Reaction of Secondary Aromatic Amines with Manganese(III) Acetate

Hiroshi Nishino* and Kazu Kurosawa
Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami 2-39-1, Kumamoto 860
(Received November 18, 1982)

The reaction of 2-(methylamino)benzophenone with manganese(III) acetate afforded 5-[(*o*-benzoylanilino)-methyl]-2-(methylamino)benzophenone, 2-aminobenzophenone, 5-formyl-2-(methylamino)benzophenone, 2-amino-5-[(*o*-benzoylanilino)methyl]benzophenone, 2-formamidobenzophenone, 2-amino-5-formylbenzophenone, and 2-(*N*-methylformamido)benzophenone. It was found that the reaction did not cause oxidative cyclization, but dimerization and conversion of *N*-methyl into *N*-formyl groups. Characterization of the products, the detailed oxidation mechanism, and the effects of the additives are discussed.

It is well known that oxidation of amino compounds with metal salts such as Hg(II), Cu(II), Co(III), Pb(IV), Ce(IV), *etc.* causes metal complex formation, *N*-acylation, *N*-dealkylation, *N,N*-coupling, and cyclization reactions. However, reaction of these compounds with manganese(III) acetate has been scarcely investigated except for the oxidation of *N,N*-dialkylarylamines.[1-3] In connection with our studies on the reaction of manganese(III) acetate with various organic substrates, we decided to investigate in detail the reaction of amino compounds, especially primary and secondary amines, with manganese(III) acetate in acetic acid.

We have previously reported that reaction of some phenolic compounds having an unsaturated side chain or aroyl group with manganese(III) acetate gave cyclic ethers in moderate yields.[4-9] We were interested in the reaction of analogous amines which may give cyclic amines because amino groups have reactivities similar to those of hydroxyl groups. We employed 2-(methylamino)benzophenone (**1**) as an amino compound whose amino group was located in a position suitable for forming a nitrogen containing six membered ring. As the result it was observed that this compound did not undergo the intramolecular oxidative cyclization, but was oxidized to give formamides in higher oxidant/substrate ratio, and dimeric compounds in lower oxidant/substrate ratio which were readily hydrolyzed to yield benzaldehydes and amines. We will describe in the present paper the detailed oxidation mechanism for the secondary amine (**1**), the effect of additives, and the synthetic application of the conversion of *N*-methyl into *N*-formyl group.

Results and Discussion

The 2-(methylamino)benzophenone (**1**) was oxidized with from one-half to eight molar equivalents of manganese(III) acetate in acetic acid at 100 °C or reflux temperature and the products were separated by TLC. The reaction conditions and the yields are summarized in Table 1.

Oxidation of **1** with one-half or one molar equivalent of manganese(III) acetate gave 5-[(*o*-benzoylanilino)-methyl]-2-(methylamino)benzophenone (**2**), 2-aminobenzophenone (**3**), and 5-formyl-2-(methylamino)benzophenone (**4**) (Table 1, Entries 1 and 2). The mass spectrum of **2** showed a parent ion peak at *m/e* 420, indicating that this product was a dimeric compound. Its NMR spectrum revealed two doublets at δ=2.88 (3H, J=4.8 Hz) and 4.26 (2H, J=4.8 Hz) for a methyl and a methylene group both coupled with an amino hydrogen, a multiplet at δ=6.34—7.66 for seventeen aromatic protons, and a broad quartet and

Table 1. Oxidation of 2-(methylamino)benzophenone (**1**) with manganese(III) acetate in acetic acid at 100 °C

Entry	Reaction conditions: Molar ratio of **1** : Oxidant	Reaction conditions: Time / min	Recovery / %	Product (yield/%)[a]: **2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	1 : 0.5	6	60	5	8	1						
2	1 : 1	7	32	10	10	6						
3	1 : 2	7	6	4	12	8	3	4	2	5		
4[b]	1 : 2	7	4	2	30	10	2	3	2	4		
5[c]	1 : 4	5	Trace		18			42	5	6		
6[b,c]	1 : 4	5	3		31			44	7	5		
7[c]	1 : 6	12	Trace		6			65	6	4		
8[c]	1 : 8	25	Trace		3			59	5	5		
9[d]	1 : 2	6	2	2	8	6	2	4	2	24		
10[e]	1 : 2	7	3	1	5	6				5	52	6
11[f]	1 : 2	7	2	1	24	5	1	5	3	5		

a) The yields were based on the substrate used. b) The reaction was carried out under nitrogen atmosphere. c) The reaction was conducted at reflux temperature. d) Formaldehyde (1 mmol) was added. e) Acetic anhydride (4 mmol) was added. f) Water (3 mmol) was added.

