; H, 6·2; N, 5·3. $C_{15}H_{17}NO_4$ requires C, 65·4; H, 6·2; N, 5·1%).

The *diketo-urethane* (I; R = CO_2Me) (30%) was obtained as needles, m.p. 65—66° (from benzene–light petroleum), $\nu_{max.}$ 1720, 1705, and 1685 cm^{-1} (Found: C, 62·9; H, 6·1; N, 5·4. $C_{13}H_{15}NO_4$ requires C, 62·6; H, 6·1, N, 5·6%).

2-*Benzylamino*-3,4-*dihydronaphthalen*-1(2H)-*one* (VI; R = H).—A suspension of 2-hydroxyimino-3,4-dihydronaphthal-

[7] A. Baeyer and F. Bloem, *Ber.*, 1882, **15**, 2154.
[8] Ger. Pat., 614,462/1933 (*Chem. Abs.*, 1935, **29**, 5994).

en-1(2*H*)-one [9] (17·5 g) and 10% palladium–charcoal (1·75 g) in ethanol (200 ml) was stirred in hydrogen (uptake 4·9 l in 1 h). Benzaldehyde (16 ml) was added and hydrogenation was continued until gas absorption ceased (*ca.* 3·7 l). After removal of catalyst, excess of concentrated hydrochloric acid was added and the solution was evaporated to dryness *in vacuo*. Trituration with acetone furnished the *amine hydrochloride* (17 g) as plates (from propan-2-ol–ether), m.p. 195—196°, $\nu_{max.}$ 1680 cm^{-1} (C=O) (Found: C, 71·2; H, 6·1; N, 4·9. $C_{17}H_{18}ClNO$ requires C, 71·0; H, 6·30; N, 4·9%). The N-*acetyl derivative* formed prisms (from benzene–light petroleum), m.p. 82—83° (Found: C, 78·0; H, 6·8; N, 4·9. $C_{19}H_{19}NO_2$ requires, C, 77·8; H, 6·5; N, 4·8%).

2-(N-*Benzylprop*-2-*ynylamino*)-3,4-*dihydronaphthalen*-1(2H)-*one* (VI; R = CH_2·C≡CH).—A mixture of the preceding hydrochloride (10 g), sodium hydrogen carbonate (10 g), freshly distilled prop-2-ynyl bromide (30 ml), and acetone (100 ml) was boiled under reflux with stirring in nitrogen for 2·5 h and filtered. Evaporation furnished an oil which was dissolved in ether (100 ml) and the solution was treated with excess of ethereal hydrogen chloride. A yellow solid was precipitated which crystallised from acetone to furnish the *base hydrochloride* (6·5), m.p. 150—151° $\nu_{max.}$ 3180 and 2120 (C≡C), and 1680 (C=O) cm^{-1} (Found: C, 73·6; H, 6·4; N, 4·4. $C_{20}H_{20}ClNO$ requires C, 73·7; H, 6·2; N, 4·3%).

Attempted Hydration of the Acetylene (VI; R = CH_2·C≡CH).—Mercury(II) sulphate (250 mg) was added to a solution of the foregoing salt (1·0 g) in 2N-sulphuric acid (5 ml) and acetic acid (10 ml) and the mixture was heated at 95° for 2·5 h. Barium chloride dihydrate (1·5 g) in water (25 ml) and 2N-hydrochloric acid (10 ml) were then added, and the mixture was heated for 5 min and filtered (charcoal). Evaporation to dryness *in vacuo* and trituration with acetone furnished *benzylaminoacetone hydrochloride* (250 mg), needles (from acetone), m.p. 170—171°, $\nu_{max.}$ 3440 (NH) and 1720 (C=O) cm^{-1}, pK_a 6·95 (Found: C, 60·0; H, 7·1; Cl, 17·9; N, 7·1%; equiv., 199. $C_{10}H_{14}ClNO$ requires C, 60·2; H, 7·1; Cl, 17·8; N, 7·0%; equiv., 200).

2-(N-*Acetonylbenzylamino*)-3,4-*dihydronaphthalen*-1(2H)-*one* (VI; R = CH_2Ac).—(*a*) A mixture of 2-(*N*-benzylprop-2-ynylamino)-3,4-dihydronaphthalen-1(2*H*)-one hydrochloride (4·5 g), mercury(II) sulphate (900 mg), 20N-sulphuric acid (6 ml), and acetic acid (30 ml) was stirred at room temperature for 6 h and then evaporated to small bulk *in vacuo*. Water and excess of sodium hydrogen carbonate were added and the free base was isolated with ethyl acetate as an oil. A solution of the latter in ether was treated with ethereal hydrogen chloride to give a gummy salt which crystallised on treatment with hot acetone to give the hydrated *diketone hydrochloride* (60%), m.p. 130—132° (frothing), $\nu_{max.}$ 1720 (aliphatic C=O) and 1685 (aromatic C=O) cm^{-1} (Found: C, 64·7; H, 6·6; N, 3·9. $C_{20}H_{22}ClNO_2,1·5H_2O$ requires C, 64·8; H, 6·8; N, 3·8%).

(*b*) A suspension of 2-benzylamino-3,4-dihydro-1(2*H*)-naphthalenone hydrochloride (3·5 g) and sodium hydrogen carbonate (6 g) in acetone (50 ml) containing purified chloroacetone (10 ml) was stirred at 60° under nitrogen for 17 h, cooled, and filtered. Evaporation of the filtrate to dryness *in vacuo* and treatment of the residual oil with ethereal hydrogen chloride as previously furnished the same product (3·0 g), m.p. 129—131°.

