Selective N,N-Dimethylation of Primary Aromatic Amines with Methyl Alkyl Carbonates in the Presence of Phosphonium Salts.

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Supporting Information

General Experimental Methods. GLC and GC/MS (70 eV) analyses were run using HP5 and HP5/MS capillary columns (30 m), respectively. ^{1}H and spectra were recorded at 300 and 400 MHz spectrometers, ^{13}C NMR at 75 and 100 MHz. Chemical shifts are reported in δ values downfield from TMS. $CDCl_3$ was used as the solvent. IR spectra were recorded at room temperature on KBr pellets.

Compounds **3a-d**, **4a-b**, **5a-g**, **6a-b**, **7a**, DMC, and K_2CO_3 were ACS grade and were employed without further purification.

Isolation and characterisation of methyl alkyl carbonates.

Methyl alkyl carbonates **1a-c** were purified by distillation under vacuum, and recovered as colorless liquids: **1a** (b.p. 92 °C / 100Pa) 72% yield (98% purity by GC); **1b** (b.p. 65 °C / 100Pa) 62% yield (99.5% purity by GC); **1c** (b.p. 39 °C / 100Pa) 60% yield (98.5% purity by GC). Full spectroscopic data of **1b** were already reported: [1] the structure of **1b** was confirmed by comparison to an authentic sample. **1a** and **1c** were characterized by GC/MS, ^{1}H NMR, and ^{13}C NMR.

2-[2-(2-Methoxyethoxy)ethoxy]ethyl methyl carbonate, 1a. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29-4.25 (m, 2H), 3.76 (s, 3H), 3.72-3.68 (m, 2H), 3.67-3.60 (m, 6H), 3.55-3.51 (m, 2H), 3.36 (s, 3H). ^{13}C NMR δ (100 MHz, $CDCl_3$), 54.9, 69.0, 67.0, 68.9, 70.51, 70.55, 70.6, 71.9, 155.7. GC-MS, 70 eV, m/z: 222 (M^+, <1%), 103 (100), 89 (12), 59 (76), 58 (27). Anal. Calcd. for $C_9H_{18}O_6$: C, 48.65; H, 8.11. Found: C, 48.72; H, 8.19.