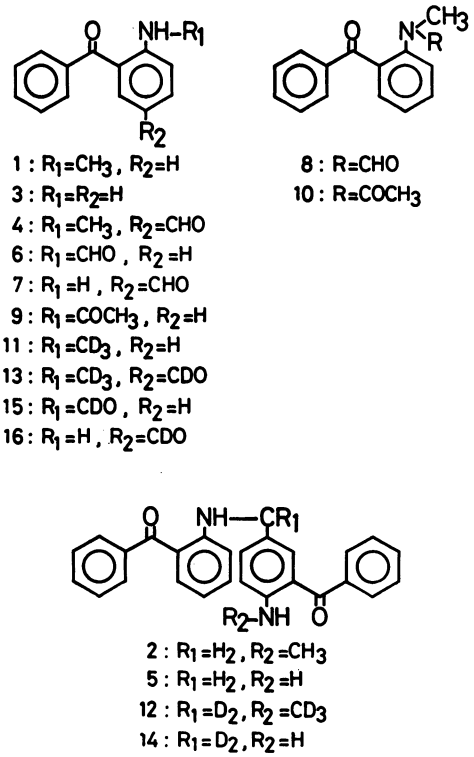


Fig. 1. 2-(Methylamino)benzophenones (**1** and **11**) and the oxidation products (**2**—**10** and **12**—**16**).

triplet at δ=8.43 (1H, J=4.8 Hz) and 8.74 (1H, J=4.8 Hz) for amino groups. The IR spectrum indicated a strong carbonyl absorption band at 1625 cm^{-1} and a broad weak absorption band at 3200—3400 cm^{-1} due to amino groups. Therefore, this spectroscopic evidence supported the structure of 5-[(*o*-benzoylanilino)methyl]-2-(methylamino)benzophenone. The product **3** was identical with an authentic sample. The NMR spectrum of **4** showed the presence of a formyl group at δ=9.61 (1H, s), and an ABX pattern of the aromatic protons at δ=6.82 (1H, d, J=9.0 Hz), 7.88 (1H, dd, J=9.0 and 1.8 Hz), and 7.94 (1H, d, J=1.8 Hz), besides a methylamino group and a phenyl group. The IR spectrum of **4** showed absorption bands at 1615, 1695, and 3300—3500 cm^{-1} due to two carbonyls, and an amino group. Accordingly, the structure of **4** was considered to be 5-formyl-2-(methylamino)benzophenone.

The compound **1** was oxidized with two molar equivalents of manganese(III) acetate to yield **2**, **3**, **4**, 2-amino-5-[(*o*-benzoylanilino)methyl]benzophenone (**5**), 2-formamidobenzophenone (**6**), and 2-amino-5-formylbenzophenone (**7**) (Table 1, Entry 3). The NMR spectrum of **5** was similar to that of **2** except for the absence of a methyl group and the appearance of a primary amino group instead of a secondary amino group. Since the molecular ion peak showed at m/e 406 in its mass spectrum, this product was deduced to be 2-amino-5-[(*o*-benzoylanilino)methyl]benzophenone which was formed by the *N*-demethylation of **2**. In the IR spectrum of **6** two carbonyls and a broad amino absorption appeared at 1640, 1710, and 3100—3600 cm^{-1}. The NMR spectrum of **6** revealed the presence of a formamido group at δ=8.40 (1H, br. s, CHO) and 10.60 (1H, br. s, –NH–). In addition, **6** was hydrolyzed with dil H_2SO_4 at reflux temperature to afford **3** (89%). Therefore, the structure of **6** was confirmed to be 2-formamidobenzophenone. The NMR spectrum of **7** which was an isomer of **6** was analogous to that of **4**, although an amino group was present instead of a methylamino group. Accordingly the structure of **7** was considered to be 2-amino-5-formylbenzophenone which is compatible both with the IR and mass spectra.

Using from four to eight molar equivalents of manganese(III) acetate, four products were obtained; these were determined to be **3**, **6**, **7**, and 2-(*N*-methylformamido)benzophenone (**8**) (Table 1, Entries 5, 7, and 8). The product (**8**) was obtained as pale yellow crystals, mp 96 °C. It showed a parent ion peak at m/e 239 in the mass spectrum, and a strong IR absorption band at 1695 cm^{-1} in chloroform. The NMR spectrum showed the presence of a methyl group (δ=3.00) and a formyl group (δ=8.10). However, the IR and NMR spectra revealed the absence of an amino hydrogen. Accordingly, this evidence suggested that the structure was 2-(*N*-methylformamido)benzophenone.

