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Catalytic Action of Azolium Salts. VIII.[1] Oxidative Aroylation with Arenecarbaldehydes Catalyzed by 1,3-Dimethylbenzimidazolium Iodide

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Refluxing of a mixture of benzaldehyde (1a), 1,3-dimethylbenzimidazolium iodide (7), *p*-nitroaniline (9b) as an oxidizing agent, and 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) in MeOH afforded methyl benzoate (2a) in good yield. Other methyl arenecarboxylates 2 were similarly obtained from arenecarbaldehydes 1. We showed that this aroylation proceeds *via* the 2-aroyl-1,3-dimethylbenzimidazolium salt (8). The 1,2,4-triazolium salt (18) and the naphtho[1,2-*d*]imidazolium salt (19) were also effective catalysts for this oxidative aroylation. However, the aroylation did not proceed with the imidazolium salt (20). In the presence of flavins (25a—c), arenecarbaldehydes 1 reacted in MeOH under aerobic conditions catalyzed by the benzimidazolium salt 7 to give the corresponding methyl arenecarboxylates 2. 1-Methyl-3-[3-(10-phenylisoalloxazin-3-yl)propyl]benzimidazolium bromide (27) is an effective complex catalyst for this oxidative aroylation.

Key words benzimidazolium salt; oxidative aroylation; arenecarbaldehyde; catalyst; flavin; complex catalyst

We have already found several new reactions catalyzed by azolium salts,[1,2] and our interest in the benzoin condensation and related reactions led us to examine oxidative aroylation with arenecarbaldehydes **1** catalyzed by azolium salts. To our knowledge, only cyanide ion (**4**) and thiazolium salt (**5**), both of which are effective catalysts in the benzoin condensation, have been reported so far as catalysts of oxidative aroylation.[3,4] The reaction proceeds through the formation of an active acylating compound (A^2 or B^2), which is generated by oxidation of the adduct of the catalysts (**4** or **5**) and benzaldehyde (**1a**), *i.e.*, benzaldehyde cyanohydrin (A^1) or the 2-(α-hydroxybenzyl)thiazolium salt (B^1), respectively, as shown in Chart 1.

In our previous papers, we reported that 1,3-dimethylbenzimidazolium iodide (**7**) catalyzed the aroylation of haloheteroarenes and benzoin condensation, resulting in the formation of nucleophilically aroylated compounds.[2] We also showed that the intermediate C^1 is the key compound by examination of the reactivity of synthetic C^1.[5] Based on the chemical similarity between cyanide ion and benzimidazolium ylide, it seems likely that C^1 could also be an important intermediate in oxidative aroylation. Here we wish to report the results of experiments designed to examine whether the benzimidazolium salts (**7**) can be used as catalysts of oxidative aroylation.

Castells *et al.* reported that the treatment of arenecarbaldehyde **1** in MeOH in the presence of nitrobenzene (**9a**) and cyanide ion (**4**) or thiazolium salt (**5**) as a catalyst gave methyl arenecarboxylate **2**. Nitro compounds **9** are effective oxidizing agents.[3] When we refluxed a solution of benzaldehyde (**1a**), a catalytic amount of the benzimidazolium salt **7**, nitrobenzene (**9a**), and 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) for 1 h, methyl benzoate (**2a**) was obtained in 72% yield. This result indicates that the benzimidazolium salt **7** is an effective catalyst for this oxidative aroylation, like cyanide ion (**4**). In this case, methyl benzoate (**2a**) was purified from the reaction mixture only with difficulty. When *p*-nitroaniline (**9b**) was used, however, methyl benzoate (**2a**) was easily purified. Among various compounds examined as oxidizing agents, only aromatic nitro compounds (**9a**, **9b**, and **9c**) were effective, as shown in Chart 3. In the subsequent experiments,

