Intramolecular Cyclisation of 2-Aminobenzophenones; a New 9-Acridone Synthesis

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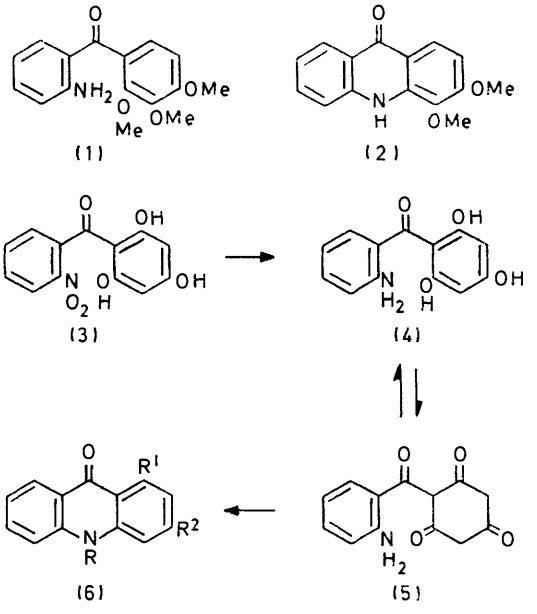
Cyclisation of 2-amino- or 2-acetamido-2'-methoxybenzophenones occurred in the presence of sodium hydride to give 9-acridones. This is a method of wide applicability for the synthesis of substituted acridones. A mechanism for the cyclisation is discussed.

In connection with studies on the synthesis of natural products under biomimetic conditions [1] we became interested in the synthesis of naturally occurring 9-acridones, a group of alkaloids found only in the plant family Rutaceae.[2] The similarity in ring number, ring size, and substituent pattern of the acridone alkaloids to xanthones [3] suggested that oxidative coupling of 2-aminobenzophenones might give the 9-acridone system in an analogous manner to that reported for the conversion of 2-hydroxybenzophenones into xanthones.[4] The poor yields which were obtained for this type of cyclisation [5] led us to investigate alternative methods for the ring closure of 2-aminobenzophenones. In our earlier oxidative experiments [5] 2'-amino-2,3,4-trimethoxybenzophenone (1) cyclised to 3,4-dimethoxy-9-acridone (2) in 7% yield, whereas reduction of 2,4,6-trihydroxy-2'-nitrobenzophenone (3) gave 1,3-dihydroxy-9-acridone (6; R = H, $R^1 = R^2 = OH$), quantitatively, presumably *via* the amine (4).[6] Our interpretation of these cyclisations involved intramolecular displacement of the adjacent *ortho*-methoxy-group by nucleophilic nitrogen, or, in the case of the amine (4), a Schiff-base-type condensation with the keto-form of the phloroglucinol ring (5). To establish the utility of this type of cyclisation a number of aminobenzophenones and their derivatives were synthesised for study.



[1] R. Breslow, *Chem. Soc. Rev.*, 1972, **1**, 553.
[2] P. Waterman, *Biochem. Syst. Ecol.*, 1975, **3**, 149 (*Chem. Abs.*, 1976, **84**, 56459).
[3] I. Carpenter, H. D. Locksley, and F. Scheinmann, *Phytochemistry*, 1969, **8**, 2013.
[4] P. Gupta and J. R. Lewis, *J. Chem. Soc.* (*C*), 1971, 629.
[5] I. H. Bowen, P. Gupta, M. S. Khan, and J. R. Lewis, *J.C.S. Perkin I*, 1972, 2524.
[6] I. H. Bowen, P. Gupta, and J. R. Lewis, *Chem. Comm.*, 1970, 1625.

Our first series of reactions was carried out with 2-acetamido-2′-methoxybenzophenones since it was considered that the action of a strong base on the acetamido-group would produce unequivocally the nitrogen nucleophile thought to be necessary for the cyclisation. Indeed treatment of 2-acetamido-2′-methoxybenzophenone (7; R = Ac, R^1 = R^2 = H) with sodium hydride in dimethyl sulphoxide gave 9-acridone (6; R = R^1 = R^2 = H) in 68% yield at room temperature. Other acetamidobenzophenones behaved in a similar manner (Table 1).

Because the original cyclisation reactions involved only amino-groups, *i.e.* in (1) and (4), the effect of sodium hydride on 2-amino-2′-methoxybenzophenones was examined and the corresponding 9-acridones were obtained in a number of cases (Table 1).