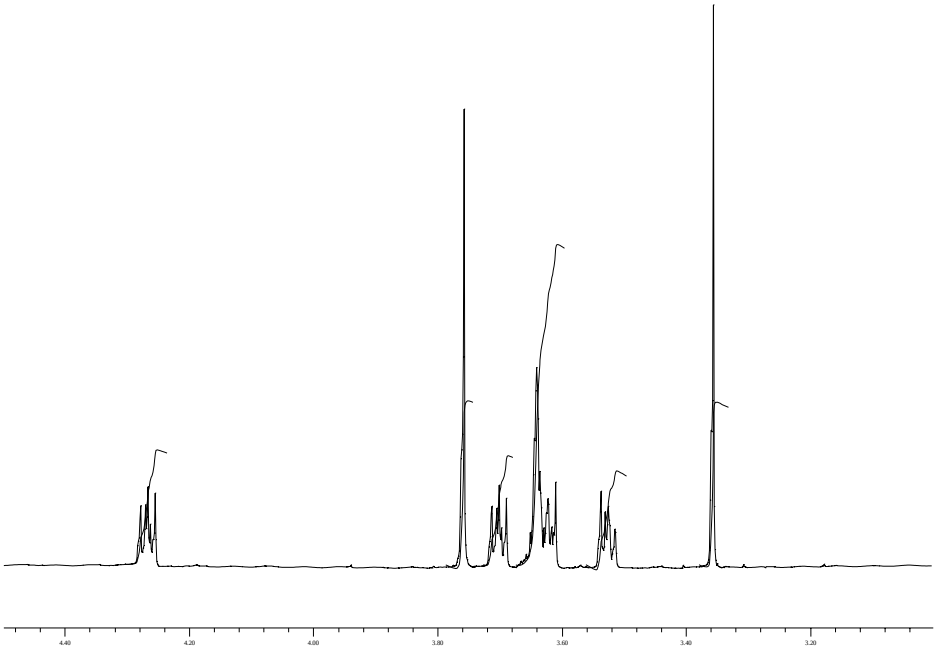

Figure 1. ^{1}H NMR of carbonate **1a**

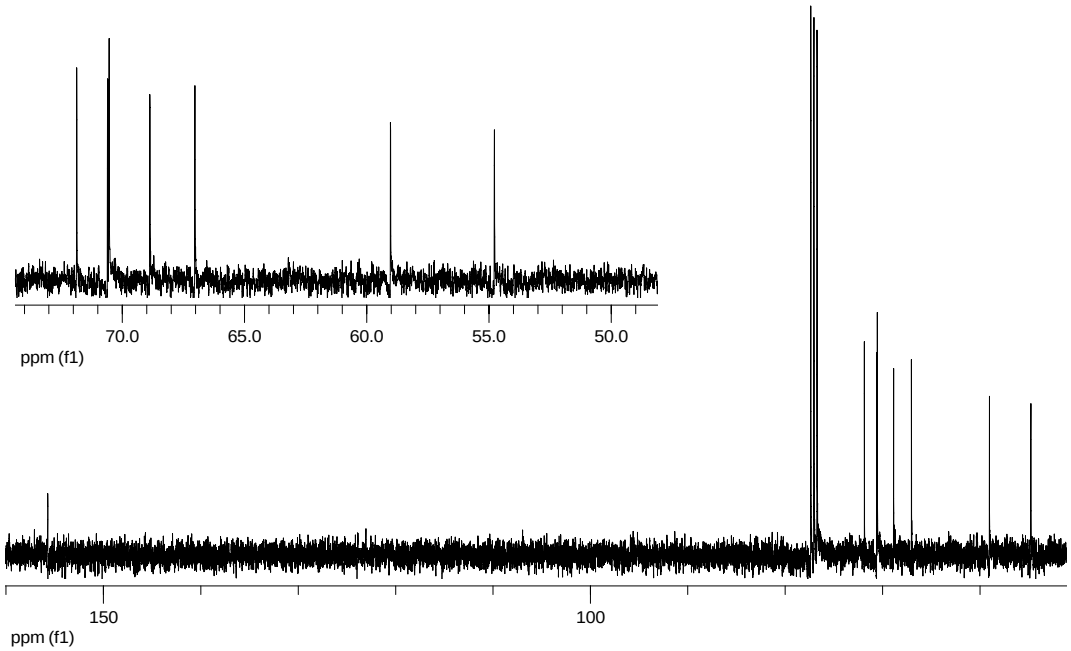

Figure 2. ^{13}C NMR of carbonate **1a**

(2-Methoxy)ethyl methyl carbonate, **1c**. [2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40 (s, 3H), 3.63 (t, 2H, J = 4.71 Hz), 3.80 (s, 3H), 4.31 (t, 2H, J = 4.70 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.8, 58.9, 66.8, 70.1, 155. 7. GC-MS, 70 eV, m/z: 134 (M^+, <1%), 103 (11), 77 (18), 59 (85), 58 (100).

