Reinvestigation of the Vilsmeier-Haack Formylation of Triphenylamine

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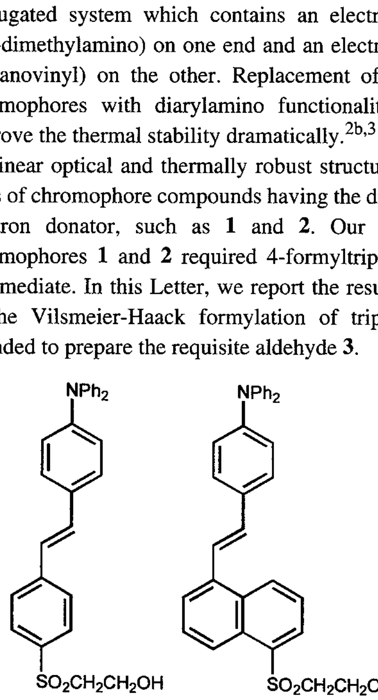
Abstract: Two previously claimed results on the Vilsmeier-Haack formylation of triphenylamine were demonstrated to be in error and the unambiguous reproducible procedures were developed to prepare 4-formyltriphenylamine (**3**) and 4,4'-diformyltriphenylamine (**4**), respectively, in good yields.

Considerable effort has been made in the last decade in the synthesis of nonlinear optical (NLO) chromophores and their incorporation into a polymer matrix to develop organic polymer-based electro-optic materials.[2] NLO chromophore molecules generally have a long-conjugated system which contains an electron-donating group *(e.g.*, *N,N*-dimethylamino) on one end and an electron-accepting group (*e.g.*, tricyanovinyl) on the other. Replacement of dialkylamino donors in chromophores with diarylamino functionalities has been shown to improve the thermal stability dramatically.[2b,3] In an effort to seek better nonlinear optical and thermally robust structures, we designed a novel class of chromophore compounds having the diphenylamino group as an electron donator, such as **1** and **2**. Our synthetic approaches to chromophores **1** and **2** required 4-formyltriphenylamine (**3**) as a key intermediate. In this Letter, we report the results of our reinvestigation of the Vilsmeier-Haack formylation of triphenylamine, which was intended to prepare the requisite aldehyde **3**.



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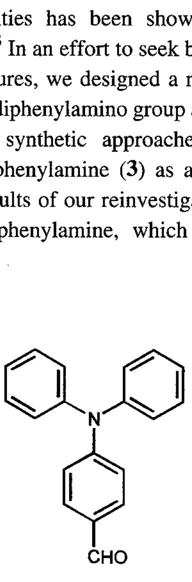

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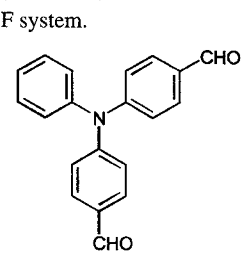
There existed two inconsistent reports in the literature regarding the formylation of triphenylamine by the Vilsmeier-Haack reagents ($POCl_3$/DMF). Wilson[4] first claimed in an early patent that treatment of triphenylamine with 8.2 equiv of $POCl_3$ in DMF gave tris(4-formylphenyl)amine (**5**) as the sole product, but Walter and his coworkers[5] later reported that Wilson's procedure led to only 4-formyltriphenylamine (**3**) and, even with longer reaction time and greater excess of the reagents, no trialdehyde **5** was produced.

With these ambiguous results in mind, we reinvestigated this formylation at first using 2 equiv of $POCl_3$ in DMF at 70 °C for 18 h. Two products, **3** and **4**, were unexpectedly detected and isolated in 71% and 23% yields, respectively. Their structures were confirmed by ^1H and ^{13}C NMR, IR, and elemental analyses.[6] By repeating Wilson's procedure,[7] we observed that the predominant product was 4,4'-diformyltriphenylamine (**4**), not the previously reported trialdehyde **5** or monoaldehyde **3**.

Attempts were then made to develop the respective practical procedures for the preparation of aldehydes **3** and **4**. We found that treatment of triphenylamine with almost an equal equivalent of $POCl_3$ in DMF at 95-100 °C for 20 h provided the monoaldehyde **3** in excellent yield (94%).[8] In this case, excess reagent ($POCl_3$) should be avoided as it resulted in the formation of the dialdehyde **4** to some extent. The dialdehyde **4** as the expected product was prepared in 71% yield along with a small amount of **3** (3%) when Ph_3N was treated with 10.5 equiv of $POCl_3$ at 95-100 °C for 6 h.[9] Treatment with less excess of $POCl_3$ increased the amount of the byproduct monoaldehyde **3**. This result of disubstitution appears to back up the proposed mechanism that the position of the equilibrium involved in the $POCl_3$/DMF system may favor the formation of the mixed amide-phosphorodichloridate cationic anhydride considered as the more electrophilic reacting species when an excess of $POCl_3$ is used.[10]

Direct preparation of the trialdehyde **5** from triphenylamine under the Vilsmeier-Haack conditions was also explored. However, this compound (**5**)[11] was obtained in only 18% isolated yield together with the dialdehyde **4** as the main product (40%) by using a large excess of $POCl_3$ (40 equiv) and prolonging heating time (48 h, 95-100 °C). The low yield of **5** apparently suggested that the intermediate(s), leading to the dialdehyde **4** after workup, may not be sufficiently electron-rich and may, therefore, retard further electrophilic substitution with the $POCl_3$/DMF system.



