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Simple and convenient synthesis of tertiary benzanilides using dichlorotriphenylphosphorane

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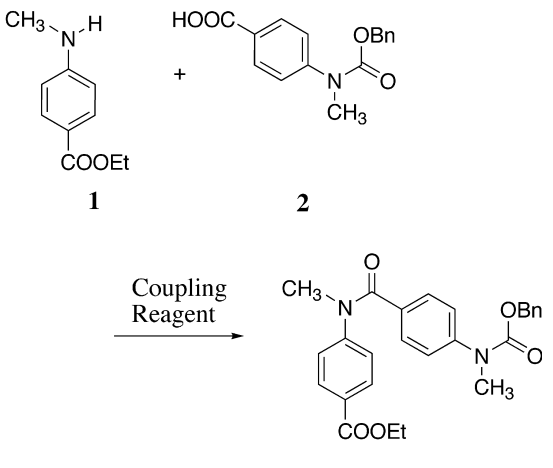
Abstract—Various tertiary benzanilide derivatives were effectively synthesized from substituted benzoic acid and *N*-monoalkylated aniline using dichlorotriphenylphosphorane in chloroform. Yields were generally high, even when an electron-withdrawing group substituted the aromatic ring of aniline, or when an electron-donating group substituted the aromatic ring of benzoic acid. Allyl, Boc, MPM and the Z group were unaffected under these conditions. © 2003 Published by Elsevier Science Ltd.

1. Introduction

Aromatic amides have been utilized as versatile fragments to construct frameworks that have various functions such as molecular recognition, conformational switching and in biological activities.[1–3] Especially, conformational alternation by *N*-alkylation of aromatic amides from *trans*[4] to *cis*[5–7] gives folded structures to such molecules.[6,7] In the classical method of synthesizing aromatic amides using thionyl chloride, the yield is sometimes not so high because the yield of acid chloride from an acid would not be quantitative. Various amide coupling reactions have been developed for peptide synthesis or amidation of weakly nucleophilic amines, but usually many additives are needed for completion of such a reaction.[8] Some of the Lewis acids, for example, boron trifluoride etherate,[9] tetrachlorosilane,[10] and titanium (IV) chloride[11] are rarely used for such couplings, as the yields are usually low, and there is a severe limitation on substituents of substrates because of their strong Lewis acidity. In the course of our search for a mild coupling reagent to couple a carboxylic acid with an *N*-alkylated secondary aniline with low nucleophilicity, we found that dichlorotriphenylphosphorane, which has been used for a synthesis of acid chloride,[12] was highly effective in a one-step amidation, and that no other additive was needed in the reaction, contrary to peptide[13] or aromatic copolyamide[14] syntheses in which this reagent is used. In this paper, we report a convenient and effective amide coupling reaction of *N*-alkylated secondary anilines with a substituted benzoic acid using dichlorotriphenylphosphorane.

2. Results and discussion

The classical peptide coupling reagents[15] such as DCC, and DCC with HOBt gave, at best, only traces of amide for the coupling reaction of substituted *N*-methylaniline **1** and substituted benzoic acid **2** (Scheme 1). The reaction using a peptide-coupling reagent for bulky or *N*-alkylated amino acid, HATU[16] or PyBop,[17] proceeded to some extent, but the yields were low because the reaction did not complete even though several equivalents of the reagent were used, and because inseparable side products were generated. On the other hand, dichlorotriphenylphosphorane cleanly produced the corresponding amide **3**, giving the best results among these dehydrating reagents. During optimization of the reaction conditions, we eventually found that 2.4 equiv. of dichlorotriphenylphosphorane effectively completed the reaction in chloroform at reflux for several hours without



1 **2** **3**

Scheme 1.

Keywords: tertiary amide; aromatic amide; coupling reagent; cyclic amide.