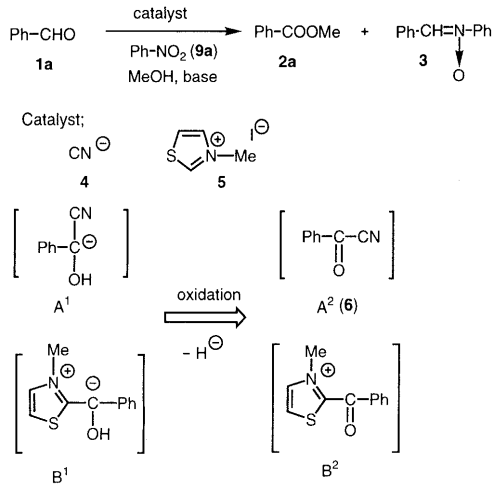

Chart 1

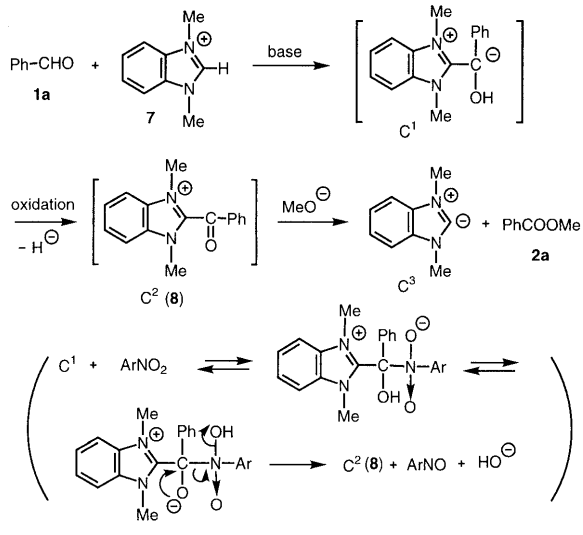

Chart 2

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p-nitroaniline (**9b**) was used as the oxidizing agent. This oxidative aroylation did not proceed in the absence of the benzimidazolium salt (**7**) or aromatic nitro compound (**9**).

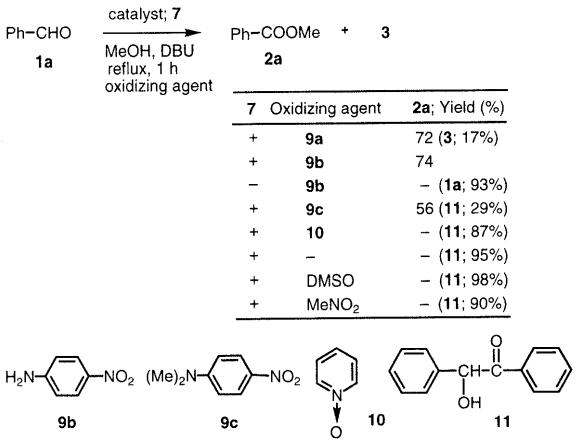
As shown in Chart 4, in the presence of the benzimidazolium salt (**7**), *p*-nitroaniline (**9b**), and DBU, several arenecarbaldehydes **1** reacted in MeOH to give the corresponding methyl arenecarboxylates **2** in good yields. In EtOH and *n*-PrOH, ethyl arenecarboxylates **16** and propyl arenecarboxylates **17** were formed. Further, benzoic acid (**15a**) was obtained when the reaction was carried out in H_2O–tetrahydrofuran (THF) mixture under basic conditions. In the absence of nucleophiles, self-oxidative aroylation proceeded, giving *O*-benzoylbenzoin (**14**) through the aroylation of benzoin (Chart 5).

The expected ester could not be produced under the above conditions by using an aliphatic aldehyde such as hexanal (**12**); only the aldol condensation product **13** was formed in 66% yield.[2d]

To elucidate the range of azolium salts effective as catalysts for this oxidative aroylation, we examined various other azolium salts. With the imidazolium salt (**20**), the reaction did not proceed and the starting benzaldehyde **1a** was recovered. Under these reaction conditions, the imidazolium salt (**20**) cannot form the imidazolium ylide, which is a key intermediate for catalytic aroylation and oxidative aroylation, because of the low acidity of the C2 hydrogen, as we established previously.[2d] In contrast, the 1,2,4-triazolium salt (**18**)[1] and the naphtho[1,2-*d*]imidazolium salt (**19**) are effective catalysts (Chart 6).

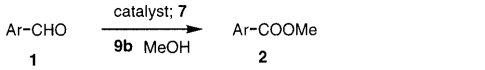
Based on the oxidative aroylation catalyzed by cyanide ion (**4**) and thiazolium salt (**5**), the reaction pathway to methyl benzoate (**2a**) from benzaldehyde (**1a**) catalyzed by the benzimidazolium salt (**7**) is considered to be as illustrated in Chart 2. Namely, the key step is the formation of the 2-aroyl-1,3-dimethylbenzimidazolium salt (C^2) by oxidation of the adduct (C^1) obtained from the benzimidazolium salt (**7**) and arenecarbaldehyde **1**. In the case of cyanide ion, it has been reported that the formation of the intermediate A^2 (benzoyl cyanide) is the key step.[3] The reactivity of benzoyl cyanide (**6**) has been well examined, and this compound **6** readily generates the benzoyl cation ($PhCO^+$), giving electrophilically benzoylated compounds.[6] The intermediate C^2 (**8**) corresponds to benzoyl cyanide (A^2, **6**). Thus, the chemical behavior of **8** should be similar to that of **6**.