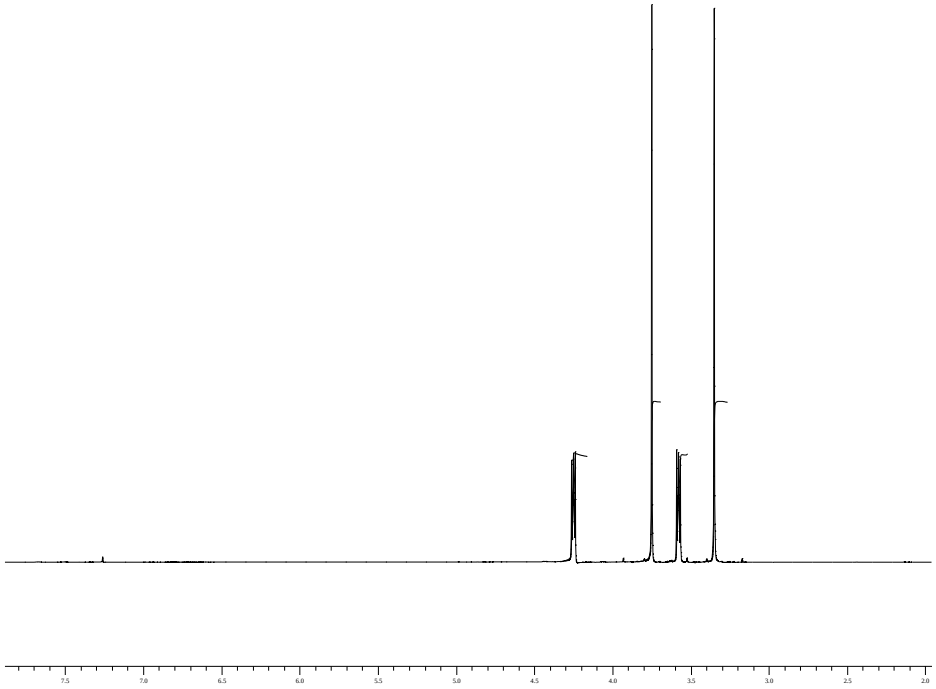

Figure 3. ^{1}H NMR of carbonate **1c**

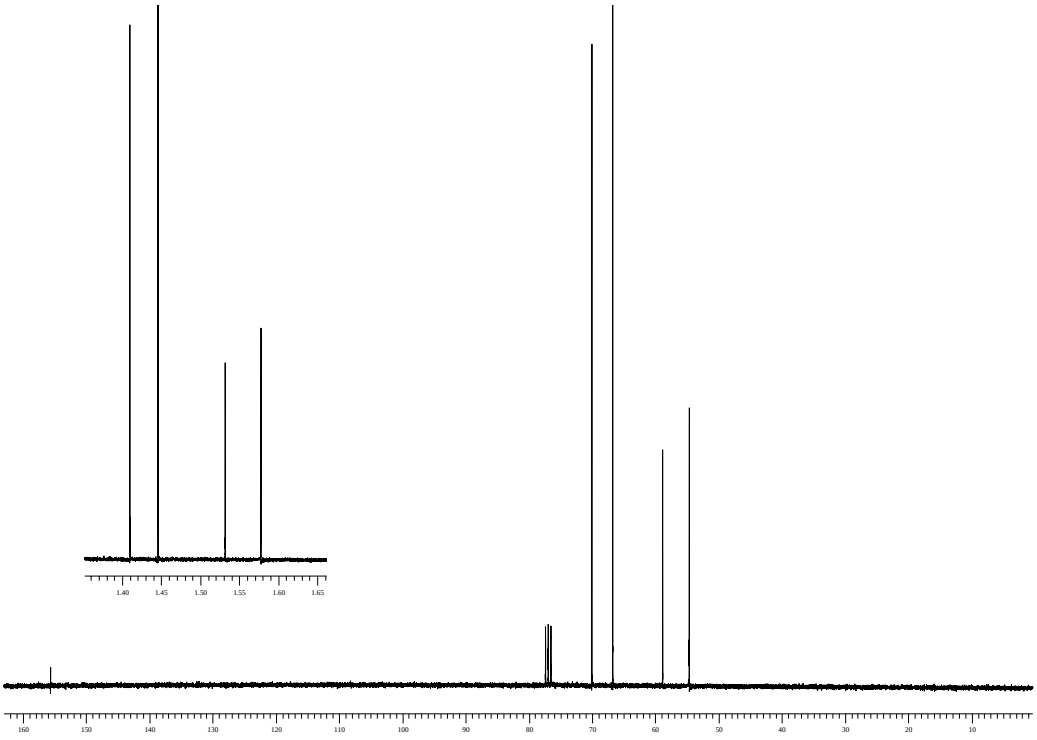

Figure 4. ^{13}C NMR of carbonate **1c**

Isolation and characterisation of N,N-dimethylanilines D_x.

N,N-dimethylanilines **D_x** were purified by FCC on silica gel F60 (eluant: petroleum ether/diethyl ether in 10:1 v/v), and characterized by ^{1}H NMR (Figures 5-11) and GC/MS. All compounds **D_x** were known products whose spectroscopic data were fully reported in the literature. **N,N-dimethyl *p*-anisidine** (98%, by GC): [3] mp 43-45 °C, lit. [4] mp 45-47 °C; ***N,N*-dimethyl *p*-toluidine** (98%, by GC): [3] pale yellow liquid, lit. [5a] bp 89-89.5 °C /11 mm; ***N,N*-dimethyl aniline** (99%, by GC): pale yellow liquid, lit. [5b] bp 77 °C / 13 mm; ***N,N*-dimethyl *p*-chloroaniline** (97%, by GC): [6] mp 32-34 °C, lit. [5c] mp 35.5 °C; **methyl *N,N*-dimethylaminobenzoate** (96%, by GC): [7] mp 100-102 °C, lit. [5d] mp 102 °C; ***N,N*-dimethyl *o*-ethyl aniline** (97%, by GC): [8] mp 132-134 °C, lit. [3] 135 °C; ***N,N*-dimethyl 2,3-dimethylaniline** (97%, by GC): [9] yellow liquid, lit. [5e] bp 75 °C / 7 mm. The structures of *N,N*-dimethyl *p*-toluidine, *N,N*-dimethyl aniline, *N,N*-dimethyl *p*-chloroaniline, and *N,N*-dimethyl 2,3-dimethylaniline were confirmed also by comparison (GC analyses) to authentic commercial samples.

***N,N*-dimethyl *p*-anisidine** (Figure 5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.89 (s, 6H), 3.79 (s, 3H), 3.80 (s, 3H), 6.78 (d, 2H, J = 9.23 Hz), 6.87 (d, 2H, J = 9.04 Hz).