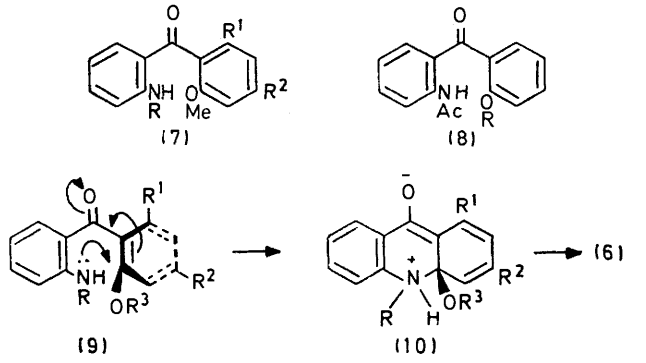
TABLE 1

Results of cyclisation reactions of benzophenones

	Temp. (°C)	Base	Acridone (%)
2′-AcNH			
2-MeO	20	NaH	68
	100	NaH	79
	20	NaOEt	0
2,4-$(MeO)_2$	20	NaH	21
	60	NaH	21
2,4,6-$(MeO)_3$	20	NaH	7
	100	NaH	7
2-Ts	20	NaH	94
2′-NH_2			
2-MeO	20	NaH	47
	100	NaH	58
	100	Me_2N·CHO	0
2,4-$(MeO)_2$	20	NaH	53
	100	NaH	58
	20	hv	0
3-HO	20	hv	0
2,4,6-$(MeO)_3$	50	NaH	35
	100	NaH	13
	100	NaOH	0
2,3,4-$(MeO)_3$	100	NaH	81
2-HO-4,6-$(MeO)_2$	50	NaH	0
2,4,6-$(MeO)_3$-imine (11; R = NH_2)	100	NaH	0

Since these cyclisations involved the displacement of a methoxy-group it was considered that its replacement by a better leaving group, *e.g.* *p*-tolylsulphonyloxy, would accelerate and enhance ring closure; this was observed when 2-acetamido-2′-*p*-tolylsulphonyloxybenzophenone (8; R = Ts) was rapidly and completely converted into 9-acridone (6; R = R^1 = R^2 = H) at room temperature by sodium hydride in dimethyl sulphoxide in less than 15 minutes.

Our interpretation of the mechanism for cyclisation involved nucleophilic displacement of the methoxy-group, but a number of other factors have been shown to be involved. The carbonyl group is a prerequisite for cyclisation since the imine (11; R = NH_2) does not cyclise under conditions where the corresponding benzophenone (7; R = H, R^1 = R^2 = OMe) does. A benzophenone containing a hydrogen-bonded carbonyl group, as in (7; R = H, R^1 = OH, R^2 = OMe), does not cyclise, but its *O*-methylated counterpart (7; R = H, R^1 = R^2 = OMe) does. The *p*-tolylsulphonyloxy-group is more rapidly displaced than the methoxy-group. These observations suggest that the intramolecular nucleophilic attack emanating from the acetamido (NHAc) or amino



(NH_2) group is best accommodated by the non-planarity of the aromatic rings consequent to the availability of an electron sink (C=O group) to accommodate the incoming negative charge [(9) ⟶ (10)]. Final displacement of OR^3 [(10) ⟶ (6)] will be enhanced by its ability to stabilise the developing negative charge.

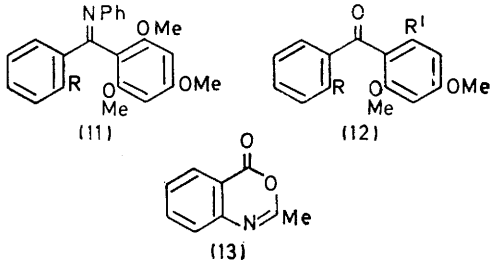
Intramolecular displacements of a similar nature but under more vigorous conditions have been reported:[7] elimination of chloride ion from a benzoylaminobenzophenone occurs with sodamide in liquid ammonia but this does not preclude the formation of a benzyne intermediate.[8] The use of carbanions to expel hydride or chloride ion in phenylacetonitriles has been reported,[9] and the use of carbanions in the synthesis of anthraquinones.[10]

