# A New Synthesis of Diacylamines

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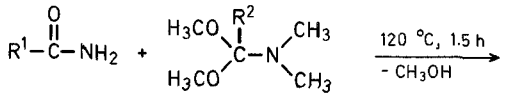
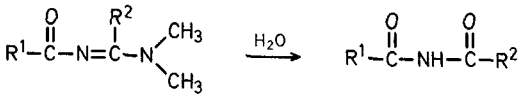
Recently, we reported a general synthesis[1,2] of isoxazoles, pyrazoles, 1,2,4-oxadiazoles, and 1,2,4-triazoles in which the dimethylaminoalkylidene moiety was utilized as a masked acyl function. We now wish to report another application of the dimethylaminoalkylidene moiety for the preparation of diacylamines.

$N^2$-Acyl-$N^1$,$N^1$-dimethylamidines **3** were prepared in good yields (41–94%) by reactions of amides **1** with dimethylformamide dimethyl acetal (**2**; $R^2 = H$) or *N,N*-dimethylacetamide dimethyl acetal (**2**; $R^2 = CH_3$). The acylamidines **3** were then hydrolyzed at room temperature in 70% aqueous acetic acid to give diacylamines **4** in almost quantitative yield. The acylamidines **3** and diacylamines **4** synthesized are presented in the Table.



**1** **2**



**3** **4**

This procedure for the preparation of diacylamines **4a–k** under mild reaction conditions is more convenient than the literature methods. *N*-Formylbenzamide has been prepared by dibenzoylation of formamide, followed by decomposition of the resulting *N*-formyldibenzamide hydrate in refluxing xylene[3] and by hydroxymethylation of benzamide, followed by oxidation of the resulting *N*-hydroxymethyl-

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benzamide[4]. Alkanoylaroylamines and dialkanoylamines have been prepared in 3–73% yields by reacting amides with acid anhydrides in the presence of a catalytical amount of hydrogen chloride[5,6], *N*-substituted diacetylamines have been prepared (31–90% yield) by reaction of primary amines with acetic anhydride in the presence of magnesium and copper(II) acetate[7], and diacylamines have been prepared in 24–84% yields by reacting amides with acid chlorides in pyridine[8]. Some halogenated diacylamines were synthesized by reacting nitriles and carboxylic acids under pressure[9,10].

Diacylamines are useful as biological agents[6,10] and reaction intermediates[11,12].

***N*-(Dimethylaminomethylene)-*p*-bromobenzamide (3c); Typical Procedure:**

A solution of *p*-bromobenzamide (100.0 g, 0.500 mol) in dimethylformamide dimethyl acetal (200 ml, 1.50 mol) is stirred at 120 °C for 1.5 h, during which time some methanol is formed and collected through a reflux condenser. After cooling, the solution deposits **3c** as colorless crystals; yield: 111.6 g (88%); m.p. 105–107 °C. Analytical and spectral data are given in the Table.

***N*-Formyl-*p*-bromobenzamide (4c); Typical Procedure:**

*N*-(Dimethylaminomethylene)-*p*-bromobenzamide (**3c**; 10.0 g, 39.2 mmol) is dissolved in 70% aqueous acetic acid (50 ml). The solution immediately deposits **4c** as colorless crystals; yield: 8.90 g (99%); m.p. 210–212 °C. Analytical and spectral data are given in the Table.