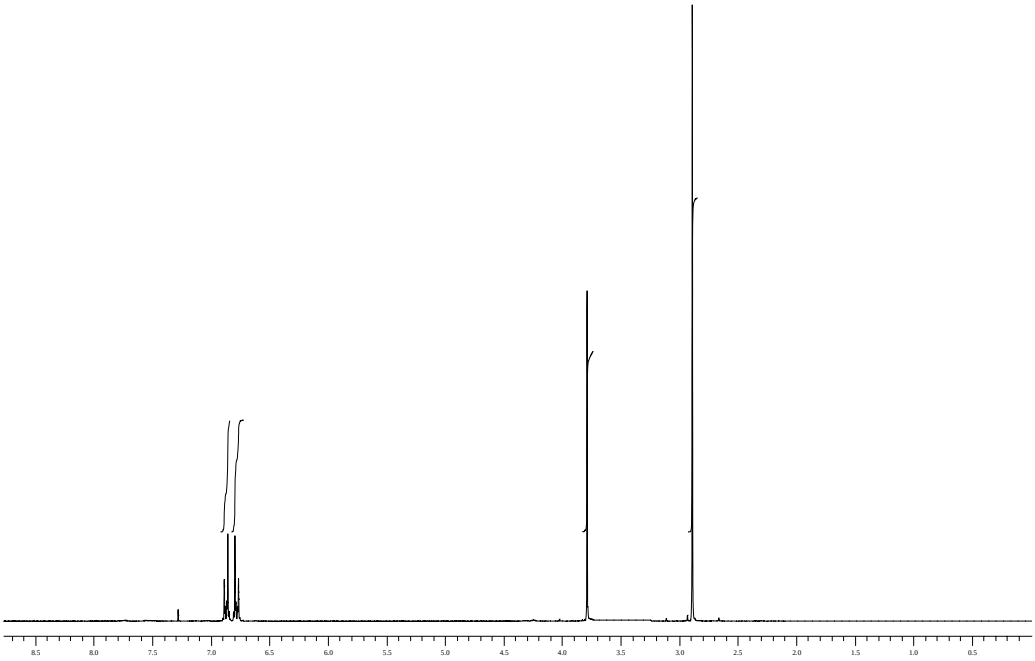

Figure 5. ^{1}H NMR of *N*,*N*-dimethyl *p*-anisidine

***N*,*N*-dimethyl *p*-toluidine** (Figure 6). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.89 (s, 6H), 6.69 (d, 2H, J = 8.85 Hz), 7.06 (d, 2H, J = 8.85 Hz).

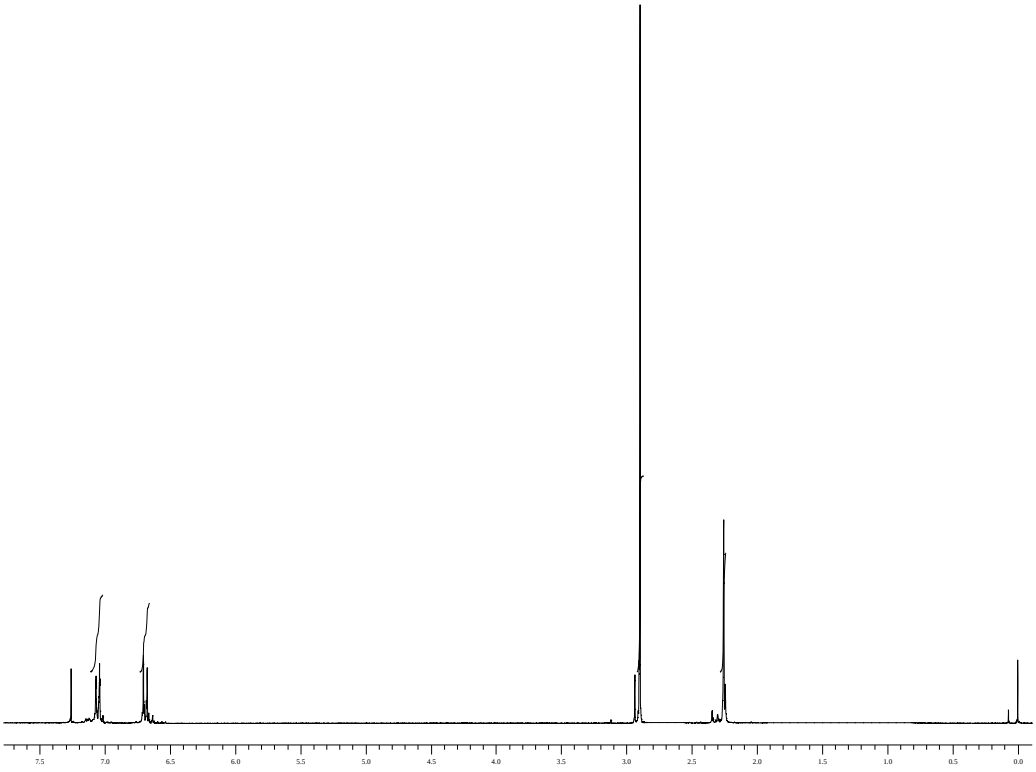

Figure 6. ^{1}H NMR of *N*,*N*-dimethyl *p*-toluidine

***N,N*-dimethyl aniline** (Figure 7). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (s, 6H), 6.68-6.77 (m, 3H), 7.20-7.28 (m, 2H).