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Table 1. Application of Ph_3PCl_2 to synthesize various amides

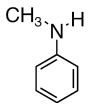
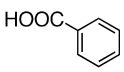
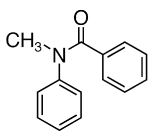
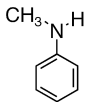
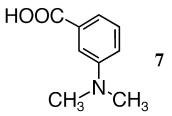
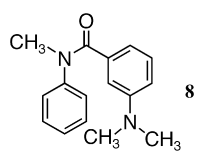
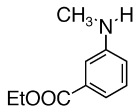
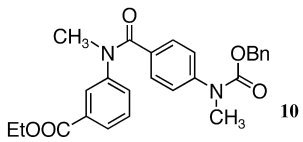
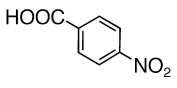
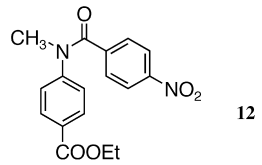
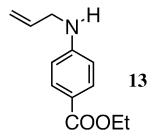
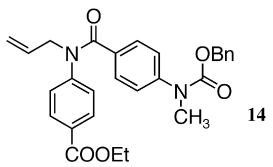
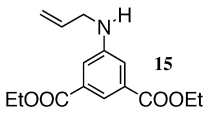
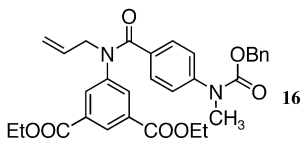
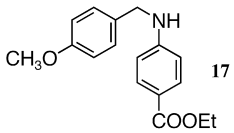
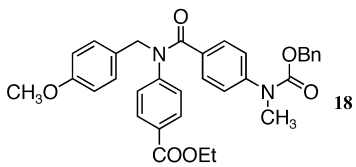
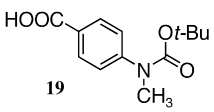
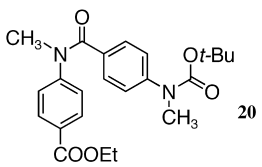
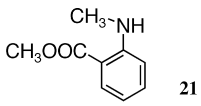
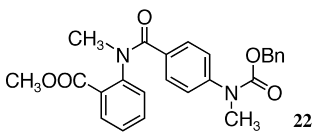
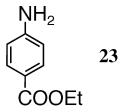
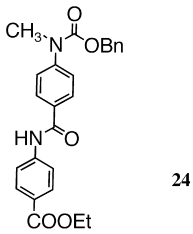
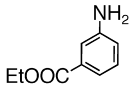
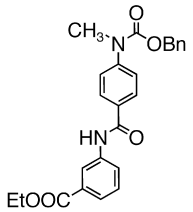
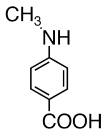
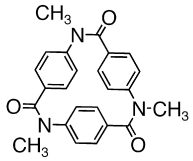
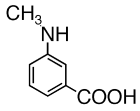
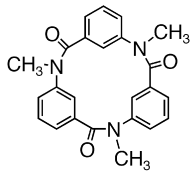
Entry	Amine	Carboxylic acid	Product	Time (h)	Yield (%)
1	 **4**	 **5**	 **6**	2.5	82
2	 **4**	 **7**	 **8**	4.5	81
3	 **9**	**2**	 **10**	3.5	86
4	**1**	 **11**	 **12**	4.0	81
5	 **13**	**2**	 **14**	5.0	80
6	 **15**	**2**	 **16**	6.5	86
7[a]	 **17**	**2**	 **18**	8.75	63
8[b]	**1**	 **19**	 **20**	3.0	92
9[b]	 **21**	**2**	 **22**	5.5	87

Table 1 (*continued*)

Entry	Amine	Carboxylic acid	Product	Time (h)	Yield (%)
10[b]	 **23**	**2**	 **24**	3.5	73
11[b]	 **25**	**2**	 **26**	3.5	89
12	 **27**		 **28**	4.0	31
13	 **29**		 **30**	4.0	59

Reaction conditions. To a solution of an amine (0.5 mmol) and a carboxylic acid (0.525 mmol) in $CHCl_3$ (10 mL) was added Ph_3PCl_2 (1.2 mmol) with stirring. The mixture was heated at reflux.