We observed no cyclisation product after irradiation of the aminobenzophenones (7; R = R^1 = R^2 = H) and (7; R = R^1 = H, R^2 = OMe) although photo-oxidation of an *o*-aminophenol results in a phenoxazin-3-one.[11]

Two general methods of synthesis of aminobenzophenones were employed: (i) direct Friedel–Crafts reaction between 2-nitrobenzoyl chloride and the appropriate phenol, and (ii) a modified procedure where 2-nitrobenzamide was first treated with phosphorus pentachloride to give the 2-nitrobenzimidoyl chloride, which was subsequently treated, in the presence of aluminium chloride, with the phenol to produce an *N*-(nitrodiphenylmethylene)aniline[12] [*e.g.* (11; R = NO_2)], the nitro-group being subsequently reduced. Method (ii) did not prove of general utility, however, owing to difficulty in hydrolysing the imines to benzophenones; a similar difficulty had been observed with 2′,2,4,6-tetrahydroxydiphenylmethyleneamine.[13] The most satisfactory synthesis involved condensation of 2-methyl-3,1-benzoxazin-

[7] R. T. Parfitt, *J. Chem. Soc.*, 1966, 87.
[8] Guo-Shyoung, J. Chen, and M. S. Gibson, *J.C.S. Perkin I*, 1975, 1138.
[9] D. W. Bayne, G. Tennant, and T. W. M. Spence, *Chem. Comm.*, 1972, 849.
[10] J. S. Davies, V. H. Davies, and C. H. Hassall, *J. Chem. Soc. (C)*, 1969, 1873.
[11] T. Ikekawa, N. Uehara, and T. Okuda, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 1705.
[12] U. R. Usgankar and G. V. Jodhar, *J. Ind. Chem. Soc.*, 1963, **40**, 27.
[13] H. Nishikawa and R. Robinson, *J. Chem. Soc.*, 1922, 839.

4-one (13) with the Grignard reagent from the appropriate bromomethoxybenzene to give directly a 2-acetamidobenzophenone.[14] Hydrolysis of the acetamide under dilute acidic conditions gave the corresponding amine, whereas under non-aqueous conditions demethylation occurred at the *ortho*-methoxy-group. The readiness of this latter type of hydrolysis is related to the ease with which methoxy-groups *peri* to a carbonyl group are preferentially demethylated by Lewis acids.



In the mass spectrometer the methoxy-acetamidobenzophenones lost an acetyl group followed by a methyl group and underwent typical aryl–carbonyl cleavages. In a few cases 9-acridone was produced (*m/e* 195), *e.g.* from 2-acetamido-2′-hydroxybenzophenone and 2-acetamido-2′-*p*-tolylsulphonyloxybenzophenone. With the amino-methoxybenzophenones loss of a methoxy-group and aryl–carbonyl cleavages were the main fragmentations. With 2-nitrobenzophenones loss of a methoxy-group and aryl–carbonyl cleavages occurred, and with 2,4,6-trihydroxy-2′-nitrobenzophenone (3) the primary fragmentation was the result of loss of NHO_2 with formation of 1,3-dihydroxyxanthone [*m/e* 228.0420 ($C_{13}H_8O_4$)].

EXPERIMENTAL

I.r. spectra were measured for KBr discs and n.m.r. spectra for solutions in $CDCl_3$ unless stated otherwise. Mass spectra were measured with an A.E.I. MS 30 spectrometer.

2,4,6-Trihydroxy-2′-nitrobenzophenone (3).—2-Nitrobenzoyl chloride (10.0 g) mixed with anhydrous aluminium chloride (8.0 g) in dry ether (50 ml) was added to dry phloroglucinol (12.0 g) in ether (50 ml) at 0 °C. The mixture was stirred for 3 h, poured into iced dilute hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with dilute hydrochloric acid and water, dried, and evaporated leaving an oil which solidified (4.5 g). Crystallisation from benzene gave (3) as *prisms* (3.2 g), m.p. 182—184°, $\lambda_{max.}$ (EtOH) 213 (log ε 4.51), 228sh (4.34), and 295 nm (4.31), $\nu_{max.}$ 3 380, 3 320 (OH), and 1 640 cm^{-1} (bonded CO), τ ($CDCl_3$–CD_3OD, 4 : 1) 1.82 (1 H, d *J* 8 Hz, 3′-H), 2.18—2.80 (3 H, m, 4′-, 5′-, and 6′-H), and 4.19 (2 H, s, 3- and 5-H) (Found: C, 56.8; H, 3.2%; M^+, 275.0429. $C_{13}H_9NO_6$ requires C, 56.7; H, 3.3%; *M*, 275.0429), *m/e* 275(5%), 229(14), 228(100), 153(11), 141(45), 134(38), and 104(22) (accurate *m/e* 228.0420; $C_{13}H_8O_4$ requires 228.0422).