When **1** was oxidized using six molar equivalents of manganese(III) acetate at reflux temperature, **6** was obtained in the highest yield (65%) for this oxidation reaction. Since in higher oxidant/substrate ratio other products were formed only in small amounts, this reaction may be a useful method for the conversion of *N*-methyl into *N*-formyl compounds.

We then investigated how additions of formaldehyde,[1] acetic anhydride,[10] and/or water[11] influence the product distribution. Addition of formaldehyde to the reaction mixture increased the yield of the *N*-methylformamide (**8**) five times, while the yield of the formamide **6** was not changed (Table 1, Entry 9). When four molar equivalents of acetic anhydride were added, formation of the formamide (**6**) was completely inhibited and acetamides (**9** and **10**) were newly produced; these were identical with compounds obtained by an alternative synthesis (Table 1, Entry 10). The formation of **9** was explained in terms of oxidative *N*-demethylation of tertiary aromatic amines.[2,3,12,13] The product yields

Table 2. Oxidation of 2-(methyl-d_3-amino)benzophenone (**11**) with manganese(III) acetate in acetic acid at 100 °C

Entry	Reaction conditions: Molar ratio of **11**: Oxidant	Reaction conditions: Time / min	Recovery / %	Product (yield/%)[a] **3**	**12**	**13**	**14**	**15**	**16**
1	1 : 2	7	5	14	7	6	4	4	1
2	1 : 4	22	Trace	17	Trace	2		34	7

a) The yields were based on the substrate used.

Table 3. Oxidation of the prodcuts (2—5) with manganese (III)acetate in acetic acid at 100 °C

Entry	Substrate	Reaction conditions: Molar ratio of Substrate : Oxidant	Reaction conditions: Time / min	Recovery / %	Product (yield/%)[a] 2	3	4	5	7	9
1	**2**	1 : 1	4	30		59	52		6	
2	**2**	1 : 2	6	11		67	76		17	
3	**1** and **3**	(1 : 1) : 1	5	47 and 93[b]	7			4		
4	**1** and **3**	(1 : 1) : 2	7	18 and 84[b]	9		1	7	8	
5	**4**	1 : 2	6	28					35	
6	**4**	1 : 4	33	2					37	
7	**3**	1 : 2	15	46						5
8	**3**	1 : 4	15	12						7
9	**5**	1 : 2	5	5		77			84	

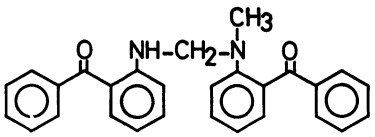
a) The yields were based on the substrate used. b) The recoveries correspond to that of **1** and **3**, respectively.

were not appreciably changed by addition of water (3 equiv.) except for **3** (Table 1, Entry 11).

In order to elucidate the reaction mechanism, we prepared and oxidized deuterated 2-(methyl-d_3-amino)-benzophenone (**11**). The reaction conditions and the yields are shown in Table 2.