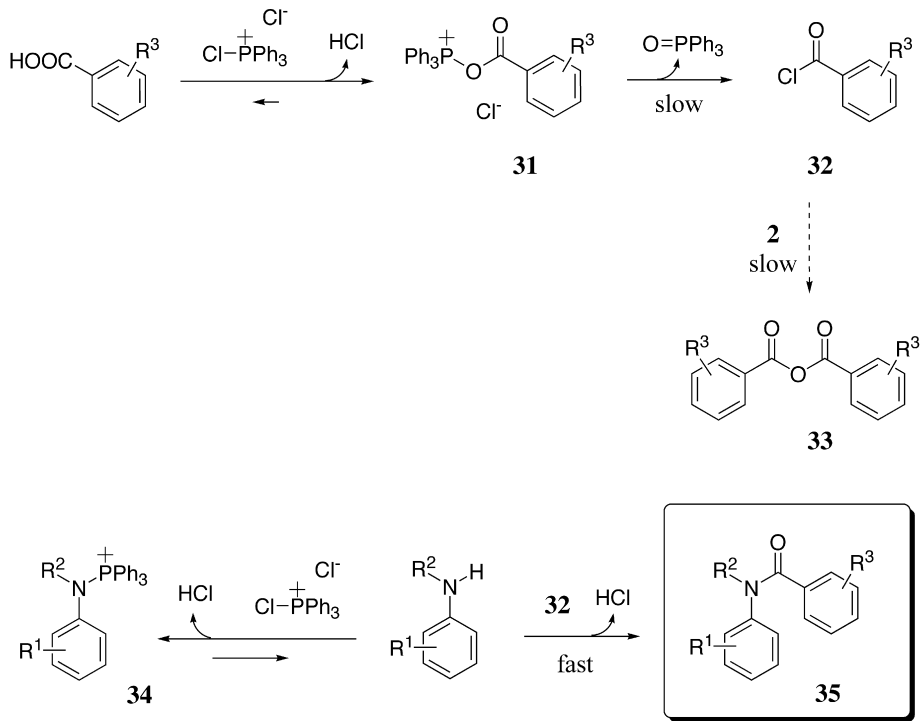
[a] Ph_3PCl_2 (2.8 equiv.).

[b] Ph_3PCl_2 (3.6 equiv.).

other additives to give the corresponding tertiary benzanilides **3** (93% yield). Excess addition over the required amount of dichlorotriphenylphosphorane lowered the yield. Even a base to trap any hydrogen chloride generated was not needed for this reaction. When triethylamine (4.8 equiv.) was added to the reaction mixture, the yield was lowered to 54% with the generation of acid anhydride (15%). In optimized conditions, a carboxylic acid, a secondary amine and dichlorotriphenylphosphorane can be mixed simultaneously before refluxing. Almost the same yield (92%) was obtained when the carboxylic acid was added to the reaction mixture after the amine and dichlorotriphenylphosphorane was mixed and refluxed in chloroform for 2 h. However, the yield was lowered (to 57%) when the aniline was added to the reaction mixture after the carboxylic acid and dichlorotriphenylphosphorane were mixed and refluxed in chloroform for 2 h.

Next, we applied conditions to synthesize various aromatic amides (Table 1). *N*-Methylaniline **4** was coupled with benzoic acid **5** to give *N*-methylbenzanilide **6** in 82% yield in 2.5 h (entry 1). The reaction effectively proceeded even when a benzoic acid or an *N*-alkylaniline had electron donating or withdrawing groups (entries 2–9). Relatively acid labile groups (All, Boc, MPM, Z) were unaffected in this condition. Where aniline had an MPM group on the amino nitrogen, additional dichlorotriphenylphosphorane was needed and the yield was relatively low with a longer reaction time; which would have been due to the steric effect of the MPM group (entry 7). Surprisingly, a coupling of methyl *N*-methylanthranylate **21** with **2** was successful (entry 9), even though amino nitrogen has the lowest nucleophilicity due to the steric effect of the methyl group on amino nitrogen, an intramolecular hydrogen bonding with the neighboring carbonyl group and its electron withdrawing ability. Primary anilines could also couple with substituted benzoic acids under similar conditions, though additional dichlorotriphenylphosphorane was needed to complete the reaction (entries 10, 11).

Because both an acid and an amine are added simultaneously in these conditions, we can easily synthesize



Scheme 2.

cyclic amides from secondary aminobenzoic acid. 4- Or 3-(methylamino)benzoic acids coupled effectively with themselves in this condition to give cyclized aromatic amides (entries 12, 13), which had previously been synthesized by a one-pot reaction using tetrachlorosilane.[18]

A possible reaction mechanism is illustrated in Scheme 2. Initially, substituted benzoic acid rapidly formed an adduct with dichlorotriphenylphosphorane in equilibrium. The adduct was gradually converted to an acid chloride **32**[12] with a small amount of acid anhydride **33**; and the acid chloride rapidly reacted with substituted aniline, which was in equilibrium with an adduct **34** of dichlorotriphenylphosphorane.[19]