To confirm that C^2 is the key intermediate in this oxidative aroylation catalyzed by 1,3-dimethylbenzimidazolium iodide (**7**), 2-benzoyl-1,3-dimethylbenzimidazolium iodide (**8**) was synthesized and its reactivity was examined. Compound **8** was synthesized from 1-methylbenzimidazole



7	Oxidizing agent	2a; Yield (%)
+	**9a**	72 (**3**; 17%)
+	**9b**	74
–	**9b**	– (**1a**; 93%)
+	**9c**	56 (**11**; 29%)
+	**10**	– (**11**; 87%)
+	–	– (**11**; 95%)
+	DMSO	– (**11**; 98%)
+	$MeNO_2$	– (**11**; 90%)

Chart 3



1	Reaction conditions: Temp.	Time (h)	2	2; Yield (%)
1b	r.t.	4	**2b**	99
1c	r.t.	5.5	**2c**	76
1d	r.t.	4	**2d**	73
1e	r.t.	8	**2e**	74
1f	reflux	2	**2f**	88
1f	r.t.	7	**2f**	– (**1f**; 87%)
1g	reflux	1	**2g**	61
1h	r.t.	6	**2h**	73
1i	r.t.	6	**2i**	82
1j	r.t.	3	**2j**	74

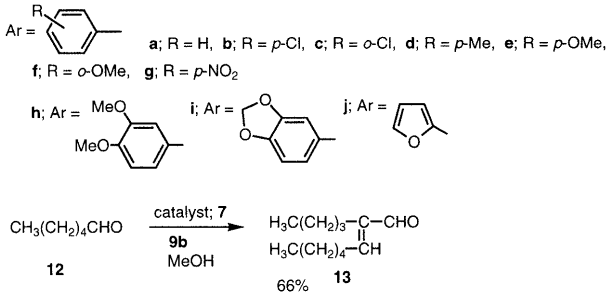
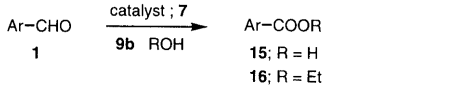


Chart 4



1	Reaction conditions: Temp.	Time (h)	R-OH	15-17	Yield (%)
1a	r.t.	4	H_2O	**15a**	69
1a	reflux	3	EtOH	**16a**	78
1a	r.t.	2	*n*-PrOH	**17a**	69
1b	reflux	4	EtOH	**16b**	79
1b	reflux	5	*n*-PrOH	**17b**	66
1e	reflux	3	EtOH	**16e**	61

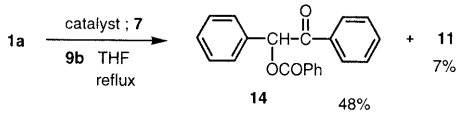
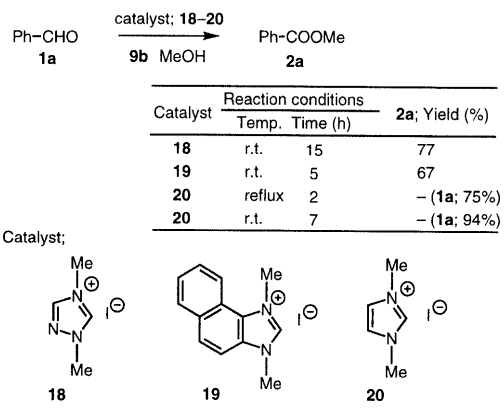


Chart 5



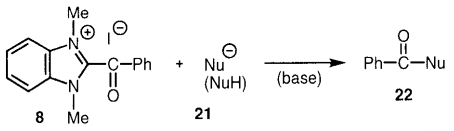
Catalyst	Reaction conditions: Temp.	Time (h)	2a; Yield (%)
18	r.t.	15	77
19	r.t.	5	67
20	reflux	2	– (**1a**; 75%)
20	r.t.	7	– (**1a**; 94%)

Chart 6

through lithiation, addition of benzonitrile, hydrolysis, and quaternization as shown in Chart 7. To our knowledge, this is the first example of preparing **8**.

Compound **8** reacted with nucleophiles (**21**), such as alcohol, amine, and active methylene compounds, to give the aroylated compounds (**22**) in good yields (Chart 7). This supports the idea that compound **8** is the key intermediate in this oxidative aroylation, and that it acts as an electrophilic aroylating agent.

It is well known that flavins (**25**) are readily reduced by a carbanion and the reduced flavin is easily oxidized by oxygen.[7] Namely, flavin acts as a catalyst in air oxidation.