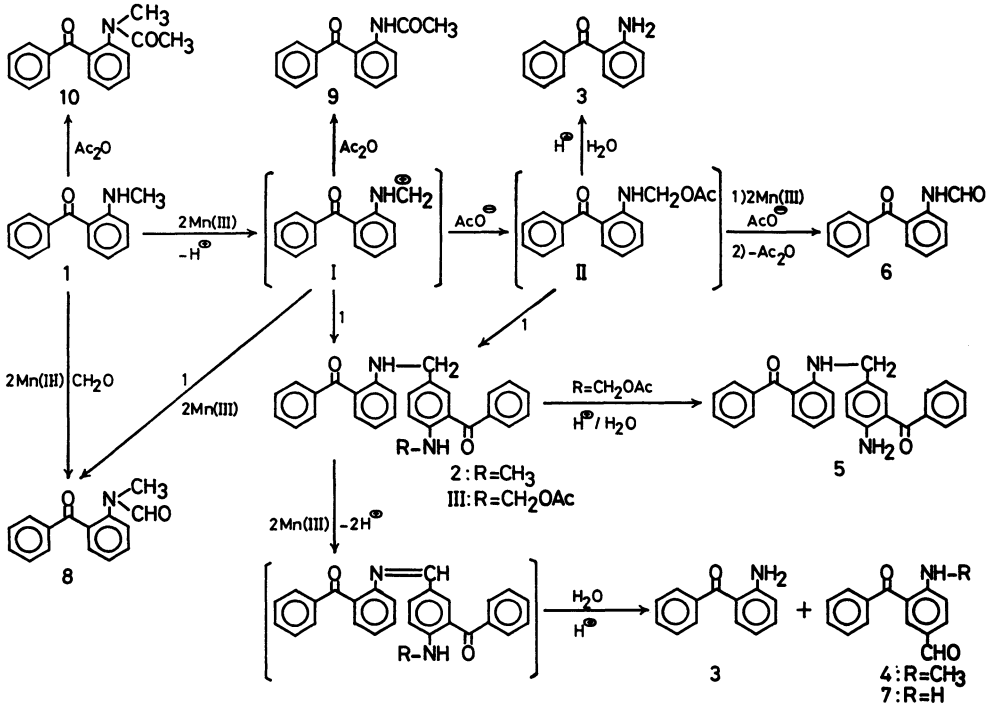
When **11** was oxidized with two molar equivalents of manganese(III) acetate in acetic acid at 100 °C, **3**, 5-[(*o*-benzoylanilino)methyl-d_2]-2-(methyl-d_3-amino)-benzophenone (**12**), 5-(formyl-*d*)-2-(methyl-d_3-amino)-benzophenone (**13**), 2-amino-5-[(*o*-benzoylanilino)methyl-d_2]benzophenone (**14**), 2-(formyl-*d*-amino)benzophenone (**14**), 2-(formyl-*d*-amino)benzophenone (**15**), and 2-amino-5-(formyl-*d*)benzophenone (**16**) were obtained. This experiment proved that the formyl group of the products, **13** and **16**, must come from the *N*-methyl group. Therefore, it suggests that the precursors of the benzaldehydes **4** or **7** must be the dimeric compound **2** or **5**, respectively. Manganese(III) acetate oxidation was then carried out for **2** and **5**, to confirm the above facts. These oxidations gave the corresponding benzaldehydes (**4** and **7**) and amine (**3**) in good yields as expected (Table 3, Entries 1, 2, and 9). The product (**4**) was also oxidized by manganese(III) acetate to **7** by the oxidative *N*-demethylation (Table 3, Entries 5 and 6).

It was thought that the dimeric compound (**5**) might



IV

Fig. 2. Dimeric intermediate (**IV**).



Scheme 1. Oxidation mechanism of 2-(methylamino)benzophenone (**1**) by manganese(III) acetate.

be formed by reaction between the intermediate carbenium cation (**I**) (formed by the oxidation of **1** with manganese(III) acetate) and the amine (**3**), presumably generated by the oxidative *N*-demethylation of **1**. However, oxidation of a 1 : 1 mixture of **1** and **3** under the above conditions gave **5** (Table 3, Entries 3 and 4) in a yield similar to that in the reaction of **1** alone (Table 1, Entry 3). This suggests that primary amines did not exist in the reaction mixture, but were formed during the work-up. We suggest that 2-(acetoxymethylamino)benzophenone (**II**) was produced from the carbenium ion (**I**) by the attack of an acetate ion. It reacted with **I** to give the dimeric compound (**III**), which was hydrolyzed to yield **5** and/or further oxidized to afford **3** and **7** during the work-up.

Reaction of the primary amine (**3**) with manganese(III) acetate gave 2-acetamidobenzophenone (**9**) as the only isolable reaction product (Table 3, Entries 7 and 8).

The mechanism for the formation of the formamide (**6**) can be explained by assuming that the intermediate (**II**) was further oxidized to **6**, since the deuterated isomer (**15**) was obtained from the oxidation of **11** and the yield of **6** was scarcely changed on oxidation of **1** under nitrogen atmosphere (Table 1, Entries 4 and 6). Formation of *N*-methylformamide (**8**), however, might be due to the reaction of **1** with formaldehyde which was produced in the reaction (**II**→**6**), since the yield of **8** was increased by the addition of formaldehyde to the reaction mixture. Alternatively, the intermediate carbenium cation (**I**) might react with the amino group of **1** to give **8** *via* an analogous dimeric intermediate (**IV**). In either event these alternative pathways could not be distinguished. The above reaction mechanism is outlined in Scheme 1.

It is characteristic of this reaction that the use of lower oxidant/substrate ratio induces dimerization, leading to aldehydes and amines. On the other hand, conversion of *N*-methyl into *N*-formyl compounds occurs preferentially at higher oxidant/substrate ratios. By contrast, however, it was found that oxidation of aromatic secondary amines with lead(IV) acetate in chloroform caused *N*-dealkylation and nuclear acetoxylation.[14] The conversion of *N*-methyl into *N*-formyl group by means of manganese(III) acetate can be useful in organic synthesis.