2-(*Acetonylamino*)-3,4-*dihydronaphthalen*-1(2H)-*one* (VII; R = H).—A solution of the preceding hydrochloride (1·7 g) in ethanol (30 ml) was stirred in the presence of 10% palladium–charcoal in hydrogen until the initial rapid absorption of gas had abated (1 ml min^{-1}). During this process, much solid separated; the mixture was heated to 80° and filtered from catalyst. The filtrate on evaporation furnished, after trituration with acetone (5 ml), the *amine hydrochloride* (90%), m.p. 204° (decomp.), $\nu_{max.}$ 1720 and 1690 cm^{-1} (Found: C, 61·30; H, 6·5; N, 5·3. $C_{13}H_{16}ClNO_2$ requires C, 61·5; H, 6·3; N, 5·5%). The N-*benzoyl derivative* formed prisms (from methanol), m.p. 152—154°, $\nu_{max.}$ 1720 and 1680 (C=O), and 1625 (CO–N<) cm^{-1} (Found: C, 74·6; H, 6·0; N, 4·4. $C_{20}H_{19}NO_3$ requires C, 74·7; H, 6·0; N, 4·4%).

Experiments on the Cyclisation of 2-(N-*Acetonylbenzamido*)-3,4-*dihydronaphthalen*-2(1H)-*one* (VII; R = Bz).—(a) *With pyrrolidine*. Pyrrolidine (2 ml) was added to a suspension of the starting amide (5·0 g) in benzene (50 ml) and the mixture was refluxed in an apparatus fitted with a water separator for 8 h. The cooled mixture was evaporated to dryness *in vacuo* to give a red viscous oil ($\nu_{max.}$ 1630 and 1608 cm^{-1}). A solution of the latter in aqueous acetic acid (1 : 1; 40 ml) containing hydrated sodium acetate (10 g) was heated at 95° for 30 min. The cooled solution furnished a buff powder (3·5 g) which crystallised from propan-2-ol (50 ml) to give 4-*benzoyl*-3,4,5,6-*tetrahydrobenzo*[f]*quinolin*-2(1H)-*one* (VIII) (1·8 g), yellow prismatic needles, m.p. 150—152°, $\lambda_{max.}$ (EtOH) 228 (ε 19,100), 279 (10,780), and 304 (13,600) nm, $\nu_{max.}$ 1730 (aliphatic C=O), 1647 (CO–N<), and 1620 cm^{-1} (Found: C, 78·9; H, 5·8; N, 4·8. $C_{20}H_{17}NO_2$ requires C, 79·2; H, 5·7; N, 4·6%). If, however, the crude red oil obtained from the cyclisation reaction, was redissolved in benzene and the solution extracted with 2N-hydrochloric acid (50 ml), the acid extract slowly deposited 5,6-*dihydro*-2-*pyrrolidin*-1-*ylbenzo*[f]*quinoline hydrochloride monohydrate* (IX) (900 mg) as yellow plates, m.p. 283° (decomp), $\lambda_{max.}$ (50%; H_2O–Me_2N·CHO) 210 (ε 26,600), 252 (18,500), 265 (20,000), 276 (18,600), and 365 (4580) nm, $\nu_{max.}$ 1617, 1592, and 1541 cm^{-1}, pK_a 3·0 and 5·6 (Found: C, 67·3; H, 6·9; Cl, 11·9; N, 9·5. $C_{17}H_{19}ClN_2,H_2O$ requires C, 67·0; H, 7·0; Cl, 11·6; N, 9·2%).

(b) *With magnesium methyl carbonate*. The starting amide (2·0 g) was added to a solution of MMC [4] [from magnesium (900 mg)] in dimethylformamide (25 ml) and the mixture was heated at 110—115° for 70 min. Solvent was then removed at 70° and 1 mmHg and the residue was dissolved in hot benzene (250 ml). The cooled solution was treated cautiously with excess of 2N-hydrochloric acid and the organic extract was washed successively with 2N-sodium carbonate and water. Removal of solvent furnished a yellow foam (1·68 g) which on crystallisation from propan-2-ol gave the *N*-benzoyl ketone (VIII) (850 mg), m.p. 151—152°, identical with the product described in (*a*).

4-*Benzyl*-4,4a,5,6-*tetrahydrobenzo*[f]*quinolin*-2(3H)-*one Hydrochloride* (X).—2-(*N*-Acetonylbenzylamino)3,4-dihydronaphthalen-1(2H)-one hydrochloride (1·0 g) was added to a solution of magnesium methyl carbonate in dimethylformamide (15 ml as before) and the mixture was heated at 110° for 1 h. After removal of solvent *in vacuo*, the residue was stirred with benzene (200 ml) and water (100 ml) for 15 min and the gelatinous mixture was filtered as rapidly as possible through kieselguhr. Evaporation of the green organic extract furnished a gum which was extracted with ether (100 ml); the ethereal extract was treated with ethereal hydrogen chloride. The gummy salt obtained

[9] F. Straus and W. Ekhard, *Annalen*, 1925, **444**, 162.

after removal of ether by decantation crystallised spontaneously on treatment with hot acetone (3 ml) to give the *base hydrochloride* (X) as a hemihydrate (120 mg), m.p. 175—177°, $\lambda_{max.}$ (EtOH) 208 (ε 21,800), 228 (10,900), and 296 (18,700) nm, $\nu_{max.}$ 1660 (conj. C=O) and 1582 cm^{-1} (Found: C, 71·4; H, 6·3; N, 4·4. $C_{20}H_{20}ClNO,0{\cdot}5H_2O$ requires C, 71·7; H, 6·3; N, 4·4%). On drying at 60° and 1 mmHg, the *anhydrous salt* was obtained (Found: C, 73·6; H, 6·2; N, 4·3. $C_{20}H_{20}ClNO$ requires C, 73·7; H, 6·2; N, 4·3%).

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