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# Green Protocol for Synthesis of Bis-indolylmethanes and Bis-indolylglycoconjugates in the Presence of Iron(III) Fluoride as a Heterogeneous, Reusable, and Eco-Friendly Catalyst

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An efficient method for the preparation of bis-indolylmethanes and bis-indolylglycoconjugates from carbonyl compounds with indoles in the presence of a catalytic amount of iron(III) fluoride under solvent-free conditions is reported. The desired products were obtained in high yields with a simple and environmentally benign procedure. The use of iron(III) fluoride is feasible because of its stability, easy handling, easy recovery, reusability, and good activity.

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Indoles and their derivatives have applications in the field of pharmaceuticals.<sup>[1]</sup> Many bis-indolylmethanes have been isolated from terrestrial and marine natural sources such as parasitic bacteria, tunicates, and sponges,<sup>[2]</sup> and some of these exhibit biological activity. The acid-catalyzed reaction of electron-rich heterocycles such as pyrroles and indoles with para-dimethylaminobenzaldehyde is known as the Ehrlich test.<sup>[3]</sup> The analogous reaction of indoles with other aromatic or aliphatic aldehydes and ketones produces azafulvenium salts. Azafulvenium salts can undergo further addition with a second indole molecule to give bisindolylmethanes.<sup>[4]</sup> Early attempts involved the use of protic acids and Lewis acids for the reaction of indoles or indolyl Grignard reagents with aldehydes, ketones,  $\alpha$ -ketoacids, imines, iminium salts, or nitrones.<sup>[5]</sup> However, many of these procedures are associated with disadvantages like long reaction time,<sup>[6a]</sup> use of expensive Lewis acids,<sup>[6b]</sup> preformed reagents,<sup>[6c-f]</sup> or extremely low yields. In recent years, several efficient methods using InCl<sub>3</sub>,<sup>[7]</sup> lanthanide triflates,<sup>[8]</sup> LiClO<sub>4</sub>,<sup>[9]</sup> I<sub>2</sub>,<sup>[10]</sup> NBS,<sup>[11]</sup> KHSO<sub>4</sub>,<sup>[12]</sup> montmorillonite,<sup>[13]</sup> HY zeolite,  $[14]_{14}$  Dy(OTf)<sub>3</sub>,  $[15]_{15}$  ZnCl<sub>4</sub>,  $[16]_{12}$ ,  $[17]_{12}$  CeCl<sub>3</sub>·7H<sub>2</sub>O/ Nal/SiO<sub>2</sub>,<sup>[18]</sup> iron(III) salts in ionic liquids,<sup>[19]</sup> polyaniline salts,<sup>[20]</sup> and ionic liquids<sup>[21]</sup> have been reported for the synthesis of bis-indolylmethanes.

Although a number of different methods have been reported for the preparation of bis-indolylmethanes, there is still a need to search for better catalysts with regard to their toxicity, handling, availability, economic viability, and operational simplicity. In view of the recent trend in catalytic process, investigations for new and less hazardous catalysts have become a priority in synthetic organic chemistry. Iron(III) chloride has been used widely as a Lewis acid catalyst in a variety of organic transformations;<sup>[19,22]</sup> however, the susceptibility of iron(III) chloride to aqueous media impedes its use for large-scale synthesis. On the other hand, iron(III) fluoride has emerged as a mild, non-toxic, inexpensive, and water-tolerant Lewis acid catalyst for various organic transformations.<sup>[23]</sup> There have been no reports on the use of iron(III) fluoride for the synthesis of bisindolylmethanes and bis-indolylglycoconjugates from carbonyl compounds under solvent-free conditions. Moreover, the catalytic applications of various reagents for the synthesis of bis-indolylmethanes have been reported frequently, but relatively few examples have been reported for the synthesis of bis-indolylglycoconjugates.<sup>[24]</sup> Therefore, a more efficient method to carry out this transformation is still highly sought.

In continuation of our program to develop reactions in aqueous, solvent-free systems,<sup>[23]</sup> we report a simple, convenient, and efficient process for the synthesis of bisindolylmethanes and bis-indolylglycoconjugates 3a-3q from carbonyl compounds 1 and 2, in which only a catalytic amount of iron(III) fluoride, a relatively environmentally acceptable chemical, is required (Scheme 1).

The electrophilic substitution reaction of indole with benzaldehyde in the presence of 5 mol% iron(III) fluoride at room temperature afforded the corresponding bis-indolylmethane within 10 min. Similarly, the scope of the reaction was assessed using structurally diverse aldehydes and ketones (Table 1). Aromatic (entries 1–10), aliphatic (entry 11),  $\alpha$ , $\beta$ -unsaturated (entry 12), and alicyclic (entry 15) aldehydes reacted smoothly with indole to afford the corresponding bis-indolylmethanes in high yields. In addition, the reaction is



Scheme 1.

