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Convenient Methods for the Preparation of *p*-Dialkylaminophenylacetylenes

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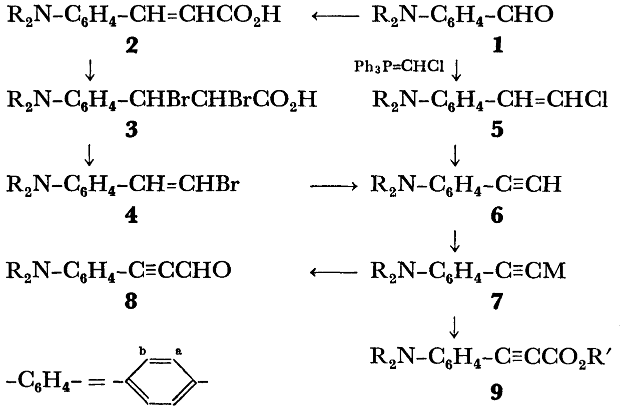
Synopsis. Two convenient methods for the preparation of *p*-dialkylaminophenylacetylenes are reported: a) Dehydrobromination of the brominated compounds obtained easily from the dialkylamino substituted cinnamic acids in acetic acid instead of chloroform; b) dehydrochlorination of the 2-chlorostyrene derivative obtained from the reaction of *p*-dimethylaminobenzaldehyde with chloromethylenetriphenylphosphorane.

In our study on ethynologs of triphenylmethane dyes,[1)] *p*-dialkylaminophenylacetylenes (**6**) are important starting materials. However, no convenient method is known for easy and large-scale production. The synthesis of *p*-dimethylaminophenylacetylene (**6**, R=CH_3) has been reported by Barbieri[2)] and by Oliver and Walton.[3)] Barbieri's method is depicted by the path (**2**→**3**→**4**→**6**) in Scheme 1. The yield of **6** based on **2** was only 18%. On the other hand, Oliver and Walton's method is made up by the reaction of *p*-dimethylaminophenylcopper with (iodoethynyl)trimethylsilane, from which **6** as trimethylsilyl derivative is obtained in 52% yield.

p-Diethylaminophenylacetylene (**6**, R=C_2H_5) has been prepared as a mixture of *p*- and *m*-isomers by the reaction of *p*-bromophenylacetylene with diethylamine in the presence of sodium amide.[4)]

Now, we wish to report here the convenient synthesis of *p*-dialkylaminophenylacetylenes and their derivatives, as outlined in Scheme 1.



Scheme 1.

The bromination of **2** to obtain **3** according to the literature[2)] has been reinvestigated unsatisfactorily in chloroform. The reaction seemed to proceed very little because **2** is almost insoluble in chloroform. However, we have found that the reaction proceeds dramatically under homogeneous conditions to give the brominated acid **3** if we use acetic acid instead of chloroform as a solvent. The bromide **4** obtained by the treatment of **3** with aq Na_2CO_3 was dehydrobrominated with several bases (*e.g.*, *n*-BuLi, $NaNH_2$, and *t*-BuOK) yielding the acetylene **6** in moderate yields. The above method seems to be easy and suitable for larger scale production. Contrary to this, Oliver and Walton's method appears to be fairly troublesome because of tedious reagents' preparation. Furthermore, we have developed an alternative route (**1**→**5**→**6**). The reaction of *p*-dimethylaminobenzaldehyde (**1**) with easily accessible chloromethylenetriphenylphosphorane[5)] generated from the corresponding phosphonium salt by the treatment with the base (*t*-BuOK or *n*-BuLi) at low temperature gave 2-chlorovinyl compound (**5**, R=CH_3), which could be easily isolated and interestingly was composed mostly of *cis*-isomers.[6)] The action of one mol of *n*-BuLi, *t*-BuOK, or $NaNH_2$ against **5** (R=CH_3) provided **6** (R=CH_3) in a high yield. Two mol of *n*-BuLi or *t*-BuOK gave the metalated compound (**7**, R=CH_3, M=Li or K), which reacted succeedingly with ethyl chloroformate to yield the ester (**9**, R=CH_3, R′=C_2H_5) and with *N*,*N*-dimethylformamide to give the aldehyde (**8**, R=CH_3).

It was clear that the general procedure for preparing ethylnyl compounds from acetyl derivatives was not applied here, since the attempted chlorination of *p*-dimethylaminoacetophenone (**10**)[7)] with PCl_5 in benzene under reflux to obtain the corresponding chloride was unsuccessful due to decomposition under several reaction conditions.[8)]

In conclusion, the preparation of **6** became easy along the route (**2**→**3**→**4**→**6**) including the modified bromination method. The alternative route (**1**→**5**→**6**) had also an advantage of being able to isolate **5** easily.