Reduction of 2,4,6-Trihydroxy-2′-nitrobenzophenone (3).—The benzophenone (3) (1.0 g) was dissolved in ethanol (30 ml) containing water (3 ml), ammonium chloride (4.0 g), and zinc dust (4.0 g) and the mixture was stirred overnight (16 h) at room temperature; it was then filtered and the ethanol removed. A solution of the residue in ethyl acetate (50 ml) was filtered, washed with water, dried ($MgSO_4$) filtered, and evaporated to give a green solid (850 mg) which crystallised from acetone to give 1,3-dihydroxy-9-acridone (6; R = R^1 = R^2 = H), m.p. *ca.* 350° (decomp.), $\lambda_{max.}$ (EtOH) 210 (log ε 4.07), 221.5 (4.18), 244(4.44), 259.5(4.29), 269(4.68), 294 (4.12), 313sh (3.72), 328 (3.88), and 392 nm (3.90).

2-Acetamido-2′-methoxybenzophenone (7; R = Ac, R^1 = R^2 = H).—2-Bromoanisole (23 g) dissolved in dry tetrahydrofuran (100 ml) was added dropwise to magnesium turnings (3 g) under nitrogen; when the Grignard reaction was complete the solution was added dropwise to 2-methyl-3,1-benzoxazin-4-one (20 g; prepared from anthranilic acid and acetic anhydride by distillation) dissolved in dry benzene, with stirring. After 2 h the mixture [14] was diluted with ice and dilute hydrochloric acid and the organic layer washed with water, dried, and evaporated to give *2-acetamido-2′-methoxybenzophenone* (19 g), which crystallised from ethanol; m.p. 146—149°, $\lambda_{max.}$ (MeOH) 211sh (log ε 4.20), 233 (4.33), 262 (3.95), 269 (3.94), and 326 nm (3.61), $\nu_{max.}$ 3 200 (NH) and 1 680 cm^{-1} (CO), τ 1.25 (1 H, d, *J* 8.5 Hz, H-2), 2.3—3.3 (7 H, complex, ArH), 6.27 (3 H, s, OCH_3), and 7.75 (3 H, s, Ac) (Found: C, 71.3; H, 5.3. $C_{16}H_{15}NO_3$ requires C, 71.4; H, 5.6%), *m/e* 269(100%), 227(32), 226(56, 212(45), 210(13), 209(32), 196(32), 135(32), 134(25), 120(20), and 104(16).

2-Amino-2′-methoxybenzophenone (7; R = H, R^1 = R^2 = H).—The foregoing acetamide (3 g) was dissolved in methanol (2.0 ml) containing concentrated hydrochloric acid (15 ml). The mixture was refluxed for 2 h, cooled and basified, and extracted with ethyl acetate. Work-up gave the *amine* (2 g), which crystallised from methanol; m.p. 110—113°, $\lambda_{max.}$ (MeOH) 207 (log ε 4.32), 227 (4.35), 262 (3.85), and 382 nm (3.74), $\nu_{max.}$ 3 470, 3 360 (NH_2), and 1 630 cm^{-1} (bonded CO), τ 2.4—3.8 (10 H, complex, ArH, NH_2) and 6.24 (3 H, s, OCH_3) (Found: C, 73.9; H, 5.8. $C_{14}H_{13}NO_2$ requires C, 74.0; H, 5.8%), *m/e* 227(100%), 226(28), 212(28), 211(10), 209(10), 196(28), 135(28), and 120(45).

Cyclisation of 2-Acetamido-2′-methoxybenzophenone.—The benzophenone (7; R = Ac, R^1 = R^2 = H) (0.5 g) was dissolved in dimethyl sulphoxide (20 ml) and sodium hydride (60%; 94 mg) was added with stirring. After 24 h at room temperature the mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with sodium hydroxide solution and water, dried, and evaporated to give a yellow solid (0.5 g), which crystallised from methanol as yellow prisms (247 mg, 68%), m.p. *ca.* 341° (decomp.), identical (mixed m.p. and u.v. spectrum) with 9-acridone (6; R = R^1 = R^2 = H).