Table 1. FeF<sub>3</sub>-catalyzed synthesis of bis(indolyl)methanes

Entry	Aldehyde/Ketone	Product	Time [min]	Yield <sup>A</sup> [%]
1	C <sub>6</sub> H <sub>5</sub> CHO	3a	10	94
2	4-ClC <sub>6</sub> H <sub>4</sub> CHO	3b	15	94
3	4-MeC <sub>6</sub> H <sub>4</sub> CHO	3c	15	95
4	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CHO	3d	15	91
5	4-MeOC <sub>6</sub> H <sub>4</sub> CHO	3e	15	93
6	3,4-(MeO) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	3f	20	92
7	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	3g	20	89
8	2-ClC <sub>6</sub> H <sub>4</sub> CHO	3h	18	88
9	3,4-(EtO) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	3i	20	91
10	3,4-(OCH <sub>2</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CHO	3j	17	93
11	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CHO	3k	15	91
12	C <sub>6</sub> H <sub>5</sub> CH=CHCHO	31	15	90
13	Thiophene-2-carboxaldehyde	3m	20	89
14	Furfural	3n	20	91
15	Cyclohexanal	30	15	88
16	Cyclopentanone	3p	25	84
17	Cyclohexanone	3q	25	89

<sup>A</sup> Yield of isolated pure product; products are characterized by IR, <sup>1</sup>H NMR, elemental analysis, and comparison with authentic samples.

applicable to ketones such as cyclopentanone and cyclohexanone. The reaction of cyclohexanone with indole gave a better yield than cyclopentanone, perhaps because of the stability of the six-membered ring compared with a five-membered ring. Further, the present protocol was successfully applied to heteroaromatic aldehydes (entries 13 and 14) to afford the corresponding bis-indolylmethanes in high yields within 20 min. It is noteworthy that these substrates reacted with equal ease in short times to furnish the products in high yields and without side reactions, which are normally encountered under acidic conditions.

In order to expand the generality of the present protocol, we employed sugar aldehyde, 1,2-*O*-isopropylidene-3-*O*-methyl- $\alpha$ -D-*xylo*-pentadialdo-1,4-furanose (Scheme 2, **a**). When indole was allowed to react with sugar-derived aldehyde **a** in the presence of 5 mol% iron(III) fluoride at room temperature, the corresponding bis-indolylglycoconjugate **4a** was obtained in good yield.

Further, we studied the catalytic ability of other iron salts such as FeCl<sub>3</sub>, FeBr<sub>3</sub> FeI<sub>3</sub>, Fe<sub>2</sub>(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O, and Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>·*n*H<sub>2</sub>O for the synthesis of bis-indolylmethanes. Among these catalysts, FeF<sub>3</sub> is more effective than other catalysts. By using 5 mol% of FeCl<sub>3</sub>, FeBr<sub>3</sub>, and FeI<sub>3</sub>, Fe<sub>2</sub>(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O, and Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>· $\alpha$ H<sub>2</sub>O, benzaldehyde was converted into the corresponding bis-indolylmethanes in 64, 45, 42, 41, and 0% yield respectively when the reaction mixture was ground under solvent-free conditions for 10 min.

This result shows the strong catalytic ability of  $FeF_3$  in comparison with  $FeCl_3$ ,  $FeBr_3$ , and  $Fel_3$ .

In view of greener chemistry, efficient recovery and reuse of the catalyst is highly desirable. In our process, the catalyst was recovered and reused efficiently without activation. The reusability of iron(III) fluoride was examined by using 4-chlorobenzaldehyde as a model substrate, and the results are described in the experimental procedure.

As compared with recently reported methods that required large<sup>[7–12]</sup> and stoichiometric amounts of catalysts,<sup>[13]</sup> the present procedure required less catalyst (5 mol%) for the reaction to proceed cleanly. Although various methods have been recently reported for this conversion, most require long reaction times,<sup>[7–9]</sup> expensive reagents<sup>[8,15–18]</sup> that are not readily available and need to be prepared,<sup>[8,14–17]</sup> and some reagents are destroyed in the workup procedure and cannot be recovered and reused.<sup>[9–12]</sup> In contrast, iron(III) fluoride as a mild, non-hygroscopic, inexpensive, eco-friendly, and commercially available reagent that affords the desired products in short reaction times and low catalyst loadings.