Experimental

The melting points were uncorrected. The IR spectra were obtained on a JASCO IRA-2 spectrophotometer. The ^{1}H NMR spectra were measured on a JEOL FX 90Q and the parameters were given in δ-values with respect to TMS used as an internal standard. The UV spectra were obtained in EtOH on a Shimadzu UV 300.

*p-Dimethylaminophenylacetylene (**6**, R=CH_3).* *From p-Dimethylaminocinnamic Acid (**2**, R=CH_3)*: *Bromination of **2***: To a solution of **2** (R=CH_3, 9.50 g, 0.05 mol) in acetic acid (300 ml) was added over 10 min bromine (8.0 g, 0.05 mol) in the same solvent (10 ml) at 16—20 °C. After the mixture had been stirred for 30 min, the solvent was evaporated. The residue was stirred with Na_2CO_3 (40 g, 0.38 mol) in water (200 ml) at room temperature for 30 min and extracted with hexane (400 ml). The extract, after being washed with brine and dried ($MgSO_4$), was concentrated to give a light brown oily substance (10.20 g); this was **4** and was used without purification in the next reaction.

Dehydrobromination. *a) By Potassium* t*-Butoxide*: To the above bromide (10.20 g) in THF (60 ml) was added *t*-BuOK (12.0 g, 0.11 mol) in THF (100 ml) over 1 h at room temperature. After stirring overnight the mixture was evaporated, worked up in the usual way, and then extracted with hexane (250 ml). The extract was washed with brine and dried ($MgSO_4$). Orange yellow crystals obtained on evaporating the solvent were dissolved in cyclohexane–benzene and passed through a short column of alumina (10 g). The filtrate was concentrated to give light yellow crystals (**6**, 2.01 g, 28% from **2**), mp 52—53 °C, lit,2) 52—53 °C, ^{1}H NMR ($CDCl_3$) $\delta=2.73$ (1H, s, ≡CH), 2.93 (6H, s, NMe_2), 6.49 (2H, d, $J=8$ Hz, H^b), and 7.25 (2H, d, $J=8$ Hz, H^a). (Found: C, 82.56; H, 7.68; N, 9.39%; M^+, 145).

b) By Sodium Amide: To a suspension of $NaNH_2$ (prepared from Na, 3.0 g, 0.13 mol in NH_3 (l) (150 ml)) was added **4** (10.45 g) which was prepared from **2** ($R=CH_3$, 9.50 g, 0.05 mol) in THF (50 ml) over 15 min at −60 °C. After being stirred overnight at −50—−30 °C, the mixture was worked up in the usual way. The residue was extracted with benzene (250 ml). The extract was washed with water and dried ($MgSO_4$). The orange-brown material obtained on evaporating the solvent was dissolved in hexane–benzene and passed through a short column of alumina (20 g). The eluate was concentrated to afford **6** (2.67 g, 37%), mp 52—53 °C.

c) By Butyllithium: To a solution of **4** (8.54 g, derived from **2**, 7.60 g, 0.04 mol) in THF (50 ml) was added *n*-BuLi in hexane (1.5 M 40.0 ml, 60 mmol) with stirring under nitrogen atmosphere at −60 °C for 1 h. From the reaction mixture worked up in the usual way, **6** (2.23 g, 38%, mp 52—53 °C) was obtained.

From p*-Dimethylaminobenzaldehyde*: p*-Dimethylamino-β-chlorostyrene (**5**, $R=CH_3$)*: To a suspension of chloromethyltriphenylphosphonium chloride5) (3.57 g, 0.01 mol) in THF (20 ml) was added a hexane solution of *n*-BuLi (1.5 M 6.7 ml, 0.01 mol) in an ice–salt bath. After the mixture being stirred for 30 min, powdered *p*-dimethylaminobenzaldehyde (1.04 g, 7 mmol) was added to the resulting orange red solution of chloromethylenetriphenylphosphorane. The mixture was stirred overnight at room temperature. The residue obtained by evaporating the solvent was extracted with heptane (300 ml). The extract was percolated through a short column of silica gel (5 g) and concentrated to give light yellow crystals (**5**, 0.96 g, 76% based on **1**), which were recrystallized from ether and exclusively composed of *cis*-isomer of **5**, as shown by ^{1}H NMR; mp 42—44 °C, IR (KBr) 1610 cm^{-1} (C=C), ^{1}H NMR ($CDCl_3$) $\delta=2.95$ (6H, s, NMe_2), 6.00 (1H, d, $J=8$ Hz, olefinic H), 6.48 (1H, d, $J=8$ Hz, olefinic H), 6.66 (2H, d, $J=9$ Hz, H^b), and 7.61 (2H, d, $J=9$ Hz, H^a).

