SYNTHESIS OF N,N-DIALKYLAMINOPHENYLACETYLENES

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N,N-Dialkylaminophenylacetylenes represent interest for obtaining polymers that are capable of forming charge-transfer complexes, and also for the synthesis of physiologically active compounds. The multistep synthesis of p-dimethylaminophenylacetylene (I) from p-bromodimethylaniline is described in the literature [1]. We obtained (I) by the chlorination of the 4-methylaminoacetophenone (II) with PCl_5 and subsequent dehydrochlorination with sodium amide in liquid ammonia, but this method could not be extended to the preparation of the other N,N-substituted aminophenylacetylenes due to the difficulty of synthesizing the corresponding aminoacetophenones. In view of this we proposed to synthesize the N,N-dialkylaminophenylacetylenes from p-bromophenylacetylene (III) and secondary amines in the presence of $NaNH_2$ in suitable solvents [2]. By analogy with the alkyl-substituted halobenzenes [3, 4], the bromine is replaced by the amino group and a mixture of the m- and p-isomers of the corresponding aminophenylacetylenes is formed in 70-90% yield (Table 1).

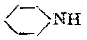
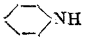
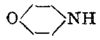
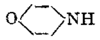
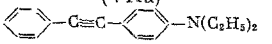
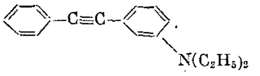
$$\underset{\text{(III)}}{p\text{-}BrC_6H_4C{\equiv}CH} + HNR^1R^2 \xrightarrow[\text{THF–HMP}\atop 40-50^\circ]{NaNH_2}$$

$$\rightarrow \underset{\text{(IV)–(VII)}}{p\text{-}R^1R^2NC_6H_4C{\equiv}CH} + \underset{\text{(IVa)–(VIIa)}}{m\text{-}R^1R^2NC_6H_4C{\equiv}CH}$$

$$R^1 = R^2 = C_2H_5\ \text{(IV), (IVa)};\quad R^1-R^2 = (CH_2)_5\ \text{(V), (Va)};$$

$$R^1-R^2 = CH_2CH_2OCH_2CH_2\ \text{(VI), (VIa)};\quad R^1 = R^2 = C_4H_9\ \text{(VII), (VIIa)}$$

TABLE 1. Synthesis Conditions, Yields, and Ratio of N,N-Dialkylaminophenylacetylene Isomers

Amine	Acetylene	Solvent	Reaction time, h	Reaction products	Ratio of isomers, %		Total yield, %
					meta	para	
$(C_2H_5)_2NH$	(III)	THF : HMP 4 : 1	9	(IV) (IVa)	59	41	82
$(C_2H_5)_2NH$	(III)	THF	38	(IV) (IVa)	40	60	90
	(III)	THF : HMP 2 : 1	3	(V) (Va)	56	44	88
	(III)	THF	35	(V) (Va)	32,5	67,5	92
	(III)	THF : HMP 4 : 1	3	(VI) (VIa)	59,5	40,5	75
	(III)	THF	35	(VI) (VIa)	32,3	67,7	94
$(C_4H_9)_2NH$	(III)	THF : HMP 4 : 1	3	(VII) (VIIa)	55	45	70
$(C_4H_9)_2NH$	(III)	THF	20—23	(VII) (VIIa)	50	50	75
$(C_2H_5)_2NH$	(VIII)	THF	3	 	55	45	94,5

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The reaction was run with excess $NaNH_2$ in either THF or a THF-hexamethylphosphorus triamide (HMP) mixture (4:1) at 40-50°C. Both the reaction time and ratio of the isomers depend on the employed solvent, and are 30-35 h in THF (ratio of m- and p-isomers = 34:66) and 3 h in THF-HMP (ratio of m- and p-isomers = 55:45). The pure m- and p-isomers were isolated by distillation through a column. The purity of the isomers was established by GLC, and the structure was confirmed by the elemental analysis, IR, and NMR spectral data.