To confirm that the reaction proceeded via an acid chloride, benzoyl chloride and *N*-methylaniline were reacted with or without dichlorotriphenylphosphorane in chloroform at reflux. As a result, the reactions were smoothly completed in 15 min to give *N*-methylbenzanilide in both cases. This means the acid chloride **32** was more reactive than the adduct **31**. On the other hand, when benzoic anhydride instead of benzoyl chloride, and *N*-methylaniline were mixed under the same conditions, the reaction did not proceed in a period of several hours even when dichlorotriphenylphosphorane was added. In the coupling reaction of **1** and **2** with dichlorotriphenylphosphorane, the production of acid anhydride **33** that would have reduced the yield of the reaction, could be avoided because the process producing the amide from acid chloride and amine was faster. Therefore, the reaction proceeded via the acid chloride **32** and the aniline, and the rate-determining step would be the formation of the acid chloride. The reason why the yield was low when triethylamine was added would be because the process forming the acid chloride **32** and the benzoic acid to the unreactive anhydride **33** was accelerated.

These mechanisms were supported by ^{1}H NMR experiments as follows. When dichlorotriphenylphosphorane was added to substituted benzoic acid **2** in $CDCl_3$ at room temperature, peaks, different from those of **2**, corresponding to an adduct of them were observed. The ratio of the adduct increased with the adding of dichlorotriphenylphosphorane, and almost all of **2** (>99%) existed as the adduct when 1.5 equiv. of dichlorotriphenylphosphorane had been added. In the same way, when dichlorotriphenylphosphorane was added to substituted aniline **1**, peaks were shifted to a lower field with the adding of dichlorotriphenylphosphorane, but the shifts did not converge even when 1.5 equiv. of dichlorotriphenylphosphorane had been added. These results indicate that the rate constant in the resulting adduct **31** is smaller than that in the resulting adduct **34**, and that the equilibrium constant at which **31** is formed is larger than that for **34**. When **1**, **2** and an equivalent of dichlorotriphenylphosphorane were mixed, 40% of **2** existed as the adduct **31**, judged by the integral of the peaks and the smaller part of **1** than that existed as the adduct **34**, judged by a shift of the chemical shifts. Additionally, when **1**, **2** and 2 equiv. of dichlorotriphenylphosphorane were mixed, almost all of **2** (>99%) existed as the adduct **31**, and some part of **1** still existed in free amino form. Therefore, 2 equiv. of dichlorotriphenylphosphorane were needed to complete the reaction, avoiding generation of the unreactive acid anhydride **33**. Additionally, one more equivalents of dichlorotriphenylphosphorane were needed when primary anilines were used because the generated secondary amide would form a complex with 1 equiv. of dichlorotriphenylphosphorane.[20]

3. Conclusion

We developed a highly efficient method for the production

of tertiary aromatic amides using dichlorotriphenylphosphorane in chloroform. The method is important, especially for the synthesis of cyclized compounds from *N*-alkylaminobenzoic acids, as a carboxylic acid and an amine can be mixed simultaneously. We believe this method provides advantages for synthesis of various functionalized oligo- and cyclic aromatic amides. We are currently exploring such applications.

4. Experimental

4.1. General

Melting points are uncorrected. IR spectra were recorded on a JASCO FT/IR-460plus spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian UNITY 400 spectrometer. Deuteriochloroform was used as solvent unless stated otherwise, and chemical shifts (δ) are referenced to tetramethylsilane or residual protonated solvent. ^{1}H NMR measurements for revealing the reaction mechanisms were performed on a Varian Mercury 300 spectrometer, and deuteriochloroform was passed through neutral aluminium oxide (Brockmann I) immediately before its use in the measurements. High and low mass spectra were obtained on a JEOL The MStation JMS-700 spectrometer. Column chromatography was performed by using Wakogel C-200 or Merck silica gel 60, and thin-layer chromatography was carried out on 0.25-mm Merck precoated silica gel glass plates (Art. 5715). All reactions were carried out under an argon atmosphere. Dehydrated chloroform for the reaction was purchased from Kanto Chemical Co., Inc. (Cat. No. 08097-05).