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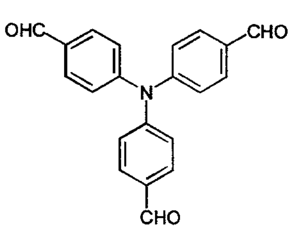

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In summary, the present work demonstrated two previously reported results on the Vilsmeier-Haack formylation of triphenylamine to be in error and found practical conditions for the preparation of aldehydes **3** and **4** in good yields. Synthesis of chromophore compound **1** and its analogues, starting with the key monoaldehyde **3**, is currently underway.[12]

References and Notes

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(6) *4-Formyltriphenylamine* (**3**): a pale yellow solid; mp 129-131 °C; R_f 0.35 (EtOAc-hexanes, 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1 H, CHO), 7.70 (d, J = 8.7 Hz, 2 H), 7.36 (t, J = 7.7-8.2 Hz, 4 H), 7.21-7.17 (m, 6 H), 7.04 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.94 (CHO), 153.32 (C_q), 146.58 (C_q), 132.45 (C_q), 130.89 (CH), 129.37 (CH), 127.51 (CH), 126.25 (CH), 120.54 (CH); IR (KBr) 1690, 1591, 1492, 1335, 1308, 1229, 1157 cm^{-1}. Anal. cacld for $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.13. Found: C, 83.49, H, 5.57; N, 5.15.

4,4'-Diformyltriphenylamine (**4**): a yellow solid; mp 141-143 °C; R_f 0.54 (EtOAc-hexanes, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 2 H, CHO), 7.77 (d, J = 8.7 Hz, 4 H), 7.41 (t, J = 7.6-8.0 Hz, 2 H), 7.30 (m, 1 H), 7.22-7.19 (m, 2 H), 7.20 (d, J = 8.6 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.88 (CHO), 152.42 (C_q), 145.92 (C_q), 131.89 (C_q), 131.69 (CH), 130.55 (CH), 127.46 (CH), 126.86 (CH), 123.64 (CH); IR (KBr) 1703, 1591, 1512, 1499, 1335, 1295, 1223, 1177, 834 cm^{-1}. Anal. cacld for $C_{20}H_{15}NO_2$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.63, H, 5.07; N, 4.63.

(7) We treated 2 g (8.15 mmol) of Ph_3N with DMF (2.62 mL, 33.49 mmol, 4.1 equiv) and $POCl_3$ (6.32 mL, 67.12 mmol, 8.2 equiv) when repeating Wilson's procedure.

(8) *Procedure for* **3**: To a mixture of Ph_3N (3 g, 12.23 mmol) and DMF (40 mL) at 0 °C was added $POCl_3$ (1.2 ml, 12.87 mmol, 1.05 equiv) dropwise with stirring. The resulting mixture was stirred at 95-100 °C under nitrogen for 20 h when TLC analysis showed that no starting material existed. The mixture was then cooled to room temperature, poured into ice-water (150 mL), and neutralized with 4 M NaOH solution. The solid was collected, washed with water, and dried. Purification by column chromatography (silica gel, EtOAc-hexanes, 1:5) afforded monoaldehyde **3** (3.14 g, 94%).

(9) *Procedure for* **4**: To a mixture of Ph_3N (1 g, 4.08 mmol) and DMF (8 mL) at 0 °C was added $POCl_3$ (4 ml, 42.91 mmol, 10.5 equiv) dropwise with stirring. The resulting mixture was stirred at 95-100 °C under nitrogen for 6 h, followed by similar workup. Purification by column chromatography (silica gel, EtOAc-hexanes, 1:4) afforded dialdehyde **4** (875 mg, 71%) along with **3** (33 mg, 3%).

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(11) *Tris(4-formylphenyl)amine* (**5**): a deep yellow solid; mp 230- 232 °C; R_f 0.36 (EtOAc-hexanes, 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 3 H, CHO), 7.81 (d, J = 8.6 Hz, 6 H), 7.29 (d, J = 8.6 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.83 (CHO), 151.59 (C_q), 133.01 (C_q), 131.68 (CH), 119.80 (CH); IR (KBr) 1703, 1598, 1578, 1512, 1321, 1282, 1223, 1177, 828 cm^{-1}. Anal. cacld for $C_{21}H_{15}NO_3$: C, 76.58; H, 4.59; N, 4.25. Found: C, 76.69, H, 4.65; N, 4.28.

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