Nu⊖ or NuH	Reaction conditions: Base	Solvent	Temp.	Time (h)	Product	Yield (%)
21a 	–	DMF	r.t.	1	**22a** 	54
21b EtOH	–	EtOH	reflux	5	**22b** PhCOOEt	80
21c ^{t}BuOK	–	DMF	r.t.	1	**22c** PhCOO^{t}Bu	61
21d $PhCH_2CN$	NaH	DMF	r.t.	1	**22d** PhCH(CN)COPh	95
21e PhCOMe	NaH	DMF	r.t.	1	**22e** $CH_2(COPh)_2$	41
21f $EtOOCCH_2CN$	NaH	DMF	r.t.	1	**22f** EtOOCCH(CN)COPh	95
21g $CH_2(COOEt)_2$	NaH	DMF	r.t.	1	**22g** $PhCOCH(COOEt)_2$	84
21h $CH_2(COMe)_2$	NaH	DMF	r.t.	1	**22h** $PhCOCH(COMe)_2$	26

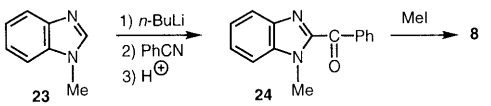
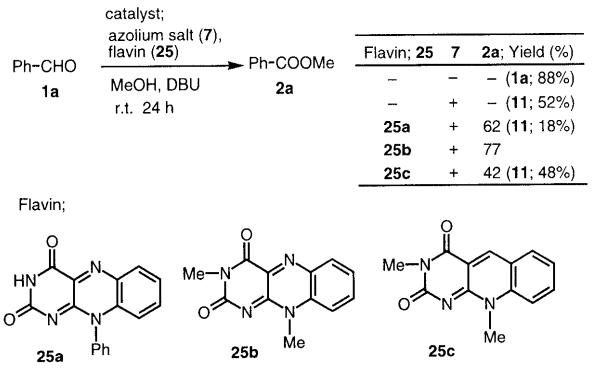
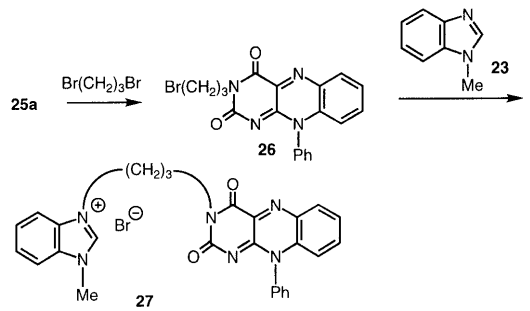


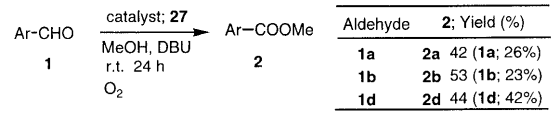
Chart 7



Flavin; **25**	**7**	**2a**; Yield (%)
–	–	– (**1a**; 88%)
–	+	– (**11**; 52%)
25a	+	62 (**11**; 18%)
25b	+	77
25c	+	42 (**11**; 48%)

Chart 8





Aldehyde	**2**; Yield (%)
1a	**2a** 42 (**1a**; 26%)
1b	**2b** 53 (**1b**; 23%)
1d	**2d** 44 (**1d**; 42%)

Chart 9

Yano *et al.* reported that flavin was an effective catalyst for the oxidation of aldehyde catalyzed by thiazolium salt.[8] We anticipated that flavins could be used in this oxidative aroylation as a catalyst in place of nitro compounds. As shown in Chart 8, in the presence of a catalytic amount of flavin (**25**) and benzimidazolium salt (**7**) under aerobic conditions, treatment of arenecarbaldehydes (**1**) in MeOH gave methyl arenecarboxylates **2** in moderate yields. However, in the absence of flavin under the conditions, only benzoin (**11**) was given in 52% yield. 10-Phenylisoalloxazine (**25a**), 3,10-dimethylisoalloxazine (**25b**), and 10-methyl-5-deazaisoalloxazine (**25c**, 5-deazaflavin) were effective catalysts.[7] This reaction can be regarded as a model of flavin-pyruvate oxidase,[9] and also as a model of double-catalytic reactions.

These results led us to design a flavin-binding benzimidazolium salt as a candidate complex catalyst for this oxidative aroylation. We synthesized 1-methyl-3-[3-(10-phenylisoalloxazin-3-yl)propyl]benzimidazolium bromide (**27**), as shown in Chart 9.

Compound **27** was found to be an effective catalyst for this oxidative aroylation. That is, treatment of benzaldehyde (**1a**) with MeOH in the presence of **27** under aerobic conditions resulted in oxidation–substitution reaction to give methyl benzoate (**2a**) in moderate yield. Similarly, other methyl arenecarboxylates **2** were formed under the same conditions in moderate yields. The catalytic activity of **27** was low, but double-catalytic action did occur. This compound can be considered as a model of a complex catalyst, such as an enzyme.

