High-pressure alkylation of bis(benzylidene)phenylenediamines

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The reactions of alkyl chlorides with bisanils (obtained from *o*-, *m*-, and *p*-phenylenediamines) under high pressure (10 kbar) were studied. Depending on the structure of the starting diamines and the solvent nature, hydrolysis of the reaction mixtures gave pure *N*-monoalkyl- or *N*,*N*′-dialkylphenylenediamines in high yields. The effect of the phase transition of the solvent on the direction of alkylation is discussed.

Key words: azomethines, anils, phenylenediamines, high-pressure alkylation.

It is known that *N*-monoalkyl- and *N*,*N*′-dialkylphenylenediamines are difficult to obtain in the individual state. The methods proposed earlier for their synthesis include (1) alkylation of nitroanilines followed by reduction of the nitro group,[1,2] (2) direct alkylation of phenylenediamines with repeated fractionation of the reaction mixtures containing mono- and polysubstitution products,[3] and (3) synthesis of an *N*-tosyl derivatives with subsequent alkylation and hydrolysis for elimination of the tosyl protection.[4]

In the preceding communication,[5] we showed that alkylation of substituted *N*-benzylideneanilines with alkyl chlorides under high pressure (5—10 kbar) is a convenient method for the synthesis of pure *N*-monoalkylanilines.

The present work is concerned with the reactions of bis(benzylidene) derivatives of *o*-, *m*- and *p*-phenylenediamines (**1a—c**, respectively) with Pr^nCl (**2**) and Bu^nCl (**3**) in solvents of different polarities (CH_2Cl_2, 1,4-dioxane, and MeCN) under the previously optimized[5] conditions (10 kbar, 50 °C, 5 h) (Scheme 1, Table 1).

As can be seen in Table 1, the alkylation gives high yields and is very selective: in each entry, either mono(alkylated) (**6**, **7**) or bis(alkylated) products (**8**, **9**) were obtained in spite of excess alkyl chlorides **2** and **3** in the reaction mixtures (see Experimental). *meta*-Derivative **1b** in any solvents afforded exclusively *N*,*N*′-dialkyl derivatives **8b** and **9b**, while monoalkylation products **6b** and **7b** were not detected. Bis(azomethines) **1a,c** react in a radically different way; in dioxane and MeCN, they yielded pure dialkyl derivatives **8a,c** and **9a,c**, while in CH_2Cl_2, only monoalkylated compounds **6a,c** and **7a,c** were obtained. Thus, the nature of both reagent **1** and the solvent strongly affects the ratio of alkylation products.

A higher reactivity of bis(azomethine) **1b** (which gives only dialkyl derivatives) relative to its isomers **1a,c** can be explained when comparing the nucleophilicity of the nonquaternized N atom of an intermediate monoimmonium salt **4** for *ortho*-, *meta*-, and *para*-isomers. The nucleophilicity of the uncharged N atom in the *meta*-salt has to be highest. A similar phenomenon associated with quaternization of aromatic diamines has been described in the literature. For instance, *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine reacts with excess MeI to give monomethyliodide, whereas the formation of bis(methyliodide) requires extremely drastic conditions.[8]

The decisive effect of solvents on the course of the reaction studied cannot be reduced to their different po-

Table 1. Yields and characteristics of *N*-monoalkyl- (**6a—c**, **7a—c**) and *N*,*N*′-dialkylphenylenediamines (**8a—c**, **9a—c**)

Product	Yield[a] (%)			M.p. /°C	MS, *m*/*z* ([M]$^+$)
	CH_2Cl_2	Dioxane	MeCN		
6a	63	0	0	Oil[b]	150
6b	0	0	0	—	—
6c	69	0	0	Oil[c]	150
7a	66	0	0	31—33.5 [d]	164
7b	0	0	0	—	—
7c	62	0	0	Oil[e]	164
8a	0	52	77	Oil	192
8b	75	58	87	Oil	192
8c	0	60	73	Oil	192
9a	0	55	81	Oil	220
9b	70	68	80	Oil	220
9c	0	61	72	52—53 [f]	220

[a] The yields were determined from the GLC data for the hydrolyzed reaction mixtures.
[b] Ref. 1: b.p. 144—148 °C (2 Torr).
[c] Ref. 6: b.p. 281 °C (760 Torr).
[d] Ref. 2: m.p. 35.8—36.2 °C.
[e] Ref. 7: m.p. 31 °C.
[f] Ref. 3: m.p. 53.7 °C.