4.2. General procedures for amide coupling of a substituted benzoic acid and a substituted aniline using dichlorotriphenylphosphorane

To a solution of an amine (0.5 mmol) and a carboxylic acid (0.525 mmol) in dry chloroform (10 mL) under argon, dichlorotriphenylphosphorane (1.2 mmol) was added with stirring. The mixture was heated at reflux for several hours (see Table 1), and the reaction mixture was poured into ice and extracted with ethyl acetate. The organic layer was washed with 4N HCl, saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated to give a crude product, which was purified by silica gel column chromatography (eluent: AcOEt–dichloromethane–MeOH) to give a corresponding amide.

4.2.1. Ethyl 4-[*N*-methyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]benzoate (3). Pale yellow oil. IR (KBr): ν=1510, 1603, 1638, 1713, 2980, 3065 cm^{-1}. ^{1}H NMR: δ 1.35 (3H, t, J=7.0 Hz), 3.26 (3H, s), 3.52 (3H, s), 4.33 (2H, q, J=7.0 Hz), 5.13 (2H, s), 7.06–7.14 (4H, m), 7.23–7.35 (7H, m), 7.91 (2H, ddd, J=9.0, 2.0, 2.0 Hz). ^{13}C NMR: δ 14.2, 37.2, 38.3, 61.1, 67.5, 124.4, 126.2, 127.8, 128.0, 128.2, 128.4, 129.5, 130.6, 132.3, 136.2, 144.7, 148.9, 155.0, 165.7, 169.8. MS (DI-EI) m/z=446 [M$^+$]. HRMS (FAB) calcd for $C_{26}H_{27}N_2O_5$ [M+H]$^+$: 447.1920, found 447.1932.

4.2.2. 3-Dimethylamino-*N*-methylbenzanilide (8). Pale yellow oil. IR (Nujol): ν=1575, 1598, 1640, 2930 cm^{-1}. ^{1}H NMR: δ 2.80 (6H, s), 3.49 (3H, s), 6.57–6.63 (2H, br m), 6.67–6.71 (1H, br m), 6.99 (1H, t, J=8.0 Hz), 7.06 (2H, d, J=7.0 Hz), 7.12 (1H, tt, J=7.5, 1.5 Hz), 7.22 (2H, t, J=7.5 Hz). ^{13}C NMR: δ 38.4, 40.4, 113.2, 113.7, 117.1, 126.2, 126.7, 128.2, 129.0, 136.3, 145.3, 149.9, 171.3. MS (DI-EI) m/z=254 [M$^+$]. HRMS (DI-EI) calcd for $C_{16}H_{18}N_2O$ [M$^+$]: 254.1419, found 254.1425.

4.2.3. Ethyl 3-[*N*-methyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]benzoate (10). Pale yellow oil. IR (KBr): ν=1510, 1585, 1603, 1650, 1710, 2980, 3038 cm^{-1}. ^{1}H NMR: δ 1.38 (3H, t, J=7.0 Hz), 3.25 (3H, s), 3.51 (3H, s), 4.36 (2H, q, J=7.0 Hz), 5.12 (2H, s), 7.06–7.14 (3H, m), 7.19–7.35 (8H, m), 7.82 (1H, ddd, J=8.0, 1.5, 1.5 Hz), 7.87 (1H, dd, J=1.5, 1.5 Hz). ^{13}C NMR: δ 14.2, 37.2, 38.5, 61.3, 67.5, 124.4, 127.2, 127.5, 127.8, 128.0, 128.4, 129.1, 129.5, 131.5, 131.8, 132.5, 136.3, 144.4, 145.0, 155.0, 165.6, 169.9. MS (DI-EI) m/z=446 [M$^+$]. HRMS (DI-EI) calcd for $C_{26}H_{26}N_2O_5$ [M$^+$]: 446.1842, found 446.1836.

4.2.4. Ethyl 4-*N*-methyl-(4-nitrobenzoyl)aminobenzoate (12). Pale yellow powder, mp 121°C. IR (KBr): ν=1603, 1658, 1722, 2925, 2980 cm^{-1}. ^{1}H NMR: δ 1.36 (3H, t, J=7.0 Hz), 3.54 (3H, s), 4.34 (2H, q, J=7.0 Hz), 7.08 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 7.45 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 7.92 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 8.05 (2H, ddd, J=9.0, 2.0, 2.0 Hz). ^{13}C NMR: δ 14.2, 38.1, 61.3, 123.3, 126.5, 129.1, 129.6, 130.9, 141.6, 147.7, 148.3, 165.4, 168.3. MS (DI-EI) m/z=328 [M$^+$]. Anal. calcd for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91; N, 8.53, found: C, 62.13; H, 5.07; N, 8.54.