In conclusion, the 1,3-dimethylbenzimidazolium salt (**7**) is an effective catalyst in oxidative aroylation using arenecarbaldehyde (**1**). The aroylation proceeds through the formation of the key intermediate (C^2) by oxidation of the adduct (C^1) obtained from benzimidazolium ylide (C^3) and arenecarbaldehyde (**1**). The flavin (**25**) can be used as a good catalyst in air oxidation. Further, the flavin-binding azolium salt (**27**) acts as an effective complex catalyst in this oxidative aroylation.

Experimental

All melting points are uncorrected. IR spectra were recorded on a JASCO A-102 diffraction grating IR spectrometer. ^{1}H-NMR spectra were measured at 60 MHz on a JEOL PMX60SI NMR spectrometer or at 270 MHz on a JEOL JNM-GSX270 FT-NMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard. Column chromatography was carried out on SiO_2.

Synthesis of Methyl Benzoate (2a) by Oxidative Aroylation General Procedure: A mixture of benzaldehyde (**1a**, 2120 mg, 20 mmol), 1,3-dimethylbenzimidazolium iodide (**7**, 274 mg, 1 mmol), DBU (0.5 ml), and an oxidizing agent (20 mmol) in MeOH (30 ml) was refluxed for 1 h with stirring under a nitrogen atmosphere. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with benzene and $CHCl_3$. The fraction eluted with benzene gave methyl benzoate (**2a**). The results obtained with other oxidizing agents are shown below.

Nitrobenzene (**9a**): The fraction eluted with benzene gave **2a** in 72% yield and the fraction eluted with $CHCl_3$ gave **3**[3b] in 17% yield.

p-Nitroaniline (**9b**): The first fraction gave **2a** in 74% yield. In the reaction in the absence of **7**, work-up as described above gave recovered **1a** in 93% yield.

p-Nitro-*N*,*N*-dimethylaniline (**9c**): The fraction eluted with benzene gave **2a** in 56% yield, and the fraction eluted with $CHCl_3$ gave **11** in 29% yield.

Pyridine *N*-oxide (**10**), DMSO: The fraction eluted with $CHCl_3$ gave

only **11**, as shown in Chart 3. $MeNO_2$: The fraction eluted with $CHCl_3$ gave **11** in 90% yield. In the case of the reaction without benzimidazolium salt, the starting benzaldehyde **1a** was recovered in 93% yield. In the case of the reaction without oxidizing agent, only benzoin (**11**) was obtained in 95% yield. These results are shown in Chart 3.

Synthesis of Methyl Arenecarboxylate (2) by Oxidative Aroylation General Procedure: A mixture of arenecarbaldehyde (**1**, 20 mmol), benzimidazolium salt (**7**, 274 mg, 1 mmol), *p*-nitroaniline (**9b**, 2760 mg, 20 mmol), and DBU (0.5 ml) in MeOH was stirred at room temperature or refluxed (the reaction conditions are shown in Chart 4). The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on SiO_2 with benzene. The first fraction gave methyl arenecarboxylate (**2**).

These results are shown in Chart 4. The structures of the esters (**2**) obtained were established by comparison of the spectral data (^{1}H-NMR and IR) with those of authentic samples.

Synthesis of Alkyl Arenecarboxylate (15, 16, and 17) by Oxidative Aroylation General Procedure: A mixture of arenecarbaldehyde (**1**, 20 mmol), benzimidazolium salt (**7**, 274 mg, 1 mmol), *p*-nitroaniline (**9b**, 2760 mg, 20 mmol), and DBU (0.5 ml) in alcohol (EtOH or *n*-PrOH, 30 ml) or H_2O (in a mixture of 5 ml of H_2O and 25 ml of THF) was stirred at room temperature or refluxed (the reaction conditions are shown in Chart 5). The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on SiO_2 with benzene. The first fraction gave alkyl arenecarboxylate (**16** or **17**). In the case of the reaction in H_2O (H_2O–THF mixture), the residue obtained by concentration of the reaction mixture was dissolved with $CHCl_3$, and the solution was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on SiO_2 with $CHCl_3$. The fraction gave benzoic acid (**15**).

These results are shown in Chart 5. The structures of the esters (**16** and **17**) and benzoic acid (**15**) obtained were established by comparison of the spectral data (^{1}H-NMR and IR) with those of authentic samples.

Self-Oxidative Aroylation of Benzaldehyde (1a) A mixture of benzaldehyde (**1a**, 2120 mg, 20 mmol), benzimidazolium salt (**7**, 274 mg, 1 mmol), *p*-nitroaniline (**9b**, 2760 mg, 20 mmol), and DBU (0.5 ml) in THF (30 ml) was refluxed for 1 h. The reaction mixture was concentrated, and the residue was purified by column chromatography on SiO_2 with benzene and $CHCl_3$. The first fraction eluted with benzene gave *O*-benzoylbenzoin (**14**) in 48% yield (1008 mg). The fraction eluted with $CHCl_3$ gave benzoin (**11**) in 7% yield (148 mg).