In order to determine if this method could be used to obtain N,N-dialkylaminophenylacetylenes in which the acetylenic hydrogen is substituted we reacted diethylamine with p-bromotolan (VIII). The reaction with (VIII) goes much more easily than with (III), and is ended in 3 h even in THF medium.

Compounds (I), (IV), (V), and (Va) were converted to the dehydro dimers by oxidative condensation.

$$p\text{-}R^1R^2NC_6H_4C{\equiv}CH \xrightarrow[\text{CuCl, Py}]{O_2} (p\text{-}R^1R^2NC_6H_4C{\equiv}C)_2$$

$$\text{(IX)—(XII)*}$$

$$R^1 = R^2 = CH_3\ \text{(IX)};\quad R^1 - R^2 = (CH_2)_5\ \text{(X)};$$

$$R^1 - R^2 = CH_2CH_2OCH_2CH_2\ \text{(XI), (XII)}$$

EXPERIMENTAL

The GLC analysis was run on a "Vyrukhrom" chromatograph equipped with a flame-ionization detector; the column had a length of 2 meters and was packed with 5% XE-60 deposited on Chromatone; the carrier gas was nitrogen, and the temperature was 150-170°. The melting points were determined on a Kofler block. The IR spectra were taken on a UR-10 instrument in CCl_4 solution, while the NMR spectra were taken on a JNM-4H-100 instrument in CCl_4 solution relative to TMS.

The p-bromophenylacetylene was obtained as described in [5], and was isolated from the reaction mixture by steam-distillation, mp 64° (from alcohol); the p-bromotolan was obtained as described in [6], mp 82°; the N,N-dimethylaminoacetophenone was obtained as described in [7], mp 102-103°.

Chlorination and Dehydrochlorination of (II). To a stirred solution of 4 g (0.0244 mole) of (II) in 35 ml of toluene at 0° was added 12.7 g (0.0488 mole) of PCl_5 in portions and then the mixture was kept at 20° for 1 h, in which connection a red tarry product deposited. With cooling, the reaction mixture was treated with liquid ammonia and the obtained yellow crystalline product was added as a suspension in toluene to $NaNH_2$ (prepared from 12.7 g of Na and 0.5 liter of liquid ammonia) in ether, after which the mixture was stirred for 2 h and then let stand overnight. The reaction mass (after removal of the ammonia) was decomposed with water, and then extracted with ether. The ether—toluene extract was evaporated, and the obtained crystalline product was dissolved in ether and passed twice through an Al_2O_3 (II activity) column. We obtained 1.53 g (43%) of (I), mp 50.5-51.5° (from alcohol); cf. [1].

Preparation of N,N-Dialkylaminophenylacetylenes. To $NaNH_2$ (from 20 g of Na in 1 liter of liquid ammonia) in 200 ml of THF-HMP mixture was added 0.4 mole of the amine, the mixture was heated at 40-45° for 30 min, and then, with vigorous stirring, a solution of 0.2 mole of (III) in 50 ml of THF-HMP was added in 30 min. The reaction course was followed via GLC by the disappearance of (III). The reaction mixture was decomposed with water, extracted with ether, the ether extracts were washed with water to remove the HMP, dried over K_2CO_3, the solvent was distilled off, and the residue was vacuum-distilled through a column.

p-Diethylaminophenylacetylene (IV), bp 84-85° (0.5 mm). m-Diethylaminophenylacetylene (IVa), bp 81° (.05 mm). Found:† C 83.11; H 8.69; N 8.20%. $C_{12}H_{15}N$. Calculated: C 83.21; H 8.73; N 8.08%. Infrared spectrum (ν, cm^{-1}): 2110 ($-C{\equiv}C-$); 3325 ($H-C{\equiv}C-$). NMR spectrum (δ, ppm): 2.89 and 2.94 (p-and m- $H-C{\equiv}C-$); 3.06 ($-CH_2-N$); 0.93 (CH_3-). 6.33-7.20 m (benzene ring).