4.2.5. Ethyl 4-[*N*-allyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]benzoate (14). Pale yellow oil. IR (Nujol): ν=1510, 1605, 1655, 1720, 2930 cm^{-1}. ^{1}H NMR: δ 1.35 (3H, t, J=7.0 Hz), 3.26 (3H, s), 4.33 (2H, q, J=7.0 Hz), 4.55 (2H, ddd, J=6.0, 1.5, 1.5 Hz), 5.13 (2H, s), 5.17 (1H, ddd, J=4.5, 3.0, 1.5 Hz), 5.21 (1H, ddd, J=11.0, 3.0, 1.5 Hz), 7.06–7.14 (4H, m), 7.22–7.36 (7H, m), 7.90 (2H, ddd, J=9.0, 2.0, 2.0 Hz). ^{13}C NMR: δ 14.3, 37.2, 53.2, 61.1, 67.5, 117.9, 124.4, 126.8, 127.8, 128.0, 128.3, 128.5, 130.0, 130.5, 132.3, 132.8, 136.2, 144.8, 147.8, 155.0, 165.7, 169.3. MS (FAB) m/z=473 [M+H]$^+$. HRMS (FAB) calcd for $C_{28}H_{28}N_2O_5$ [M$^+$]: 472.1998, found 472.2005.

4.2.6. Diethyl 5-[*N*-allyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]isophthalate (16). Pale yellow amorphous. IR (KBr): ν=1512, 1600, 1650, 1698, 1710, 2925, 2980, 3078 cm^{-1}. ^{1}H NMR: δ 1.37 (6H, t, J=7.0 Hz), 3.24 (3H, s), 4.35 (4H, q, J=7.0 Hz), 4.55 (2H, d, J=6.0 Hz), 5.11 (2H, s), 5.17 (1H, d, J=6.0 Hz), 5.20 (1H, s), 5.90–6.01 (1H, m), 7.12 (2H, br d, J=9.0 Hz), 7.22–7.35 (7H, m), 7.89 (2H, d, J=1.5 Hz), 8.45 (1H, t, J=1.5 Hz). ^{13}C NMR: δ 14.2, 37.2, 53.2, 61.6, 67.5, 118.5, 124.4, 127.8, 128.1, 128.5, 128.5, 129.4, 131.9, 132.1, 132.3, 132.5, 136.2, 144.0, 144.7, 154.9, 164.9, 169.7. MS (DI-EI) m/z=544 [M$^+$]. HRMS (FAB) calcd for $C_{31}H_{33}N_2O_7$ [M+H]$^+$: 545.2288, found 545.2288.

4.2.7. Ethyl 4-[*N*-4-methoxybenzyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]benzoate (18). Pale

yellow oil. IR (KBr): ν=1512, 1603, 1650, 1710, 2840, 2940 cm^{-1}. ^{1}H NMR: δ 1.34 (3H, t, J=7.0 Hz), 3.25 (3H, s), 3.77 (3H, s), 4.31 (2H, q, J=7.0 Hz), 5.08 (2H, s), 5.12 (2H, s), 6.80 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 6.97 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 7.09 (2H, br d, J=9.0 Hz), 7.19 (2H, d, J=9.0 Hz), 7.22–7.36 (7H, m), 7.84 (2H, ddd, J=9.0, 2.0, 2.0 Hz). ^{13}C NMR: δ 14.5, 37.5, 53.5, 55.4, 61.4, 67.7, 114.1, 124.6, 127.5, 128.0, 128.3, 128.6, 128.7, 129.4, 129.8, 130.0, 130.7, 132.7, 136.5, 144.9, 147.8, 155.2, 159.2, 166.0, 169.8. MS (FAB) m/z=553 [M+H]$^+$. HRMS (FAB) calcd for $C_{33}H_{32}O_6N_2$ [M$^+$]: 552.2272, found 552.2260.