Found: C, 66.13; H, 6.70; N, 7.78%; M^+, 183. Calcd for $C_{10}H_{12}NCl$: C, 66.11; H, 6.66; N, 7.71%; M, 183.

*Dehydrochlorination of **5** ($R=CH_3$)*: To a solution of **5** (0.20 g, 1.1 mmol) in THF was added *n*-BuLi in hexane (1.5 M 2.0 ml, 3 mmol) for 30 min in an ice–salt bath under nitrogen atmosphere. After being stirred for 1 h, the mixture was quenched by adding water (50 ml). The aq layer was extracted with benzene (50 ml). The combined organic layer was dried ($MgSO_4$) and evaporated to give **6** ($R=CH_3$) as light yellow crystals (0.15 g, 94%, mp 52—53 °C). The use of *t*-BuOK instead of *n*-BuLi gave nearly the same result. The yield by $NaNH_2$ in NH_3(l) was 61%.

p*-Diethylaminophenylacetylene (**6**, $R=C_2H_5$)*: According to the same procedure as used for the dimethyl derivative, the bromination of **2** ($R=C_2H_5$)9) was done. The successive dehydrobromination of **4** by *n*-BuLi, $NaNH_2$, and *t*-BuOK gave **6** in 42,10) 28,11) and 27%12) based on **2**, respectively: bp 116 °C (4 mmHg); IR (Neat) 3290 (≡CH) and 2090 cm^{-1} (C≡C); MS M^+, 173, M, 173; ^{1}H NMR ($CDCl_3$) $\delta=1.16$ (6H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.34 (4H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 2.94 (1H, s, ≡CH), 6.56 (2H, d, $J=9$ Hz, H^b), and 7.32 (2H, d, $J=9$ Hz, H^a).

Ethyl p*-Dimethylaminophenylpropiolate (**9**, $R=CH_3$, $R'=C_2H_5$)*: To a solution of **5** ($R=CH_3$, 2.00 g, 11 mmol) in THF (20 ml) was added *n*-BuLi in hexane (1.5 M 8.00 ml, 12 mmol) with stirring under nitrogen atmosphere in an ice–salt bath. After the mixture was stirred for 1 h, an excess of ethyl chloroformate (3.3 g, 30 mmol) was added; the resulting mixture was stirred overnight, and extracted with benzene (200 ml). The extract was passed through a short column of alumina (10 g) and concentrated to give yellow crystals (0.96 g, 40%), mp 36—38 °C. UV: 335 (ε 36000); IR (KBr) 2200 (C≡C) and 1700 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) $\delta=1.65$ (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.35 (6H, s, NMe_2) 4.50 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 6.49 (2H, $J=9$ Hz, H^b), and 7.15 (2H, $J=9$ Hz, H^a). Found: C, 71.70; H, 6.99; N, 6.52%; M^+, 217. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45%; M, 217.

p*-Dimethylaminophenylpropynal (**8**, $R=CH_3$)*: To a solution of **5** ($R=CH_3$, 1.02 g, 5.6 mmol) in THF (40 ml) was added *n*-BuLi in hexane (1.5 M 5.0 ml, 7.5 mmol) with stirring under nitrogen atmosphere in an ice–salt bath. After 1 h, an excess of DMF (1 ml) was added and stirred for 1 h. The reaction mixture was worked up with 1% H_2SO_4 and extracted with benzene (200 ml). Crude crystals obtained here by concentrating the extract were dissolved in benzene (3 ml). The solution was passed through a short column of alumina (10 g) and concentrated to give **8** as light yellow crystals (0.39 g, 40%), mp 86—88 °C, IR (KBr) 2200 (C≡C) and 1660 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) $\delta=3.18$ (6H, s, NMe_2), 6.60 (2H, d, $J=8$ Hz, H^b), 7.41 (2H, d, $J=8$ Hz, H^a), and 9.32 (1H, s, CHO); UV: 365 (ε 15200). Found: C, 76.05; H, 6.39; N, 7.66%; M^+, 174. Calcd for $C_{10}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09%; M, 174.

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10) The yield by GLPC analysis (5% FFAP, 200 °C) of the distillate containing *p*-diethylaminostyrene (18%).

11) The yield by GLPC analysis (5% FFAP, 200 °C) of the distillate containing *N,N,p*-triethylaniline (18%).

12) Isolated yield by distillation.