Experimental

Measurements. The IR spectra were measured on a JASCO IRA-1 grating spectrometer. The ^{1}H-NMR spectra were recorded on a Hitachi Perkin-Elmer R-24 spectrometer (60 MHz) with tetramethylsilane as an internal standard; the chemical shifts are reported in δ values. The mass spectra were obtained with a JEOL JMS-DX300 mass spectrometer. The HPLC analyses were performed on an ALTEX model 330/110A/153 isocratic liquid chromatograph equipped with a HY-ODS-5U column, eluting with methanol or 70% aqueous methanol. The melting points were taken on a Yanagimoto micromelting point apparatus and are uncorrected.

Preparation of the Materials. 2-(Methylamino)benzophenone (**1**) was synthesized by the methylation of 2-aminobenzophenone which was obtained from the commercial sample of Wako Pure Chemical Industries, Ltd. The 2-aminobenzophenone (10 mmol) was heated under reflux for 12 h with dimethyl sulfate (15 mmol) in dry acetone (50 ml) containing anhydrous potassium carbonate (2 g). The solvent was removed *in vacuo* and the residue was triturated with water. The aqueous reaction mixture was extracted with chloroform, followed by column chromatography on silica gel (Wakogel C-100) using chloroform as eluent to give **1** (55%); yellow needles (from hexane), mp 68.5 °C (lit,[15] mp 69 °C); IR ($CHCl_3$) 1620 (C=O) and 3250—3400 cm^{-1} (NH); NMR ($CDCl_3$) δ=2.91 (3H, s, CH_3), 6.34—7.69 (9H, m, aromatic), 8.47 (1H, br. s, NH). Found: C, 79.41; H, 6.18; N, 6.41%. Calcd for $C_{14}H_{13}ON$: C, 79.59; H, 6.20; N, 6.63%.

2-(Methyl-d_3-amino)benzophenone (**11**) was also obtained from the same methylation of the 2-aminobenzophenone with dimethyl-d_6 sulfate which was available from E. Merck AG.; 43%; yellow needles (from hexane), mp 69.0—69.5 °C; IR ($CHCl_3$) 1620 (C=O) and 3250—3600 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.32—7.72 (9H, m, aromatic), and 8.48 (1H, br. s, NH). Found: C, 78.46; H+D/2, 6.19; N, 6.51%. Calcd for $C_{14}H_{10}D_3ON$: C, 78.47; H+D/2, 6.11; N, 6.54%.

*Oxidation of **1** and **11**.* The compound **1** (1 mmol) was dissolved in acetic acid (25 ml) and suitable amounts of manganese(III) acetate dihydrate[16] were added. The mixture was heated on a water bath until the brown color of Mn(III) ion disappeared (see Table 1). The solvent was removed *in vacuo* and the residue was triturated with 2 M (1 M=1 mol dm^{-3}) hydrochloric acid (25 ml), followed by extraction with chloroform. The products were separated on TLC (Wakogel B-10) with chloroform as the developing solvent, and simultaneously tested by HPLC. The deuterated compound **11** (1 mmol) was also oxidized by the procedure described above. It was found that substantial quantities of unidentified tarry materials were formed in both reaction mixture besides the isolated products.

*Oxidation Products of **1**.* *5-[(o-Benzoylanilino)methyl]-2-(methylamino)benzophenone (**2**)*: Yellow liquid; IR ($CHCl_3$) 1625 (C=O) and 3200—3400 cm^{-1} (NH); NMR ($CDCl_3$) δ=2.88 (3H, d, J=4.8 Hz, CH_3), 4.26 (2H, d, J=4.8 Hz, $-CH_2-$), 6.34—7.66 (17H, m, aromatic), 8.43 (1H, q, J=4.8 Hz, –NH–), and 8.74 (1H, t, J=4.8 Hz, –NH–); MS *m/e* (rel intensity), 420 (M^+, 22), 405 (4), 239 (3), 224 (100), 196 (6), 180 (2), 146 (5), 132 (2), 118 (3), 105 (10), 91 (9), and 77 (23). Found: *m/e* 420.19424. Calcd for $C_{28}H_{24}O_2N_2$: M, 420.18378.

*2-Aminobenzophenone (**3**)*: Yellow needles (from hexane), mp 105—106 °C (lit,[17] mp 107 °C).