To conclude, the present procedure clearly demonstrates that conversion of aldehydes, ketones, and sugar aldehydes into bis-indolylmethanes and bis-indolylglycoconjugates using iron(III) fluoride as a mild, cheap, and commercially available catalyst under solvent-free conditions is a valid alternative to existing methods. It also offers several advantages including high product yields products, cleaner reactions, operational simplicity, and easy workup.

# Experimental

Melting points were measured by using a Buchi R-535 apparatus. IR spectra were recorded on a Bomem MB FT-IR spectrometer. <sup>1</sup>H NMR spectra were recorded on a Varian Gemini-200 spectrometer. Mass spectra were recorded on a VG Micromass-7000 H (70 eV). CHN analyses were recorded on a Vario EL analyzer.

## Experimental Procedure

A mixture of indole (2 mmol), 4-chlorobenzaldehyde (1 mmol), and iron(III) fluoride (0.05 mmol) under solvent-free conditions was ground in a mortar and pestle at room temperature for an appropriate time. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with water (10 mL), and the mixture was extracted with ethyl acetate ( $2 \times 10$  mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and solvent was removed under reduced pressure to furnish a crude product that was further purified by column chromatography on silica gel (ethyl acetate/hexane 1/9). The aqueous layer was then separated and evaporated under reduced pressure to afford the catalyst. The recovered catalyst was then reused for the reaction of a fresh lot of 4-chlorobenzaldehyde (1 mmol) with indole (2 mmol) to afford 90% yield of the corresponding product after 20 min. The recovered catalyst was reused for four consecutive reactions of 4-chlorobenzaldehyde



## Scheme 2.

(1 mmol) with indole (2 mmol), affording 88, 85, 82, and 80% yields of the corresponding products, respectively, in 25, 30, 35 and 40 min.

### Compound 3a

Solid, mp 125–126°C. (Found: C 85.8, H 5.5, N 8.6%. Calc. for C<sub>23</sub>H<sub>18</sub>N<sub>2</sub> (322.14): C 85.7, H 5.6, N 8.7%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 750, 1095, 1455, 1600, 1620, 3055, 3415 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.90 (s, 1H, Ar–CH), 6.65 (s, 2H), 7.00 (t, 2H, *J* 7.0), 7.22 (m, 3H), 7.30 (m, 2H), 7.35 (m, 6H), 7.95 (br s, 2H, NH).

## Compound 3b

Solid, mp 75–77°C. (Found (HR-MS): 356.1070. Calc. for  $C_{23}H_{17}ClN_2$ : 356.1080.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1090, 1450, 1490, 3055, 3415 (NH).  $\delta_H$  (CDCl<sub>3</sub>) 5.80 (s, 1H, Ar–CH), 6.65 (s, 2H), 7.05 (t, 2H, *J* 8.3), 7.15 (t, 2H, *J* 7.9), 7.25–7.35 (m, 8H), 7.95 (br s, 2H, NH).

# Compound 3c

Solid, mp 94–96°C. (Found: C 85.4, H 5.9, N 8.0%. Calc. for  $C_{24}H_{20}N_2$  (349.45): C 85.7, H 6.0, N 8.3%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 775, 1055, 1220, 1515, 1610, 2930, 3040, 3415 (NH).  $\delta_{H}$  (CDCl<sub>3</sub>) 2.35 (s, 3H, Ar–CH<sub>3</sub>), 5.85 (s, 1H, Ar–CH), 6.70 (s, 2H), 7.05 (t, 2H, *J* 7.2), 7.1 (d, 2H, *J* 7.6), 7.25–7.29 (m, 6H), 7.5 (d, *J* 7.6, 2H), 7.98 (br s, 2H, NH).

## Compound 3d

Solid, mp 216–218°C. (Found: C 75.3, H 4.5, N 11.6%. Calc. for  $C_{23}H_{17}N_3O_2$  (367.40): C 75.2, H 4.7, N 11.4%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1340, 1455, 1510, 1595, 3050, 3420 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.98 (s, 1H, Ar–CH), 6.70 (s, 2H), 7.00–7.05 (m, 3H), 7.35 (d, 3H, *J* 8.0), 7.40 (d, 2H, *J* 8.2), 7.50 (d, 2H, *J* 8.8), 8.05 (br s, 2H, NH), 8.15 (d, 2H, *J* 8.8).