2′-Acetamido-2,4-dimethoxybenzophenone (7; R = Ac, R^1 = H, R^2 = OMe).—4-Bromo-1,3-dimethoxybenzene (18.4 g) was converted into the Grignard reagent in tetrahydrofuran (100 ml) and added to the benzoxazinone (13) (13.7 g) dissolved in benzene (50 ml) at 0 °C. After stirring for 2 h the mixture was worked up in the usual way to give an oil which crystallised from benzene–methanol (1 : 1) to give the *acetamide* as a pale yellow solid (4.0 g), m.p. 93—95°, $\lambda_{max.}$ (EtOH) 208.5 (log ε 4.32), 231sh (4.33), 236 (4.35), 263 (3.95), 270 (3.95), and 323 nm (3.82), $\nu_{max.}$ 3 260 (NH), 1 685 (CONH), 1 625 cm^{-1} (CO), τ 1.27 (1 H, m, H-3′), 2.4—3.6 (6H, complex, ArH), 6.12 (3 H, s, 4-OCH_3), 6.27 (3 H, s, 2-OCH_3), and 7.74 (3 H, s, Ac) (Found: C, 68.1; H, 5.4. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7%), *m/e* 299(40%), 257(14), 256(100), 242(20), 240(20), 239(11), 226(20), 165(63), 139(40), and 119(32).

[14] W. A. Lothrop and P. A. Goodwin, *J.A.C.S.*, 1943, **65**, 363.

N-[(2-*Nitrophenyl*)-(2,4,6-*trimethoxyphenyl*)*methylene*]*aniline* (11; R = NO_2).—The imidoyl chloride (20 g) prepared from 2-nitrobenzanilide [12] was treated directly with 1,3,5-trimethoxybenzene (26 g) in ether (100 ml) containing aluminium chloride (11 g) for 3 h at 0 °C. The mixture was poured into ice–dilute hydrochloric acid and the organic layer separated, washed several times with dilute hydrochloric acid and water, dried, and evaporated to give a mixture (40 g) which was separated by chromatography on silica gel. Elution with benzene produced 1,3,5-trimethoxybenzene (11 g), followed by the *imine* (11; R = NO_2) (18 g) which crystallised from ethanol as pale yellow prisms, m.p. 172—174°, $\lambda_{max.}$ (MeOH) 207 (log ε 4.68), 260 (3.82), 270 (3.68), 288 (3.67), and 305 nm (3.48), $\nu_{max.}$ 1 620 cm^{-1}, τ [$(CD_3)_2CO$] 2.15—3.45 (9 H, complex, ArH), 3.82 (2 H, s, 3- and 5-H), 6.22 (3 H, s, 4-OMe), and 6.39 (6 H, s, 2- and 6-OMe) (Found: C, 67.5; H, 4.9. $C_{22}H_{20}N_2O_5$ requires C, 67.35; H, 5.1%), *m/e* 392(40%), 375(40), 347(13), 346(71), 344(32), 300(32), 270(100), 202(32), and 178(45).

2′-*Amino*-2,4,6-*trimethoxybenzophenone* (7; R = H, R^1 = R^2 = OMe).—The nitro-compound (12; R = NO_2, R^1 = OMe) (10 g) was dissolved in acetic acid (80 ml) containing water (15 ml), and iron powder (314 g) was added over 80 min. The mixture was heated for 2 h at *ca.* 95 °C, cooled, filtered, diluted with water, and worked up to give a mixture (8.2 g), which on silica gel chromatography and elution with benzene followed by benzene–ethyl acetate (9 : 1) gave first the *aminobenzophenone* (7; R = H, R^1 = R^2 = OMe) (4.5 g), which crystallized from methanol as yellow plates, m.p. 182—184°, $\lambda_{max.}$ (EtOH) 207 (log ε 4.70), 229 (4.40), 260 (3.87), and 3.61 nm (3.79), $\nu_{max.}$ 3 475, 3 350 (NH_2) and 1 630 cm^{-1}, τ 2.6—3.75 (6 H, complex, NH_2, ArH), 3.75 (2 H, s, 3- and 5-H), 6.18 (3 H, s, 4-OMe), and 6.32 (6 H, s, 2- and 6-OMe) (Found: C, 66.7; H, 5.9. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 6.0%), *m/e* 287(56%), 256(32), 195(16), 168(100), 120(13), and 119(32). Continued elution with benzene–ethyl acetate (9 : 1) gave the aminodiphenylmethyleneaniline (11; R = NH_2) (2.5 g), which crystallised from methanol as yellow prisms, m.p. 166—168°, $\lambda_{max.}$ (MeOH) 208 (log ε 4.68), 234 (4.61), 262sh (3.99), and 351 nm (3.86), $\nu_{max.}$ 3 475 and 3 240 cm^{-1} (NH_2), τ 2.6—3.6 (11 H, complex, NH_2, ArH), 4.04 (2 H, s, 3- and 5-H), 6.28 (3 H, s, 4-OMe), and 6.42 (6 H, s, 2- and 6-OMe) (Found) C, 72.6; H, 5.8. $C_{22}H_{22}N_2O_3$ requires C, 72.9; H, 6.1%), *m/e* 362(32%), 332(11), 331(100), 270(32), 195(5), and 181(8).