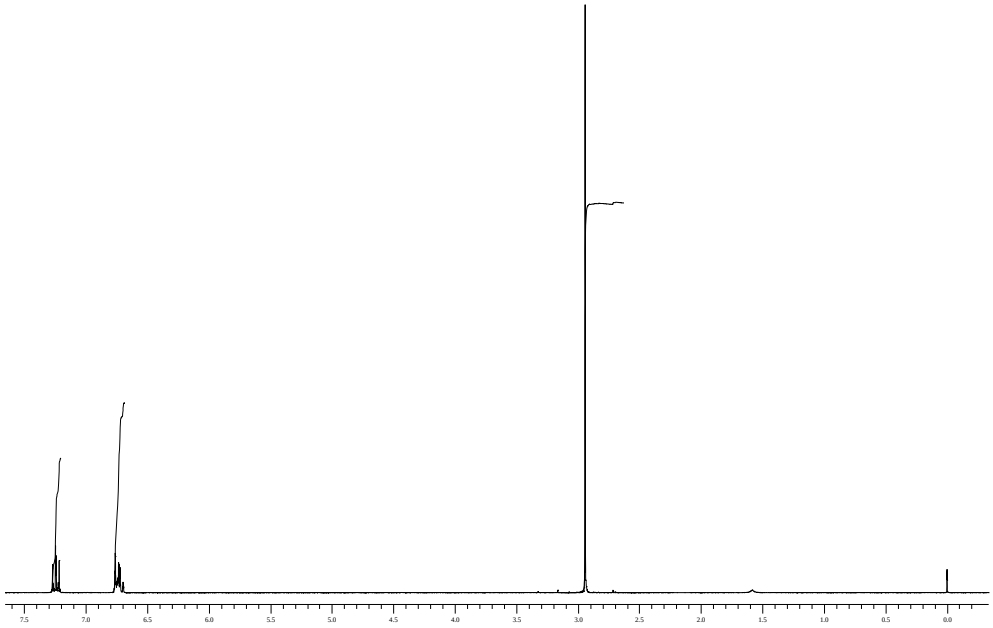

Figure 7. ^{1}H NMR of *N*,*N*-dimethylaniline

***N,N*-dimethyl *p*-chloroaniline** (Figure 8). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (s, 6H), 6.66 (d, 2H, J = 9.23 Hz), 7.19 (d, 2H, J = 9.23 Hz).

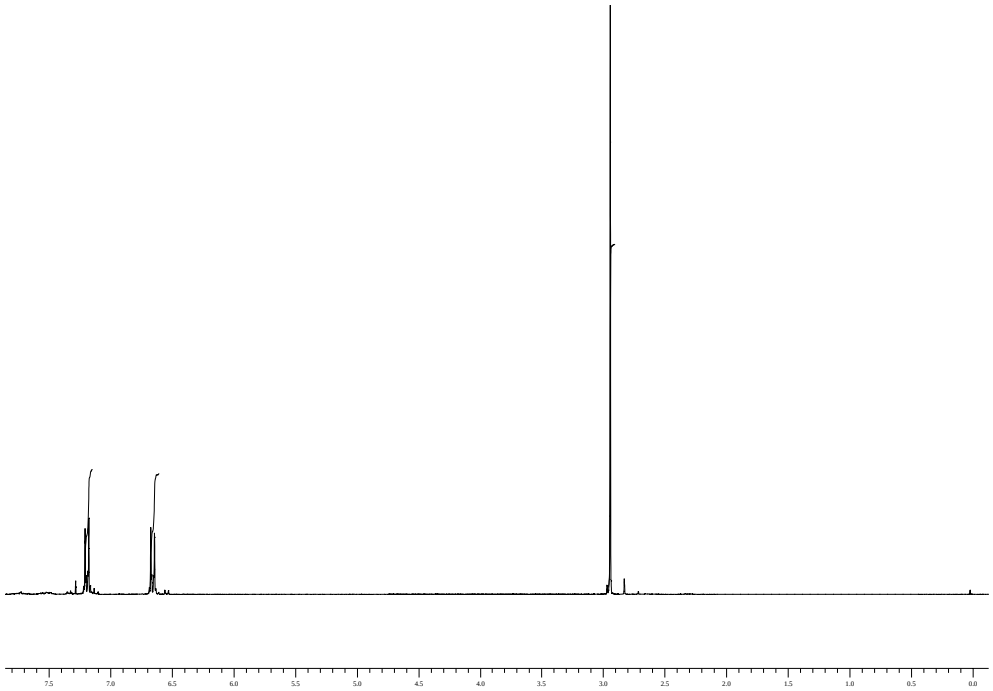

Figure 8. ^{1}H NMR of *N*,*N*-dimethyl *p*-chloroaniline

Methyl *N,N*-dimethyl aminobenzoate (Figure 9). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.05 (s, 6H), 3.87 (s, 3H), 6.66 (d, 2H, J = 9.04 Hz), 7.92 (d, 2H, J = 9.04 Hz).