1,4-Dimethyl-1*H*-1,2,4-triazolium Iodide (18) A solution of 1-methyl-1,2,4-triazole[10] (10 g, 0.12 mol) and MeI (20.6 g, 0.145 mol) in 30 ml of MeOH was placed in a sealed tube and heated at 100 °C for 2 h. The solvent was removed and the separated solid was recrystallized from acetone to give 1,4-dimethyl-1,2,4-triazolium salt (**18**) in 51% yield (13.7 g). Colorless scales, mp 119—123 °C. *Anal.* Calcd for $C_4H_8N_3I$: C, 21.35; H, 3.58; N, 18.67. Found: C, 21.32; H, 3.45; N, 18.45. ^{1}H-NMR (DMSO-d_6) δ: 4.12 (3H, s, N-CH_3), 4.15 (3H, s, N-CH_3), 9.26 (1H, s, C^3-H), 10.25 (1H, s, C^5-H). ^{13}C-NMR (DMSO-d_6) δ: 34.2 (q), 38.8 (q), 143.2 (d, C^3), 145.1 (d, C^5).

1,3-Dimethylnaphtho[1,2-*d*]imidazolium Iodide (19) A solution of naphtho[1,2-*d*]imidazole (10 g, 0.055 mol), MeI (34 g, 0.24 mol), and sodium methoxide (prepared from 2.74 g of Na and 50 ml of MeOH) was placed in a sealed tube and heated at 100 °C for 2 h. The solvent was removed under reduced pressure and the separated solid was recrystallized from MeOH–acetone to give naphto[1,2-*d*]imidazolium salt (**19**) in 60% yield (11.7 g). Colorless prisms, mp 233—235 °C. *Anal.* Calcd for $C_{13}H_{13}IN_2$: C, 48.17; H, 4.04; N, 8.64. Found: C, 47.67; H, 4.14; N, 8.42. ^{1}H-NMR (DMSO-d_6) δ: 4.12 (3H, s, N-CH_3), 4.43 (3H, s, N-CH_3), 7.55—8.70 (6H, m, aromatic H), 9.60 (1H, s, C^2-H).

Catalytic Action of Azolium Salts (18, 19, and 20) for Oxidative Aroylation with Benzaldehyde (1a) A mixture of benzaldehyde (**1a**, 2120 mg, 20 mmol), azolium salt (**18**, 225 mg; **19**, 324 mg, or **20**, 224 mg, 1 mmol), DBU (0.5 ml), and *p*-nitroaniline (**9b**, 2760 mg, 20 mmol) in MeOH (30 ml) was stirred at room temperature or refluxed under a nitrogen atmosphere (reaction conditions are shown in Chart 6). The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with benzene. The first fraction gave methyl benzoate (**2a**). In the case of the reaction catalyzed by **20**, the first fraction gave the recovered benzaldehyde (**1a**). These results are shown in Chart 6.

2-Benzoyl-1-methyl-1*H*-benzimidazole *n*-Butyllithium (64 ml, 100 mmol, 1.62 mol/l in hexane) was added to a stirred solution of tetramethylethylenediamine (TMEDA) (19 ml) in 50 ml of THF at −78 °C. A solution of 1-methyl-1*H*-imidazole (13.2 g, 100 mmol) in THF (50 ml) was added dropwise to the resulting solution over 1 h, and then a solution of benzonitrile (10.3 g, 100 mmol) was further added dropwise over 1 h at −78 °C. The resulting mixture was stirred for 1 h at −78 °C, the cooling bath was removed, and the whole was stirred for an additional 1 h. Hydrogen chloride (20%, 10 ml) was added to the mixture and the resulting mixture was further stirred for 1 h, poured into ice-H_2O mixture and extracted with benzene. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The fraction eluted with *n*-hexane–AcOEt (7 : 1) gave 2-benzoyl-1-methyl-1*H*-benzimidazole in 66% (15.6 g) yield. Colorless needles (EtOH), mp 72—74 °C. *Anal.* Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.11; N, 11.86. Found: C, 76.06; H, 5.11; N, 11.82. IR (KBr) cm^{-1}: 1660 (CO). ^{1}H-NMR ($CDCl_3$) δ: 4.13 (3H, s, N-CH_3), 7.25—7.72 (6H, m, aromatic H), 7.75—8.07 (1H, m, aromatic H), 8.24—8.51 (2H, m, aromatic H).