# Compound 3e

Solid, mp 187–188°C. (Found: C 81.7, H 5.8, N 8.0%. Calc. for  $C_{24}H_{20}N_2O$  (352.43): C 81.8, H 5.7, N 8.0%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1220, 1240, 1455, 1505, 1610, 2930, 3415 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 3.75 (s, 3H, CH<sub>3</sub>), 5.80 (s, 1H, Ar–CH), 6.65 (s, 2H), 6.80 (d, 2H, *J* 8.2), 7.05 (t, 2H, *J* 7.2), 7.15 (t, 2H, *J* 7.2), 7.20 (s, 2H), 7.35–7.40 (m, 4H), 7.98 (br s, 2H, NH).

## Compound 3f

Solid, mp 197–199°C.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 765, 1005, 1235, 1495, 1620, 2980, 3060, 3445 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 3.75 (s, 3H), 3.82 (s, 3H), 5.75 (s, 1H), 6.72 (d, 2H, *J* 2.4), 6.80 (d, 2H, *J* 8.2), 6.85 (s, 1H), 6.90 (d, 2H, *J* 8.2), 7.05 (t, 2H, *J* 8.0), 7.35 (t, 4H, *J* 8.2), 10.45 (br s, 2H, NH). *m/z* 382 (100%, M<sup>+</sup>), 265 (10), 245 (50), 69 (20).

# Compound 3g

Solid, mp 153–154°C.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 775, 1015, 1250, 1475, 1610, 2975, 3050, 3450 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.83 (s, 1H), 6.75 (d, 2H, *J* 2.4), 6.87 (m, 1H), 6.95 (m, 2H), 6.92–7.02 (m, 4H), 7.2 (s, 1H), 7.25 (t, 2H, *J* 8.2), 7.40 (s, 1H), 7.92 (br s, 2H, NH). *m*/*z* 390 (100%, M<sup>+</sup>), 392 (60, [M+2]<sup>+</sup>), 274 (80), 245 (50), 204 (20), 176 (5), 117 (10).

#### Compound 3h

Solid, mp 73–74°C. (Found: (HR-MS): 356.1070. Calc. for C<sub>23</sub>H<sub>17</sub>ClN<sub>2</sub>: 356.1080.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1015, 1045, 1095, 1340, 1415, 1455, 1620, 3050, 3410 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 6.30 (s, 1H, Ar–CH), 6.70 (s, 2H), 7.05 (t, 2H, *J* 8.2), 7.10–7.20 (m, 6H), 7.35–7.41 (m, 4H), 7.97 (br s, 2H, NH).

# Compound 3i

Solid, mp 185–187°C.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 765, 1015, 1230, 1495, 1625, 2990, 3100, 3420 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.35 (t, 3H, *J* 8.0), 1.42 (t, 3H, *J* 7.0), 3.95 (q, 2H, *J* 7.0), 4.05 (q, 2H, *J* 7.0), 5.75 (s, 1H), 6.63 (d, 2H, *J* 2.4), 6.75 (m, 2H), 6.80 (m, 1H), 6.95 (t, 2H, *J* 8.2), 7.05 (t, 2H, *J* 8.2), 7.30 (m, 4H), 7.95 (br s, 2H, NH). *m/z* 410 (70%, M<sup>+</sup>), 266 (10), 248 (20), 215 (5), 160 (60), 135 (100), 121 (30), 91 (40), 69 (20).

# Compound 3j

Solid, mp 96–98°C.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 765, 1075, 1210, 1490, 1615, 3100, 3475 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.82 (s, 1H, CH), 5.90 (d, 2H), 6.65 (d, 2H, *J* 2.4), 6.72 (d, 1H, *J* 8.4), 6.85 (d, 2H, *J* 8.4), 7.05 (t, 2H, *J* 8.4), 7.20 (t, 2H, *J* 8.4), 7.25 (d, 2H, *J* 8.4), 7.35 (d, 2H, *J* 8.4), 7.95 (br s, 2H, NH). *m*/*z* 366 (100%, M<sup>+</sup>), 245 (60), 204 (30), 57 (20), 43 (25).

#### Compound 3k

Solid, mp 67–69°C. (Found: C 83.5, H 8.2, N 8.1%. Calc. for  $C_{23}H_{26}N_2$  (330.47): C 83.4, H 7.9, N 8.5%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 790, 1095, 1335, 1450, 1620, 3055, 3410 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 0.85 (t, 3H, *J* 7.0), 1.25–1.35 (m, 8H), 2.20 (m, 2H), 4.60 (t, 1H, *J* 7.6), 7.00–7.05 (m, 4H), 7.15 (t, 2H, *J* 8.0), 7.30 (d, 2H, *J* 8.0), 7.55 (d, 2H, *J* 7.2), 7.95 (br s, 2H, NH).