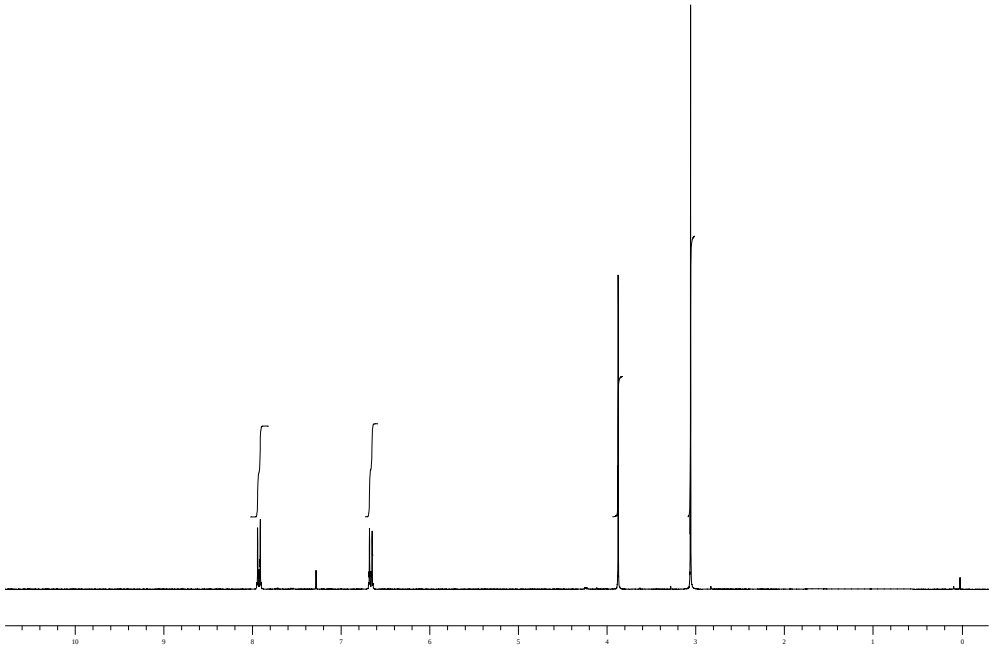

Figure 9. ^{1}H NMR of methyl *N,N*-dimethylaminobenzoate

***N,N*-dimethyl *o*-ethylaniline** (Figure 10). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 3H, J = 7.54 Hz), 2.68 (s, 6H), 2.73 (q, 2H, J = 7.54 Hz), 6.99-7.25 (m, 5H).

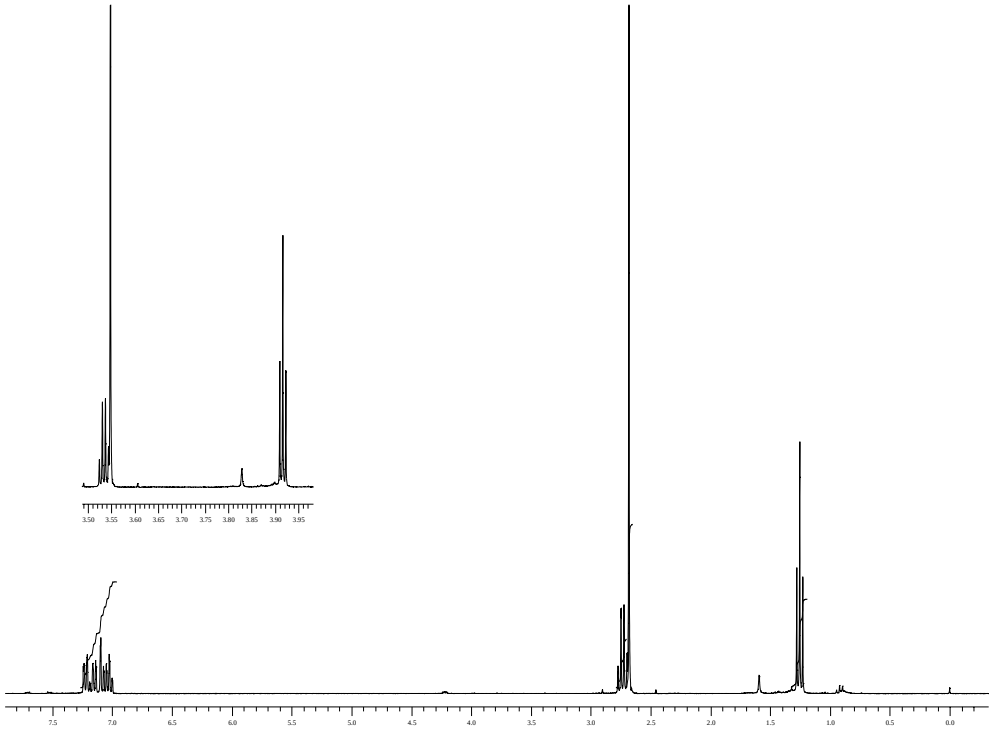

Figure 10. ^{1}H NMR of *N,N*-dimethyl *o*-ethylaniline

***N,N*-dimethyl 2,3-dimethylaniline** (Figure 11). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3H), 2.27 (s, 3H), 2.67 (s, 6H), 6.85-6.95 (m, 2H), 7.03-7.1 (m, 1H).