**Table.** $N^2$-Acyl-$N^1$,$N^1$-dimethylamidines **3** and Diacylamines **4**

| Product | $R^1$ | $R^2$ | Yield [%] | m.p. or b.p./torr | Molecular formula[a] or Lit. m.p. | $^1$H-N.M.R. ($CDCl_3$) $\delta$ [ppm] |
|---|---|---|---|---|---|---|
| **3a** | 3,5-di-$H_3CO$—$C_6H_3$ | H | 94 | 108–110 °C | 108–110 °C[2] | 3.10 (s, 3H); 3.14 (s, 3H); 3.80 (s, 6H); 6.58 (t, 1H); 7.42 (d, $J$ = 1.5 Hz, 2H); 8.54 (s, 1H) |
| **3b** | 4-$H_3CO$—$C_6H_4$ | H | 88 | 89–91 °C | $C_{11}H_{14}N_2O_2$ (206.2) | 3.04 (s, 3H); 3.10 (s, 3H); 3.78 (s, 3H); 6.88 (d, $J$ = 4.5 Hz, 2H); 8.03 (d, $J$ = 4.5 Hz, 2H); 8.54 (s, 1H) |
| **3c** | 4-Br—$C_6H_4$ | H | 88 | 105–107 °C | $C_{10}H_{11}BrN_2O$ (255.1) | 3.08 (s, 3H); 3.11 (s, 3H); 7.74 (d, $J$ = 4.0 Hz, 2H); 8.14 (d, $J$ = 4.0 Hz, 2H); 8.57 (s, 1H) |
| **3d** | 4-$O_2N$—$C_6H_4$ | H | 91 | 141–143 °C | 141–143 °C[2] | 3.18 (s, 3H); 3.24 (s, 3H); 8.25 (q, 4H); 8.62 (s, 1H)[b] |
| **3e** | 3-pyridyl | H | 81 | 64–66 °C | 64–66 °C[2] | 3.14 (s, 6H); 7.32 (m, 1H); 8.45 (m, 1H); 8.66 (m, 2H); 9.41 (s, 1H) |
| **3f** | $C_2H_5$ | H | 41 | 80 °C/1.3 | $C_6H_{12}N_2O$ (128.2) | 1.13 (t, $J$ = 7.0 Hz, 3H); 2.46 (q, $J$ = 7.0 Hz, 2H); 3.08 (s, 3H); 3.13 (s, 3H); 8.39 (s, 1H) |
| **3g** | 3,5-di-$H_3CO$—$C_6H_3$ | $CH_3$ | 90 | 90–92 °C | 90–92 °C[2] | 2.29 (s, 3H); 3.11 (s, 6H); 3.81 (s, 6H); 6.57 (t, 1H); 7.31 (d, $J$ = 1.5 Hz, 2H) |
| **3h** | 3,4,5-tri-$H_3CO$—$C_6H_2$ | $CH_3$ | 91 | 121–123 °C | 121–123 °C[2] | 2.32 (s, 3H); 3.16 (s, 6H); 3.89 (s, 3H); 3.92 (s, 6H); 7.45 (s, 2H) |
| **3i** | 4-Br—$C_6H_4$ | $CH_3$ | 90 | 133–135 °C | 133–135 °C[2] | 2.29 (s, 3H); 3.10 (bs, 6H); 7.48 (d, $J$ = 4.0 Hz, 2H); 8.00 (d, $J$ = 4.0 Hz, 2H) |
| **3j** | 4-$O_2N$—$C_6H_4$ | $CH_3$ | 89 | 141–142 °C | $C_{11}H_{13}N_3O_3$ (235.2) | 2.39 (s, 3H); 3.19 (s, 3H); 3.25 (s, 3H); 8.23 (q, 4H) |
| **3k** | t-$C_4H_9$ | $CH_3$ | 88 | 95 °C/1.3 | $C_9H_{18}N_2O$ (170.2) | 1.17 (s, 9H); 2.15 (s, 3H); 3.04 (s, 6H) |
| **4a** | 3,5-di-$H_3CO$—$C_6H_3$ | H | 98 | 182–184 °C | $C_{10}H_{11}NO_4$ (209.2) | 3.80 (s, 6H); 6.73 (t, 1H); 8.19 (d, $J$ = 1.0 Hz, 2H); 9.24 (s, 1H); 11.59 (s, 1H)[b] |
| **4b** | 4-$H_3CO$—$C_6H_4$ | H | 95 | 203–205 °C | $C_9H_9NO_3$ (179.2) | 3.87 (s, 3H); 7.05 (d, $J$ = 4.5 Hz, 2H); 8.05 (d, $J$ = 4.5 Hz, 2H); 9.26 (s, 1H); 11.56 (s, 1H)[b] |
| **4c** | 4-Br—$C_6H_4$ | H | 99 | 210–212 °C | $C_8H_6BrNO_2$ (228.1) | 7.73 (d, $J$ = 8.7 Hz, 2H); 7.96 (d, $J$ = 8.7 Hz, 2H); 9.25 (s, 1H); 11.78 (s, 1H)[b] |
| **4d** | 4-$O_2N$—$C_6H_4$ | H | 97 | 202–205 °C | $C_8H_6N_2O_4$ (194.1) | 8.27 (d, $J$ = 4.0 Hz, 2H); 8.40 (d, $J$ = 4.0 Hz, 2H); 9.26 (s, 1H); 11.97 (s, 1H)[b] |
| **4e** | 3-pyridyl | H | 65 | 164–166 °C | $C_7H_6N_2O_2$ (150.1) | 7.61 (m, 1H); 8.38 (m, 1H); 8.81 (m, 1H); 9.14 (d, $J$ = 1.0 Hz, 1H); 9.28 (s, 1H)[b] |
| **4f** | $C_2H_5$ | H | 65 | 64–66 °C | $C_4H_7NO_2$ (101.1) | 1.21 (t, $J$ = 7.0 Hz, 3H); 2.47 (q, $J$ = 7.0 Hz, 2H); 9.12 (d, $J$ = 10 Hz, 1H); 9.48 (bs, 1H) |
| **4g** | 3,5-di-$H_3CO$—$C_6H_3$ | $CH_3$ | 95 | 161–163 °C | $C_{11}H_{13}NO_4$ (223.2) | 2.37 (s, 3H); 3.81 (s, 6H); 7.09 (t, 1H); 7.12 (d, $J$ = 1.5 Hz, 2H); 10.95 (bs, 1H)[b] |
| **4h** | 3,4,5-di-$H_3CO$—$C_6H_2$ | $CH_3$ | 92 | 171–174 °C | $C_{12}H_{15}NO_5$ (253.2) | 2.40 (s, 3H); 3.74 (s, 3H); 3.86 (s, 6H); 7.31 (s, 2H); 10.98 (s, 1H)[b] |
| **4i** | 4-Br—$C_6H_4$ | $CH_3$ | 96 | 152–154 °C | $C_9H_8BrNO_2$ (242.1) | 2.35 (s, 3H); 7.75 (d, $J$ = 10 Hz, 2H); 7.82 (d, $J$ = 10 Hz, 2H); 11.06 (bs, 1H)[b] |
| **4j** | 4-$O_2N$—$C_6H_4$ | $CH_3$ | 99 | 225–227 °C | $C_9H_8N_2O_4$ (208.2) | 2.35 (s, 6H); 8.10 (d, $J$ = 9 Hz, 2H); 8.38 (d, $J$ = 9 Hz, 2H); 11.29 (bs, 1H)[b] |
| **4k** | t-$C_4H_9$ | $CH_3$ | 95 | 67–70 °C | $C_7H_{13}NO_2$ (143.2) | 1.28 (s, 9H); 2.50 (s, 3H); 8.70 (bs, 1H) |

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.4, H ±0.3, N ±0.3, Hal ±0.2), exception **3f** N −0.7%.

[b] DMSO-$d_6$ solution.

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