2′-*Acetamido*-2,4,6-*trimethoxybenzophenone* (7; R=Ac, R^1 = R^2 = OMe).—The aminobenzophenone (7; R = H, R^1 = R^2=OMe) (0.76 g) was dissolved in acetic acid (glacial; 5 ml) and acetic anhydride (5 ml) was added. The mixture was heated on a steam-bath for 1 h, poured into water, and extracted with ether. The extract was washed with dilute aqueous sodium hydroxide and water, dried, and evaporated to give a solid (0.82 g), which crystallised from ethanol to give the *acetamide* (7; R = Ac, R^1 = R^2 = OMe), m.p. 142—143°, $\lambda_{max.}$ (MeOH) 212 (log ε 4.44), 234 (4.45), 266 (4.09), 270 (4.07), and 333 nm (3.75), $\nu_{max.}$ 3 240 (NH), 1 700 (CONH), and 1 680 cm^{-1} (CO), τ −1.85 (1 H, s, NH), 1.24 (1 H, m, 3′-H), 2.3—3.2 (3 H, complex, ArH), 3.83 (2 H, s, 3- and 5-H), 6.17 (3 H, s, 4-OMe), 6.33 (6 H, s, 2- and 6-OMe), and 7.76 (3 H, s, Ac) (Found: C, 65.9; H, 5.7. $C_{18}H_{19}NO_5$ requires C, 65.6; H, 5.8%), *m/e* 329(20%), 256(18), 195(13), and 167(100).

Cyclisation of 2′-*Acetamido*-2-*methoxybenzophenones*.—The acetamide was dissolved in dimethyl sulphoxide and treated with base at the appropriate temperature (as indicated). The mixture was poured into water and extracted with ethyl acetate, and the product from the extract was crystallised from acetone and compared with an authentic sample. Table 2 gives the results.

2-*Acetamido*-2′-*hydroxybenzophenone* (8; R = H).—2-Acetamido-2′-methoxybenzophenone (8; R = Me) (5 g) was dissolved in chlorobenzene (130 ml) containing aluminium chloride (anhydrous, 5 g) and the mixture was refluxed for 1 h, poured into iced hydrochloric acid and extracted with ether (2 × 300 ml). The organic layer yielded an oil which crystallised from benzene as *needles*, m.p. 102—104°, $\lambda_{max.}$ (MeOH) 220.5 (log ε 4.28), 235 (4.28), 264 (4.04), and 326 nm (3.70), $\nu_{max.}$ 3 220 (OH), 1 670 ($CONH_2$), and 1 640 cm^{-1} (bonded CO), τ −1.46br (1 H, s, 2′-OH), 0.65br (1 H, NH), 1.6 (1 H, d, *J* 9 Hz, 3′-H), 2.3—3.3 (7 H, complex, ArH), 7.83 (3 H, s, Me) (Found: C, 70.6; H, 5.2. $C_{15}H_{13}NO_3$ requires C, 70.6; H, 5.2%), *m/e* 255(20%), 212(18), 211(18), 190(10), and 93(100).