4.2.8. Ethyl 4-[*N*-methyl-4-(*N*-methyl-*tert*-butoxycarbonylamino)benzoylamino]benzoate (20). Pale yellow oil. IR (KBr): ν=1510, 1605, 1648, 1710, 2930, 2980 cm^{-1}. ^{1}H NMR: δ 1.36 (3H, t, J=7.0 Hz), 1.39 (9H, s), 3.19 (3H, s), 3.51 (3H, s), 4.33 (2H, q, J=7.0 Hz), 7.05–7.10 (4H, m), 7.25 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 7.90 (2H, ddd, J=9.0, 2.0, 2.0 Hz). ^{13}C NMR: δ 14.3, 28.2, 36.8, 38.2, 61.1, 80.7, 124.3, 126.3, 128.1, 129.3, 130.5, 131.7, 145.3, 149.0, 154.2, 165.7, 170.0. MS (FAB) m/z=413 [M+H]$^+$. HRMS (FAB) calcd for $C_{23}H_{29}N_2O_5$ [M+H]$^+$: 413.2076, found 413.2039.

4.2.9. Methyl 2-[*N*-methyl-4-(*N*-methylbenzyloxycarbonylamino)benzoylamino]benzoate (22). Pale yellow oil. IR (KBr): ν=1510, 1603, 1648, 1710, 2950, 3038 cm^{-1}. ^{1}H NMR: δ 3.22 (3H, s), 3.42 (3H, s), 3.85 (3H, s), 5.10 (2H, s), 7.02 (2H, br d, J=8.0 Hz), 7.18–7.29 (5H, m), 7.29–7.38 (4H, m), 7.43 (1H, br t, J=8.0 Hz), 7.76 (1H, br d, J=8.0 Hz). ^{13}C NMR: δ 37.3, 38.4, 52.5, 67.4, 124.1, 127.3, 127.7, 128.0, 128.2, 128.4, 129.0, 129.8, 131.6, 133.1, 136.3, 144.2, 144.7, 155.0, 165.9, 169.7. MS (FAB) m/z=433 [M+H]$^+$. HRMS (FAB) calcd for $C_{25}H_{25}N_2O_5$ [M+H]$^+$: 433.1763, found 433.1777.

4.2.10. Ethyl 4-[4-(*N*-methylbenzyloxycarbonylamino)-benzoylamino]benzoate (24). White powder, mp 130°C. IR (KBr): ν=1590, 1605, 1650, 1703, 2980, 3310 cm^{-1}. ^{1}H NMR: δ 1.40 (3H, t, J=7.0 Hz), 3.36 (3H, s), 4.37 (2H, q, J=7.0 Hz), 5.21 (2H, s), 7.30–7.40 (7H, m), 7.74 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 7.81 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 8.04 (2H, ddd, J=9.0, 2.0, 2.0 Hz), 8.14 (1H, br s). ^{13}C NMR: δ 14.3, 37.3, 60.9, 67.8, 119.1, 125.1, 126.2, 127.8, 128.0, 128.2, 128.6, 130.8, 131.4, 142.1, 146.6, 155.1, 165.1, 166.1. MS (DI-EI) m/z=432 [M$^+$]. Anal. calcd for $C_{25}H_{24}N_2O_5$: C, 69.43; H, 5.59; N, 6.48, found: C, 69.43; H, 5.61; N, 6.50.

4.2.11. Ethyl 3-[4-(*N*-methylbenzyloxycarbonylamino)-benzoylamino]benzoate (26). Pale yellow powder, mp 102°C. IR (KBr): ν=1592, 1608, 1665, 1688, 1715, 2980, 3398 cm^{-1}. ^{1}H NMR: δ 1.39 (3H, t, J=7.0 Hz), 3.36 (3H, s), 4.37 (2H, q, J=7.0 Hz), 5.20 (2H, s), 7.28–7.40 (7H, m), 7.44 (1H, t, J=7.0 Hz), 7.80–7.86 (3H, m), 8.06 (1H, dd, J=8.0, 2.5 Hz), 8.11 (1H, br s), 8.13 (1H, dd, J=2.0, 2.0 Hz). ^{13}C NMR: δ 14.3, 37.3, 61.2, 67.8, 121.0, 124.6, 125.1, 125.5, 127.7, 128.0, 128.2, 128.5, 129.2, 131.3, 131.5, 136.1, 138.1, 146.5, 155.1, 165.1, 166.2. MS (FAB) m/z=433 [M+H]$^+$. Anal. calcd for $C_{25}H_{24}N_2O_5$: C, 69.43; H, 5.59; N, 6.48, found: C, 69.38; H, 5.68; N, 6.57.

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