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*For (XII) the R^1R^2N groups are found in the 3,3' positions.

†The analysis is given for the mixture of isomers.

p-Piperidinophenylacetylene (V), mp 73-74° (from heptane). Found: C 84.05; H 8.16; N 7.37%.

m-Piperidinophenylacetylene (Va), bp 107-107.5° (1 mm). Found: C 84.24; H 8.46; N 7.66%. $C_{13}H_{15}N$. Calculated: C 84.28; H 8.16; N 7.57%. Infrared spectrum (ν, cm^{-1}): 2118 (-C≡C-); 3325 (H-C≡C-); 2800-2950 ($-CH_2-$). NMR spectrum (δ, ppm): 2.75 and 2.82 (p- and m-H-C≡C-); 1.52 ($-CH_2-$); 3.05 (CH_2-N-); 6.57-7.24 m (benzene ring).

p-Morpholinophenylacetylene (VI), mp 145.5-146.5° (from heptane). Found: C 76.90; H 6.99; H 7.48%.

m-Morpholinophenylacetylene (VIa), bp 128.5-129.5° (1.5 mm). Found: C 76.77; H 7.07; N 7.59%. $C_{12}H_{13}NO$. Calculated: C 76.99; H 7.09; N 7.72%. Infrared spectrum (ν, cm^{-1}): 2100 (-C≡C-); 3300 (H-C≡C-); 2800-2950 ($-CH_2-$). NMR spectrum (δ, ppm): 2.82 and 2.86 (p- and m- -H-C≡C-); 3.00 ($-CH_2-N-$); 3.68 (CH_2-O-); 6.56-7.23 m (benzene ring).

p-Dibutylaminophenylacetylene (VII), bp 110° (0.5 mm). Found: C 83.48; H 10.21; N 6.22%.

m-Dibutylaminophenylacetylene (VIIa), bp 110° (1 mm). Found: C 83.55; H 10.27; N 6.18%. 3323 (H-C ≡ C-). NMR spectrum (δ, ppm): 2.76 and 2.80 (p- and m H-C ≡ C-); 3.05 ($-CH_2-N-$); 1.27 ($-CH_2-$); 0.85 (CH_3-); 6.31-7.21 m (benzene ring).

4-Diethylaminotolan, mp 113.7-114.6° (from heptane). Found: C 86.80; H 7.80; N 5.79%.

3-Diethylaminotolan, mp 64-65.2° (from heptane). Found: C 86.61; H 7.76; N 5.86%. $C_{18}H_{19}N$. Calculated: C 86.72; H 7.68; N 5.62%.

Oxidative dimerization of (I). A mixture of 0.8 g (0.0055 mole) of (I) and 0.15 g (0.0015 mole) of CuCl in 20 ml of pyridine was shaken in a O_2 atmosphere. When the calculated amount of oxygen has been absorbed the mixture was poured into water, and the obtained precipitate was filtered, dissolved in dioxane, and passed through Al_2O_3 (II activity). We obtained 0.6 g (75%) of (IX), mp 239-241° (from dioxane). Found: N 9.54%. $C_{20}H_{20}N_2$. Calculated: N 9.71%.

In a similar manner were obtained (X) (97.5% yield, mp 273-275°. Found: N 7.47%. $C_{26}H_{28}N_2$. Calculated: N 7.60%); (XI) (80%, mp 328°. Found: N 7.93%. $C_{24}H_{24}N_2O_2$. Calculated: N 7.52%); (XII)(90% yield, mp 205°. Found: N 7.41%. $C_{24}H_{24}N_2O_2$. Calculated: N 7.52%).

CONCLUSIONS

A method was proposed for the synthesis of some m- and p-N,N-substituted aminophenylacetylenes via the reaction of secondary amines with p-bromophenylacetylene. The ratio of the isomers varies as a function of the reaction conditions.

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