2-*Acetamido*-2′-*p-tolylsulphonyloxybenzophenone* (8; R = Ts).—The hydroxybenzophenone (8; R = H) (1.47 g) was dissolved in dry pyridine (20 ml) and toluene-*p*-sulphonyl chloride (1.2 g) was added. The mixture was heated for 1 h on a steam-bath, cooled, and poured into dilute hydrochloric acid–ice; the yellow precipitate was collected, washed with dilute hydrochloric acid and water, and dried under reduced pressure. The *toluene*-p-*sulphonate* (8; R = Ts) crystallised from ethanol as a yellow solid (0.5 g), m.p. 122—124°, $\lambda_{max.}$ (MeOH) 205 (log ε 4.64), 229, (4.58), 266 (4.08), 274 (4.07), and 333 nm (3.64), $\nu_{max.}$ 1 670 cm^{-1} (C=O), τ 1.31 (1 H, d, *J* 8 Hz, 3′-H), 3.3—4.2 (12 H, complex, ArH), 7.66 (3 H, s, ArMe), and 7.76 (3 H, s, COMe) (Found: C, 64.7; H, 4.9. $C_{22}H_{19}NO_5$ requires C, 64.5; H, 4.7%), *m/e* 409(45%), 367(22), 236(10), 202(100), 195(50), 134(18), and 91(16).

Cyclisation of the 2′-*Acetamido*-2-*toluene*-p-*sulphonate* (8; R = Ts).—The tosylate (66 mg) was dissolved in dimethyl sulphoxide (10 ml) and sodium hydride (benzene-washed; 32 mg from a 60% dispersion) was added at room temperature. After 40 min, t.l.c. showed the absence of starting material and the mixture was worked up in the usual way to give 9-acridone (6; R = R^1 = R^2 = H) (31 mg, 94%), m.p. and mixed m.p. *ca* 340°. A repeat reaction showed complete convesion after 15 min.

2′-*Amino*-2,4-*dimethoxybenzophenone* (7; R = R^1 = H, R^2 = OMe).—The acetamide (7; R = Ac, R^1 = H, R^2 = OMe) (1 g) was heated in ethanol (25 ml) containing concentrated hydrochloric acid (5 ml) for 3 h. Cooling, basifying (NaOH) and extracting with ether gave an oil (0.9 g). Purification on silica gel and elution with benzene–ethyl acetate (95 : 5) gave the *amine* (7; R = R^1 = H, R^2 = OMe), which crystallised from methanol as yellow plates, m.p. 127—128°, $\lambda_{max.}$ (EtOH) 209 (log ε 4.45), 233 (4.52), 261 (4.09), and 377 nm (3.92), $\nu_{max.}$ 3 320, 3 340 (NH_2), and 1 640 cm^{-1} (CO), τ 2.5—3.0 and 3.2—4.0 (9 H, complex, ArH, NH_2), 6.20 (3 H, s, 2-OMe), and 6.31 (3 H, s, 4-OMe) (Found: C, 70.2; H, 5.9. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9%), *m/e* 257(94%), 256(100), 232(20), 230(10), 226(22), 145(56), 138(45), 110(32), 109(71), and 92(40).

2′-*Amino*-2,3,4-*trimethoxybenzophenone* (1). This amine, prepared according to the method previously described,[5] had m.p. 126°, *m/e* 287 (100%), 286(63), 256(25), 241(13), 195(22), 168(45), 153(14), 120(56), 119(14), and 92 (35).

2-*Hydroxy*-4,6-*dimethoxy*-2′-*nitrobenzophenone* (12; R = NO_2R^1 = H).—2,4,6-Trimethoxy-2′-nitrobenzophenone (12; R = NO_2, R^1 = OMe) (300 mg) was dissolved in dichloromethane (50 ml) and cooled to 0 °C, and tribromoborane (0.5 g) in dichloromethane (5 ml) was added slowly. The mixture was left at 0 °C for 10 min and at room temperature overnight.

TABLE 2

Cyclisation of 2′-acetamidobenzophenones

	Wt. (g)	Solvent	Base [mol]	Temp. (°C)	Time (h)	Product acridone	Yield (%)
2-MeO	0.5	Me_2SO	NaH [1.1]	20	2	Acridone	26
	0.5	Me_2SO	NaH [1.5]	20	24	Acridone	68
	0.5	Me_2SO	NaH [1.5]	100	2	Acridone	79
	0.1	EtOH	NaOEt [10]	20	48	Nil	0
	0.1	EtOH	NaOEt [10]	78	48	Nil	0
2,4-$(MeO)_2$	0.5	Me_2SO	NaH [1.1]	20	6	3-MeO	21
2,4,6-$(MeO)_3$	0.5	Me_2SO	NaH [1.5]	20	2	1,3-$(MeO)_2$	Trace
	0.5	Me_2SO	NaH [2]	20	30	1,3-$(MeO)_2$	7
	0.5	Me_2SO	NaH [2]	100	0.5		7