2-Benzoyl-1,3-dimethylbenzimidazolium Iodide (8) A solution of 2-benzoyl-1-methyl-1*H*-benzimidazole (12.3 g, 52 mmol) and methyl iodide (12 ml) in *N*,*N*-dimethylformamide (DMF) (12 ml) was heated at 80 °C for 16 h. Ether (20 ml) was added to the mixture, and the crystals that separated were collected and dried to give **8** (18.9 g, 96%), yellowish granules, mp 251—252 °C. IR (KBr) cm^{-1}: 1670 (CO). *Anal.* Calcd for $C_{16}H_{15}IN_2O$: C, 50.81; H, 4.00; N, 7.40. Found: C, 50.52; H, 4.05; N, 7.13. IR (KBr) cm^{-1}: 1670 (CO). ^{1}H-NMR (DMSO-d_6) δ: 4.13 (6H, s, 2 × N-CH_3), 7.60—8.30 (9H, m, aromatic H).

Reaction of 2-Benzoyl-1,3-dimethylbenzimidazolium Iodide (8) with Nucleophiles (21) *N*-Benzoylmorpholine (**22a**): A solution of morpholine (0.23 ml, 2.64 mmol) and the benzimidazolium salt (**8**, 500 mg, 1.32 mmol) in DMF (4 ml) was stirred at room temperature for 1 h. The reaction mixture was poured into ice-H_2O, acidified with dil.-HCl, and extracted with benzene. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography with $CHCl_3$. The fraction gave **22a**, colorless needles (*n*-hexane), mp 74—76 °C (lit.,[11] 73.5—74 °C).

Ethyl Benzoate (**22b**): A solution of benzimidazolium salt (**8**, 500 mg, 1.32 mmol) in EtOH (20 ml) was refluxed for 5 h. The reaction mixture was concentrated under reduced pressure. The residue was poured into ice-H_2O and extracted with benzene. Work-up as described for the preparation of **22a** gave **22b**.

tert-Butyl Benzoate (**22c**): A mixture of potassium *tert*-butoxide (673 mg, 4.5 mmol) and benzimidazolium salt (**8**, 500 mg, 1.32 mmol) in DMF (10 ml) was stirred at room temperature for 1 h. The reaction mixture was poured into ice-H_2O and extracted with benzene. Work-up as described for the preparation of **22a** gave **22c**, colorless oil (lit.,[12] bp 96 °C/2 mmHg). IR (KBr) cm^{-1}: 1710 (CO).

Benzoylphenylacetonitrile (**22d**): A mixture of phenylacetonitrile (0.35 ml, 3 mmol) and NaH (60% in oil, 126 mg, 3.2 mmol) in DMF (10 ml) was stirred for 10 min. Benzimidazolium salt (**8**, 1140 mg, 3 mmol) was added to the resulting mixture, and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured into ice-H_2O and extracted with benzene. Work-up as described for the preparation of **22a** gave **22d**, colorless scales (*n*-hexane), mp 82—83 °C. IR (KBr) cm^{-1}: 2250 (CN), 1680 (CO). ^{1}H-NMR ($CDCl_3$) δ: 5.66 (1H, s, CH), 7.24—7.66 (8H, m, aromatic H), 7.90—8.10 (2H, m, aromatic H).

Dibenzoylmethane (**22e**): Work-up as described for the preparation of **22d** gave **22e**. Colorless needles (*n*-hexane), mp 77—79 °C (lit.,[13] 77—78 °C). ^{1}H-NMR ($CDCl_3$) δ: 6.81 (2H, s, CH_2), 7.23 (6H, m, aromatic H), 7.83—8.10 (4H, m, aromatic H).

Ethyl 2-Benzoylcyanoacetate (**22f**): Work-up as described for the preparation of **22d** gave **22f**. Colorless columns (MeOH–H_2O), mp 40—41 °C. IR (neat) cm^{-1}: 2400—3200 (enol-OH), 2250 (CN), 1660 (CO). ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, t, J=8 Hz, CH_3), 4.37 (2H, q, J=8 Hz, CH_2), 7.45—7.73 (3H, m, aromatic H), 7.89—8.17 (2H, m, aromatic H), 14.3 (1H, b, OH). MS *m/z*: 217 (M^+).

Diethyl 2-Benzoylmalonate (**22g**): Work-up as described for the preparation of **22d** gave **22g**. Colorless oil. IR (neat) cm^{-1}: 1750 (CO), 1690 (CO). ^{1}H-NMR ($CDCl_3$) δ: 1.73 (6H, t, J=7 Hz, 2 × CH_3), 4.24 (4H, q, J=7 Hz, 2 × CH_2), 5.24 (1H, s, CH), 7.38—7.65 (3H, m, aromatic H), 7.77—8.03 (2H, m, aromatic H). MS *m/z*: 220 ($M^+ - CO_2$).