#### Compound 31

Semisolid.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 765, 990, 1050, 1475, 1595, 2960, 3110, 3450 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.95 (s, 1H), 6.42 (d, 1H, *J* 16.0), 6.65 (d, 2H, *J* 2.2), 7.05 (t, 2H, *J* 8.0), 7.15 (t, 2H, *J* 8.0), 7.30 (m, 4H), 7.40 (m, 3H), 7.55 (m, 2H), 7.75 (d, 1H, *J* 16.0), 7.95 (br s, 2H, NH). *m/z* (EI) 346 (20%, M<sup>+</sup>), 321 (100), 244 (80), 205 (30), 122 (15), 77 (10).

## Compound 3m

Solid, mp 152–154°C. (Found: C 76.7, H 5.0, N 8.5%. Calc. for C<sub>21</sub>H<sub>16</sub>N<sub>2</sub>S (328.10): C 76.8, H 4.9, N 8.5%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1250, 1455, 1710, 3410 (NH).  $\delta_{H}$  (CDCl<sub>3</sub>) 6.15 (s, 1H, Ar–CH), 6.86 (s, 2H), 6.90–7.47 (m, 1H), 7.95 (br s, 2H, NH).

# Compound 3n

Solid, mp 113–115°C.  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 665, 750, 790, 940, 1010, 1045, 1095, 1145, 1160, 1215, 1248, 1345, 1410, 1450, 1505, 1555, 1610, 1725, 2850, 2920, 3055, 3120, 3414, 3896.  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 5.80 (s, 1H), 5.95 (d, 1H, *J* 3.4), 6.22 (d, 1H, *J* 2.4), 6.75 (d, 1H, *J* 2.4), 6.95 (t, 2H), 7.10 (t, 2H), 7.25–7.45 (m, 5H), 7.90 (br s, 2H, NH). *m/z* 312 (8%, M<sup>+</sup>), 137 (28), 105 (16), 91 (93), 43 (100).

#### Compound 30

Solid, mp 137–139°C.  $\nu_{max}$  (KBr)/cm $^{-1}$ 775, 1040, 1290, 1575, 1610, 2990, 3010, 3420 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.22 (m, 6H) 1.95 (m, 4H), 2.24

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(m, 1H), 4.40 (m, 1H), 6.96 (d, 2H, J 2.4), 7.05 (m, 2H), 7.10 (m, 2H), 7.25 (d, 2H, J 8.2), 7.45 (d, 2H, J 8.0), 7.95 (br s, 2H, NH). m/z 328 (30%, M<sup>+</sup>), 246 (80), 130 (25), 84 (60), 57 (90), 41 (100).

# Compound 3p

Solid, mp 73–74°C. (Found: C 84.0, H 6.7, N 9.3%. Calc. for  $C_{21}H_{20}N_2$ : C 84.0, H 6.7, N 9.3%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 775, 1010, 1490, 1585, 1610, 2965, 3430 (NH).  $\delta_H$  (CDCl<sub>3</sub>) 1.72 (m, 4H), 2.40 (m, 4H), 6.70 (t, 2H, *J* 8.2), 6.95 (m, 4H), 7.25 (d, 2H, *J* 8.2), 7.42 (d, 2H, *J* 8.0), 7.98 (br s, 2H, NH).

# Compound 3q

Solid, mp 119–120°C. (Found: C 84.1, H 7.1, N 9.0%. Calc. for  $C_{22}H_{22}N_2$ : C 84.1, H 7.1, N 9.9%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 785, 1015, 1235, 1480, 1580, 1620, 2950, 3030, 3450 (NH).  $\delta_H$  (CDCl<sub>3</sub>) 1.82 (m, 6H), 2.50 (m, 4H), 6.80 (t, 2H, *J* 8.2), 7.05 (m, 4H), 7.24 (d, 2H, *J* 8.0), 7.55 (d, 2H, *J* 8.0), 7.98 (br s, 2H, NH).

# Compound 4a

Solid, mp 102–103°C. (Found: C 71.8, H 6.3%. Calc. for C<sub>25</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>: C 71.8, H 6.3%.)  $\nu_{max}$  (KBr)/cm<sup>-1</sup> 1010, 1075, 1160, 1305, 1510, 1710, 1725, 2935, 2990, 3390 (NH).  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.22 (s, 3H), 1.60 (s, 3H), 3.10 (s, 3H), 3.30 (d, 1H, *J* 4.2), 4.50 (d, 1H, *J* 5.2), 4.98 (t, 2H, *J* 17.2), 5.80 (d, 1H, *J* 5.2), 6.75–7.22 (m, 8H), 7.33–7.50 (m, 1H), 7.65 (d, 1H, *J* 6.5), 9.98 (br s, 2H, NH).

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