TABLE 3

Cyclisation of 2′-aminobenzophenones

	Wt. (g)	Solvent	Base [mol]	Temp. (°C)	Time (h)	Product acridone	Yield (%)
2-MeO	0.1	Me_2SO	NaH [6]	20	48	Acridone	47
	0.5	Me_2SO	NaH [1.5]	100	7.5	Acridone	58
	0.1	$Me_2N{\cdot}CHO$	$Me_2N{\cdot}CHO$	100	48	Nil	0
2,4-$(MeO)_2$	0.35	Me_2SO	NaH [1.5]	20	7	3-MeO	23
	0.1	Me_2SO	NaH [6]	20	48	3-MeO	53
	0.5	Me_2SO	NaH [6]	100	1.5	3-MeO	58
2,4,6-$(MeO)_3$	0.35	Me_2SO	NaH [1.5]	100	11	1,3-$(MeO)_2$	13
	0.1	Me_2SO	NaH [6]	50	8	1,3-$(MeO)_2$	35
	0.1	Me_2SO	NaOH [excess]	20	120	Nil	0
2,3,4-$(MeO)_3$	0.5	Me_2SO	NaH [1.5]	100	0.75	3,4-$(MeO)_2$	81
2-HO-4,6-$(MeO)_2$	0.28	Me_2SO	NaH [4]	50	9	Nil	0
2,4,6-$(MeO)_3$-imine (11; R = NH_2)	0.5	Me_2SO	NaH [1.5]	100	5	Nil	0

Water was added and the organic layer washed several times with water, dried, and evaporated to give an oil (280 mg), which crystallised from methanol to yield the *nitro-compound* (12; R = NO_2, R^1 = OH), m.p. 133—135°, $\lambda_{max.}$ (MeOH) 216 (log ε 4.14) and 295 nm (4.06), $\nu_{max.}$ 3 400 (OH) and 1 638 cm^{-1} (bonded CO), τ −13.16 (1 H, s, 2-OH), 2.85 (1 H, dd, 3′-H), 2.2—2.9 (3 H, complex, ArH), 6.18 (3 H, s, 4-OMe), and 6.71 (3 H, s, 6-OMe) (Found: C, 59.4; H, 4.5. $C_{15}H_{13}NO_6$ requires C, 59.4; H, 4.3%), *m/e* 303(4%), 181(4.5), 169(100), 141(13), 134(5), and 104(6).

2′-*Amino-2-hydroxy-4,6-dimethoxybenzophenone* (12; R = NH_2, R^1 = OH).—The nitro-compound (12; R = NO_2, R^1 = OH) (1.8 g) was dissolved in ethanol (120 ml) containing water (20 ml), ammonium chloride (4 g), and zinc moss (12 g), and the mixture was stirred for 8 h at room temperature. Filtration and evaporation gave a solid which was extracted with chloroform. Work up of the extract gave an oil (1.26 g). Trituration with methanol gave a solid which crystallised from ether to give the *amine* (12; R = NH_2, R^1 = OH), m.p. 61—63°, $\lambda_{max.}$ (MeOH) 212 (log ε 4.54), 231 (4.45), 262 (3.96), and 374 nm (3.88), $\nu_{max.}$ 3 480, 3 360 (NH_2), 3 170br (OH), and 1 620 cm^{-1} (bonded CO), τ −10.75br (1 H, 2-OH), 2.75—2.90 (4 H, m, NH, 3′- and 4′-H), 3.2—3.6 (2 H, multiplet, 5′- and 6′-H), 3.85 and 4.05 (2 H, dd, *J* 2 Hz, 3- and 5-H), 6.18 (3 H, s, 4-OMe), and 6.49 (3 H, s, 6-OMe) (Found: M^+, 273.0999. $C_{15}H_{15}NO_4$ requires *M*, 273.1001), *m/e* 273(20), 181(14), 120(100), 106(11), and 93(11%).

Cyclisation of 2′-Amino-2-*methoxybenzophenones*.—The results are summarised in Table 3.

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