3-Benzoylpentan-2,4-dione (**22h**): Work-up as described for the preparation of **22d** gave **22h**. Colorless oil. IR (neat) cm^{-1}: 3400 (enol-OH), 1550—1670 (CO). ^{1}H-NMR ($CDCl_3$) δ: 2.01 (6H, s, 2 × CH_3), 7.40—7.75 (3H, m, aromatic H), 7.85—8.06 (2H, m, aromatic H), 17.06 (1H, b,

OH). MS *m/z*: 204 (M^+). These results are shown in Chart 7.

Oxidative Aroylation Catalyzed by Flavin (25a, 25b, and 25c) and Benzimidazolium Salt (7) General Procedure: A mixture of benzaldehyde (**1a**, 2120 mg, 20 mmol), 1,3-dimethylbenzimidazolium iodide (**7**, 274 mg, 1 mmol), DBU (0.5 ml), and flavin (1 mmol) in MeOH (30 ml) was stirred at room temperature for 24 h under aerobic conditions. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with benzene and $CHCl_3$. The fraction eluted with benzene gave methyl benzoate (**2a**).

In the case of the reaction catalyzed by **25a** and **25c**, the fraction eluted with $CHCl_3$ gave benzoin (**11**). In the presence of only the benzimidazolium salt (**7**) as the catalyst, benzoin (**11**) alone was obtained in 52% yield (1102 mg). In the absence of both catalysts, flavin (**25**) and benzimidazolium salt (**7**), the starting benzaldehyde (**1a**) was recovered in 88% yield (1866 mg).

3-(3-Bromopropyl)-10-phenylisoalloxazine (26) 1,3-Dibromopropane (25.0 g) and K_2CO_3 (10 g) were added to a solution of 10-phenylisoalloxazine (**25a**,[14] 1.5 g, 5.2 mmol) in 60 ml of DMF and the mixture was stirred for 1 h at 80 to 85 °C. Potassium carbonate was filtered off and the filtrate was concentrated under reduced pressure. Methanol (50 ml) was added to the residue and warmed. The separated solid was collected and dried to give **26** in 68% yield (1.45 g). 3-(3-Bromopropyl)-10-phenylisoalloxazine (**26**): yellow powder, mp 245—246 °C. IR (KBr) cm^{-1}: 1650 (CO). *Anal.* Calcd for $C_{19}H_{15}BrN_4O_2$: C, 55.47; H, 3.65; N, 13.63. Found: C, 55.50; H, 3.67; N, 13.68. ^{1}H-NMR (DMSO-d_6) δ: 2.23 (2H, septet, $J=7$ Hz, CH_2), 3.37 (2H, t, $J=7$ Hz, CH_2Br), 4.10 (2H, t, $J=7$ Hz, CH_2N), 7.06—8.30 (9H, m, aromatic H).

1-Methyl-3-[3-(10-phenylisoalloxazin-3-yl)propyl]benzimidazolium Bromide (27) A solution of 3-(10-phenylisoalloxazin-3-yl)propyl bromide (**26**, 1.0 g, 2.43 mmol) and 1-methyl-1*H*-benzimidazole (1.6 g, 12.2 mmol) in 50 ml of benzene was heated in a sealed tube for 7 h at 100 °C. The separated solid was collected, dried and recrystallized from acetone–MeOH to give **27** in 72% yield (950 mg), yellowish orange prisms, mp 271 °C. IR (KBr) cm^{-1}: 1650 (CO). *Anal.* Calcd for $C_{27}H_{23}BrN_6O_2$: C, 59.68; H, 4.27; N, 15.47. Found: C, 59.38; H, 4.43; N, 15.21. ^{1}H-NMR (DMSO-d_6) δ: 3.05—3.25 (2H, m, CH_2), 4.05 (3H, s, Me), 4.35—4.70 (4H, m, $2\times CH_2N$), 7.20—8.20 (13H, m, aromatic H), 9.56 (1H, s, imidazole C^2-H).

Oxidative Aroylation Catalyzed by Complex Catalyst (27) A mixture of arenecarbaldehyde (**1a**, 2120 mg; **1b**, 2810 mg; or **1d**, 2400 mg; 20 mmol), the flavin-binding benzimidazolium salt (**27**, 111 mg, 0.1 mmol), and DBU (0.2 ml) in MeOH (30 ml) was stirred at room temperature for 24 h under aerobic conditions. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on SiO_2 with benzene and $CHCl_3$. The first fraction eluted with benzene gave methyl arenecarboxylate (**2**). The second fraction gave the recovered starting material **1**.

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References and Notes

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