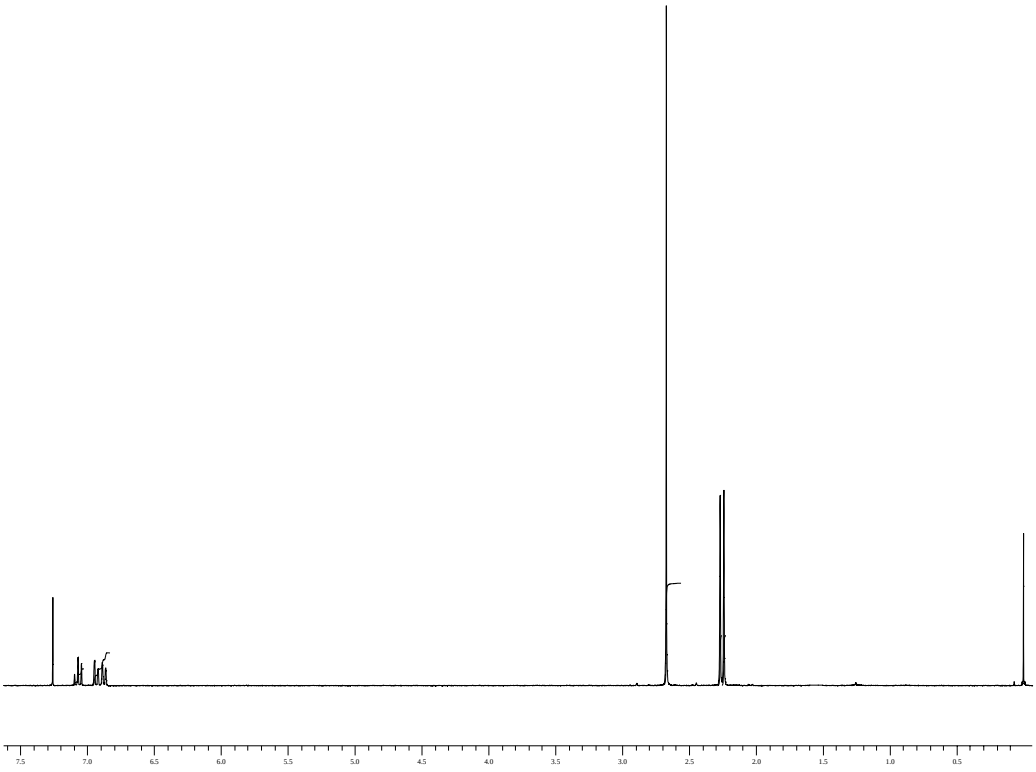

Figure 11. ^{1}H NMR of *N,N*-dimethyl 2,3-dimethylaniline

N-Ethyl,N-methyl *m*-toluidine (**7b**, [10] Scheme 6) was not isolated from the reaction mixture: its structure was assigned by GC/MS: 149 (M^+, 38), 134 (M^+-Me, 100), 120 (M^+-Et, 4), 119 (15), 118 (14), 91 (24), 65 (12).

IR Investigations

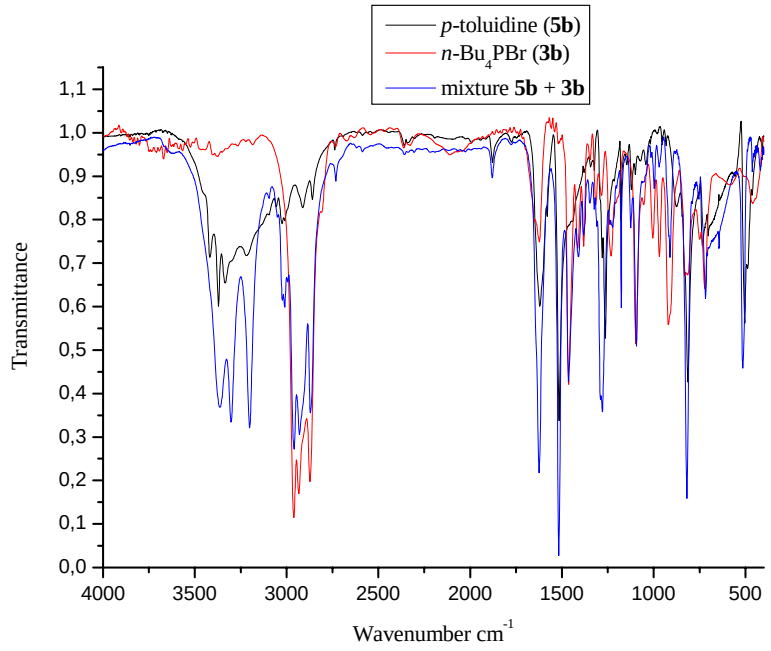

Figure 1. Overlap of IR spectra of pure *p*-toluidine (**5b**, black), pure *n*-Bu_4PBr (**3b**, red), and a mixture of **5b** and **3b** (blue), recorded at room temperature.