*5-Formyl-2-(methylamino)benzophenone (**4**)*: Pale yellow needles (from hexane), mp 136 °C; IR ($CHCl_3$) 1615 and 1695 (C=O), and 3300—3500 cm^{-1} (NH); NMR ($CDCl_3$) δ=3.05 (3H, d, J=5.4 Hz, CH_3), 6.82 (1H, d, J=9.0 Hz, $H_{(3)}$), 7.4—7.7 (5H, m, aromatic), 7.88 (1H, dd, J=9.0 and 1.8 Hz, $H_{(4)}$), 7.94 (1H, d, J=1.8 Hz, $H_{(6)}$), 9.20 (1H, br. s, –NH–), and 9.61 (1H, s, CHO); MS *m/e* (rel intensity), 239 (M^+, 100), 238 (70), 210 (5), 134 (6), 105 (16), 91 (5), and 77 (30). Found: C, 75.28: H, 5.50; N, 5.83%. Calcd for $C_{15}H_{13}O_2N$: C, 75.30; H, 5.48; N, 5.85%.

*2-Amino-5-[(o-benzoylanilino)methyl]benzophenone (**5**)*: Yellow liquid; IR ($CHCl_3$) 1625 (C=O) and 3320—3480 cm^{-1} (NH); NMR ($CDCl_3$) δ=4.26 (2H, d, J=4.2 Hz, $-CH_2-$), 6.04 (2H, br. s, NH_2), 6.39—7.67 (17H, m, aromatic), and 8.76 (1H, br. s, –NH–); MS *m/e* (rel intensity), 406 (M^+, 23), 210 (100), 196 (71), 132 (16), 120 (32), 105 (25), 92 (20), and 77 (44). Found: *m/e* 406.16058. Calcd for $C_{27}H_{22}O_2N_2$: M, 406.16813.

*2-Formamidobenzophenone (**6**)*: Pale yellow liquid; IR ($CHCl_3$) 1640 and 1710 (C=O), and 3100—3600 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.90—8.67 (9H, m, aromatic), 8.40 (1H, br. s, CHO), and 10.60 (1H, br. s, –NH–); MS *m/e* (rel intensity), 225 (M^+, 38), 196 (100), 120 (7), 105 (17), and 77

(23). Found: *m/e* 225.08177. Calcd for $C_{14}H_{11}O_2N$: M, 225.07898.

2-Amino-5-formylbenzophenone (7): Pale yellow crystals (from benzene/hexane), mp 131—132 °C; IR ($CHCl_3$) 1615 and 1700 (C=O), and 3320—3490 cm^{-1} (NH); NMR ($CDCl_3$) δ= 6.76 (1H, d, J=8.4 Hz, $H_{(3)}$), 6.95 (2H, br. s, NH_2), 7.25—8.05 (5H, m, aromatic), 7.72 (1H, dd, J=8.4 and 1.8 Hz, $H_{(4)}$), 7.88 (1H, d, J=1.8 Hz, $H_{(6)}$), and 9.56 (1H, s, CHO); MS *m/e* (rel intensity), 225 (M^+, 97), 224 (100), 208 (5), 196 (14), 148 (25), 120 (11), 105 (25), and 77 (32). Found: C, 74.82; H, 4.97; N, 6.02%. Calcd for $C_{14}H_{11}O_2N$: C, 74.65; H, 4.92; N, 6.22%.

2-(N-Methylformamido)benzophenone (8): Pale yellow crystals (from benzene/hexane), mp 96 °C; IR ($CHCl_3$) 1695 cm^{-1} (C=O); NMR ($CDCl_3$) δ=3.00 (3H, s, CH_3), 7.18—7.95 (9H, m, aromatic), and 8.10 (1H, s, CHO); MS *m/e* (rel intensity), 239 (M^+, 27), 210 (100), 194 (92), 134 (92), 105 (47), and 77 (100). Found: *m/e* 239.09281. Calcd for $C_{15}H_{13}O_2N$: M, 239.09463.

Oxidation Products of 11. 5-[(o-Benzoylanilino)methyl-d_2*]-2-(Methyl-*d_3*-amino)benzophenone (12)*: Yellow liquid; IR ($CHCl_3$) 1625 (C=O) and 3200—3600 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.36—7.61 (17H, m, aromatic), 8.41 (1H, br. s, -NH-), and 8.74 (1H, br. s, -NH-); MS *m/e* (rel intensity), 425 (M^+, 20), 229 (100), 151 (20), 105 (22), and 77 (45).

*5-(Formyl-*d*)-2-(methyl-*d_3*-amino)benzophenone (13)*: Yellow needles (from hexane), mp 136 °C; IR ($CHCl_3$) 1610 and 1675 (C=O), and 3150—3600 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.83 (1H, d, J=9.0 Hz, $H_{(3)}$), 7.25—7.68 (5H, m, aromatic), 7.88 (1H, dd, J=9.0 and 1.8 Hz, $H_{(4)}$), 7.94 (1H, d, J=1.8 Hz, $H_{(6)}$), and 9.18 (1H, br. s, -NH-); MS *m/e* (rel intensity), 243, (M^+, 100), 197 (20), 166 (26), 105 (27), and 77 (90).