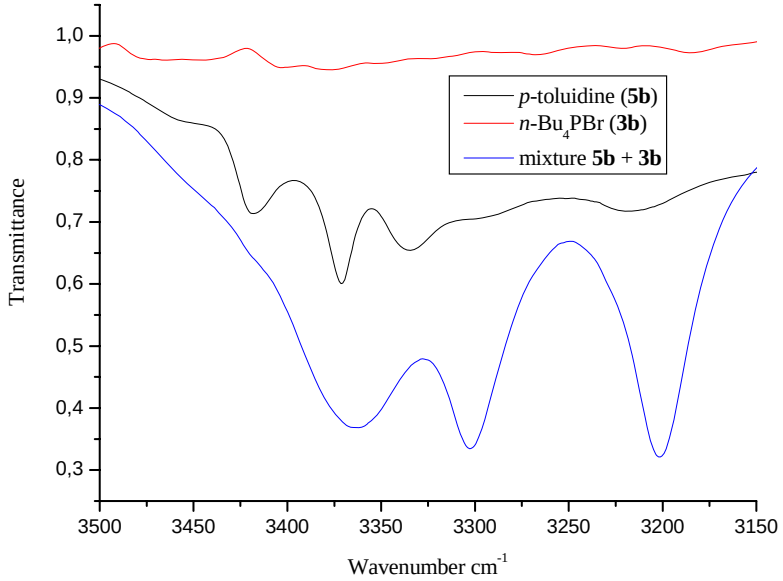

Figure 2. Enlargement of Figure 1 between 3500 and 3150 cm^{-1}.

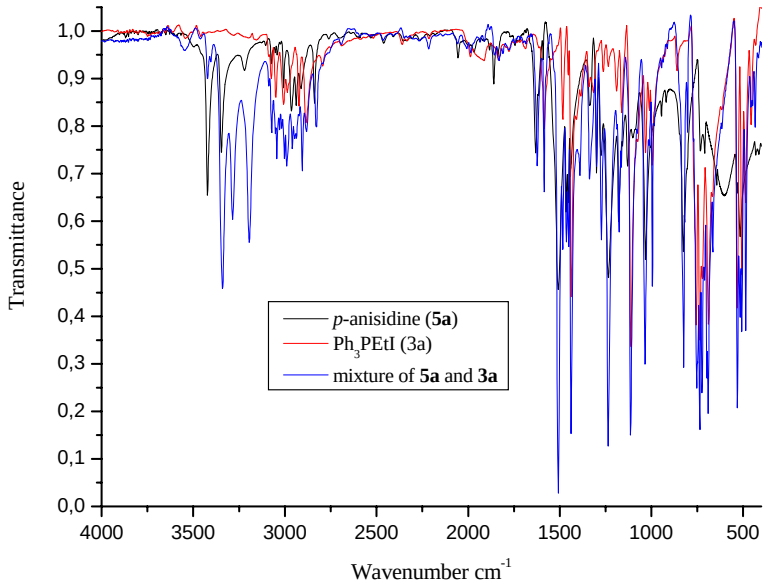

Figure 3. Overlap of IR spectra of pure *p*-anisidine (**5a**, black), [11] pure Ph_3PEtI (**3a**, red), and a mixture of **5a** and **3a** (blue), recorded at room temperature.

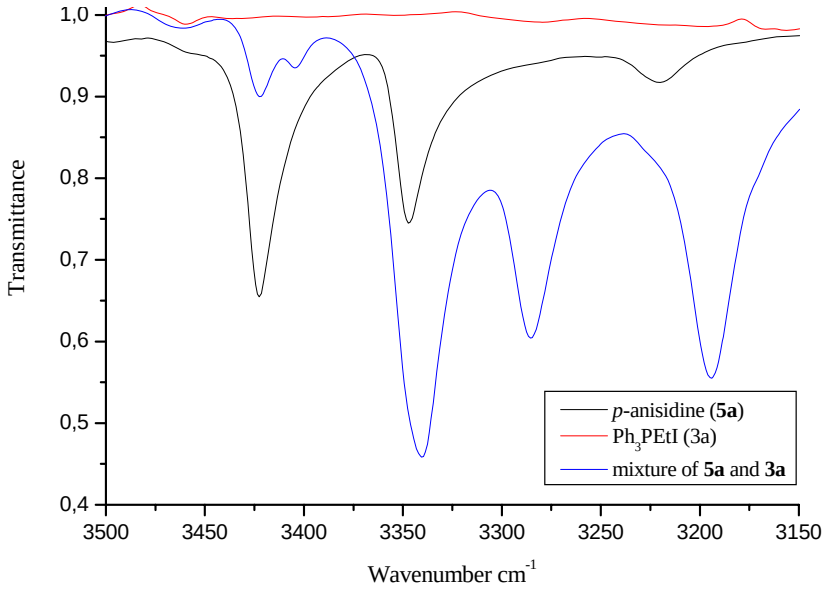

Figure 4. Enlargement of Figure 4 between 3500 and 3150 cm^{-1}.

IR spectra were recorded on commercial *p*-anisidine (**5a**), *p*-toluidine (**5b**), ethyltriphenyl phosphonium iodide (**3a**), and tetrabutylphosphonium bromide (**3b**). Mixtures of **5a** and **3a**, of **5b** and **3a**, and of **5b** and **3b**, were equimolar.

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