2-Amino-5-[(o-benzoylanilino)methyl-d_2*]benzophenone (14)*: Yellow liquid; IR ($CHCl_3$) 1625 (C=O) and 3340—3500 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.05 (2H, br. s, NH_2), 6.41—7.69 (17H, m, aromatic), and 8.79 (1H, br. s, -NH-); MS *m/e* (rel intensity), 408 (M^+, 12), 212 (36), 167 (10), 105 (43), and 77 (100).

*2-(Formyl-*d*-amino)benzophenone (15)*: Pale yellow liquid; IR ($CHCl_3$) 1645 and 1680 (C=O), and 3100—3650 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.93—8.71 (9H, m, aromatic), and 10.61 (1H, br. s, -NH-); MS *m/e* (rel intensity), 226 (M^+, 20), 197 (100), 167 (10), 121 (27), and 77 (78).

*2-Amino-5-(formyl-*d*)benzophenone (16)*: Pale yellow needles (from benzene/hexane), mp 132—133 °C; IR ($CHCl_3$) 1610 and 1690 (C=O), and 3320—3490 cm^{-1} (NH); NMR ($CDCl_3$) δ=6.77 (1H, d, J=9.0 Hz, $H_{(3)}$), 6.95 (2H, br. s, NH_2), 7.22—7.69 (5H, m, aromatic), 7.78 (1H, dd, J=9.0 and 1.8 Hz, $H_{(4)}$), and 7.94 (1H, d, J=1.8 Hz, $H_{(6)}$); MS *m/e* (rel intensity), 226 (M^+, 25), 149 (15), 105 (30), and 77 (100).

Oxidation of a Mixture of 1 and Formaldehyde. The compound **1** (1 mmol) was dissolved in acetic acid (25 ml), and aqueous formaldehyde (37%, 1 mmol) and manganese(III) acetate (2 mmol) were added to it. The mixture was heated at 100 °C for 6 min, followed by treatment in a manner similar to that described above, which gave **2** (2%), **3** (8%), **4** (6%), **5** (2%), **6** (4%), **7** (2%), and **8** (24%).

Oxidation of 1 in Acetic Acid Containing Acetic Anhydride. A mixture of **1** (1 mmol), acetic anhydride (4 mmol), and manganese(III) acetate (2 mmol) were heated at 100 °C for 7 min in acetic acid (25 ml). This oxidation gave **2** (1%), **3** (5%), **4** (6%), **8** (5%), **9** (52%), and **10** (6%).

2-Acetamidobenzophenone (9): Colorless crystals (from hexane), mp 88.0—88.5 °C (lit,[18] mp 88 °C); IR ($CHCl_3$) 1640 and 1710 (C=O), and 3100—3650 cm^{-1} (NH); NMR ($CDCl_3$) δ=2.17 (3H, s, $COCH_3$), 6.88—8.67 (9H, m, aromatic), and 10.74 (1H, br. s, -NH-); MS *m/e* (rel intensity), 239 (M^+, 30), 196 (100), 134 (13), 120 (28), 105 (15), 92 (24), and 77 (55).

2-(N-Methylacetamido)benzophenone (10): Colorless needles (from hexane), mp 80—81 °C; IR ($CHCl_3$) 1650 and 1680 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.84 (3H, s, $COCH_3$), 3.04 (3H, s, CH_3), and 7.20—7.84 (9H, m, aromatic); MS *m/e* (rel intensity), 253 (M^+, 10), 210 (86), 194 (48), 148 (100), 105 (8), and 77 (20). Found: *m/e* 253.10693. Calcd for $C_{16}H_{15}O_2N$: M, 253.11028.

Acetylation of 1 and 3: The compound **1** (33.3 mg) and acetic anhydride (0.1 ml) were heated at 100 °C for 6 h in pyridine (5 ml) to yield **10** (39.9 mg, 99%). The product **3** (1 mmol) was treated with acetic anhydride (1.5 mmol) in pyridine (5 ml) overnight to give **9** (99%).

Oxidation of a Mixture of 1, Formaldehyde, and Acetic Anhydride. A mixture of **1** (1 mmol), aqueous formaldehyde (37%, 1 mmol), acetic anhydride (3 mmol), and manganese(III) acetate (2 mmol) were heated on a water bath for 6 min in acetic acid (25 ml) to afford **2** (trace), **3** (8%), **4** (6%), **8** (25%), **9** (25%), and **10** (8%).

Oixdation of a Mixture of 1 and Water. The compound **1** (1 mmol), water (3 mmol), and manganese (III) acetate (2 mmol) were heated in acetic acid (25 ml) at 100 °C for 7 min to give **2** (1%), **3** (24%), **4** (5%), **6** (6%), **7** (3%), and **8** (5%).

Oxidation of 2. The product **2** (54.7 mg) was heated at 100 °C for 4 min with manganese(III) acetate (36.5 mg) in acetic acid (5 ml) to yield **3** (15.1 mg, 59%), **4** (16.1 mg, 52%), and **7** (1.7 mg, 6%) which was determined by HPLC.

Oxidation of 3. A mixture of **3** (1 mmol) and manganese(III) acetate (2 mmol) was heated in acetic acid (25 ml) at 100 °C for 15 min. The reaction mixture was treated in a manner similar to that described above to give intractable tarry materials and **9** (5%) as the only isolable reaction product.

Oxidation of 4. A mixture of **4** (31.3 mg) and manganese(III) acetate (76.7 mg) was heated in acetic acid (5 ml) at 100 °C for 6 min to yield **7** (10.2 mg, 35%) and unidentified products (10.2 mg).

Oxidation of 5. A mixture of **5** (32.9 mg) and manganese(III) acetate (45.0 mg) was heated in acetic acid (5 ml) at 100 °C for 5 min to give **3** (12.3 mg, 77%) and **7** (15.3 mg, 84%).

Oxidation of a Mixture of 1 and 3. A mixture of **1** (0.5 mmol) and **3** (0.5 mmol) was dissolved in acetic acid (25 ml) and the mixture was oxidized with manganese(III) acetate (1 mmol) to give **2** (9%), **4** (1%), **5** (7%), and **7** (8%).

Hydrolysis of 6. The product **6** (17.5 mg) was heated under reflux for 1 h in dil H_2SO_4 (5 ml), which was extracted with chloroform, followed by recrystallization from hexane to give **3** (13.7 mg, 89%).

The authors wish to thank Mr. Masanori Tsumura of the Ichikawa Chemical Co. Ltd., Higashi Osaka, for his measurements of the MS spectra, and also wish to thank Dr. John F. W. McOmie of Bristol University, England, for his helpful discussion and for reading the manuscript.

References

1) T. Aratani and M. J. S. Dewar, *J. Am. Chem. Soc.*, **88**, 5479 (1966).

2) B. Rindone and C. Scolastico, *Tetrahedron Lett.*, **1974**, 3379.

3) G. Galliani, B. Rindone, and C. Scolastico, *Tetrahedron Lett.*, **1975**, 1285.

4) K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **42**, 1456 (1969).
5) K. Kurosawa and J. Higuchi, *Bull. Chem. Soc. Jpn.*, **45**, 1132 (1972).
6) K. Kurosawa, Y. Sasaki, and M. Ikeda, *Bull. Chem. Soc. Jpn.*, **46**, 1498 (1973).
7) K. Nogami and K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **47**, 505 (1974).
8) S. Ueda and K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **50**, 193 (1977).
9) K. Kurosawa and F. Araki, *Bull. Chem. Soc. Jpn.*, **52**, 529 (1979).
10) E. I. Heiba, R. M. Dessau, and W. J. Koehl, Jr., *J. Am. Chem. Soc.*, **91**, 138 (1969).
11) E. I. Heiba, R. M. Dessau, and P. C. Rodewald, *J. Am. Chem. Soc.*, **96**, 7977 (1974).
12) G. Galliani and B. Rindone, *J. Chem. Soc., Perkin Trans. 2*, **1976**, 1803.
13) G. Galliani and B. Rindone, *J. Chem. Soc., Perkin Trans. 1*, **1980**, 828.
14) G. Galliani and B. Rindone, *J. Chem. Res. (S)*, **1980**, 178.
15) G. Kempter and E. Schiewald, *J. Prakt. Chem.*, **28**, 169 (1965); *Chem. Abstr.*, **63**, 4236f (1965).
16) P. J. Andrulis, Jr., M. J. S. Dewar, R. Dietz, and R. L. Hunt, *J. Am. Chem. Soc.*, **88**, 5473 (1966).
17) S. Inagaki, *J. Pharm. Soc. Jpn.*, **59**, 1 (1939); *Chem. Abstr.*, **33**, 3790 (1939).
18) W. C. Lothrop and P. A. Goodwin, *J. Am. Chem. Soc.*, **65**, 363 (1943).