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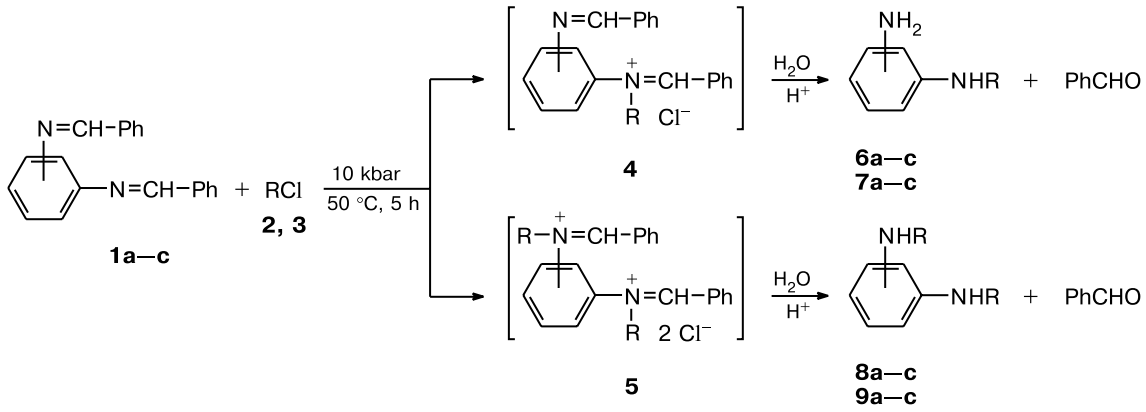
Scheme 1



R = Pr^n (**2**, **6a**—**c**, **8a**—**c**); Bu^n (**3**, **7a**—**c**, **9a**—**c**)

1, 6—9: the substituents are in *ortho*- (**a**), *meta*- (**b**), and *para*-positions (**c**)

larities. Compounds **1a,c** in dioxane (ε = 2.21) and MeCN (ε = 36.2) yield only dialkyl derivatives, whereas their reactions in CH_2Cl_2, with an intermediate dielectric constant (ε = 8.9), afford monoalkyl derivatives only, which clearly indicates the activating effects of dioxane and MeCN on the process. The polar properties of the latter solvents seem not to be so important here. Apparently, this effect is due to their crystallization under a pressure of 10 kbar, while CH_2Cl_2 remains liquid and does not activate the process further.

Acceleration of other reactions under high pressures due to solvent crystallization and possible reasons for this phenomenon have been described earlier (see Ref. 9 and references cited therein).

Experimental

Melting points were determined on a Boetius hot stage. ^{1}H NMR spectra were recorded on a Bruker AC-200 instrument in $CDCl_3$. GLC and MS analyses were carried out on a Finnigan MAT INCOS-50 instrument (EI, 70 eV, capillary column 30 m × 0.25 mm with polydimethylsiloxane (0.25 μm) as a grafted phase). Bis(azomethines) **1a**—**c** were prepared according to the known procedures.[10—12]

Alkylation of bis(azomethines) 1a—c under high pressure (general procedure). A solution of a bis(azomethine) (**1a**—**c**) (1 mmol) and an alkyl chloride (**2** or **3**) (2.2 mmol) in 1 mL of CH_2Cl_2, dioxane, or MeCN in a Teflon tube was kept at 50 °C and a pressure of 10 kbar for 5 h. The reaction mixture was cooled, concentrated *in vacuo*, acidified with 20% HCl (3 mL), and refluxed for 10 min. After cooling, benzaldehyde was extracted with Et_2O (2×5 mL). The aqueous layer was alkalified with a solution of NaOH to strongly alkaline reaction, the alkylated phenylenediamine was extracted with Et_2O (3×5 mL), and the extract was analyzed by GLC.[5] Analytically pure amines were obtained by precipitation of compounds **6**—**9** from the ethereal extract as picrates by adding a solution of picric acid (2.5 mmol) in 2 mL of EtOH. The picrates were filtered off, washed with 2 mL of EtOH, dried, and eluted with $CHCl_3$ through an Al_2O_3 layer (h = 1 cm) to separate off the picric acid. The eluates were concentrated to give analytically pure amines as oils or low-melting solids.

6a. ^{1}H NMR, δ: 1.00 (t, 3 H, Me, J = 7 Hz); 1.45—1.65 (m, 2 H, CH_2); 2.70—2.90 (m, 2 H, NCH_2); 2.90—3.30 (3 H, NH_2, NH); 6.40—6.90 (m, 4 H, H arom.).

6c. ^{1}H NMR, δ: 1.00 (t, 3 H, Me, J = 7 Hz); 1.40—1.60 (m, 2 H, CH_2); 2.60—2.80 (m, 2 H, NCH_2); 2.90—3.60 (3 H, NH_2, NH); 6.65—6.75 (m, 4 H, H arom.).

7a. ^{1}H NMR, δ: 0.95 (t, 3 H, Me, J = 7 Hz); 1.20—1.60 (m, 4 H, $(CH_2)_2$); 2.60—2.80 (m, 2 H, NCH_2); 2.90—3.60 (3 H, NH_2, NH); 6.50—7.00 (m, 4 H, H arom.).

7c. ^{1}H NMR, δ: 1.00 (t, 3 H, Me, J = 8 Hz); 1.20—1.50 (m, 4 H, $(CH_2)_2$); 2.70—2.90 (m, 2 H, NCH_2); 3.00—3.50 (3 H, NH_2, NH); 6.65—6.75 (m, 4 H, H arom.).

8a. Found (%): C, 74.60; H, 10.72; N, 14.45. $C_{12}H_{20}N_2$. Calculated (%): C, 74.95; H, 10.48; N, 14.57. ^{1}H NMR, δ: 1.00 (t, 6 H, 2 Me, J = 7 Hz); 1.30—1.70 (m, 4 H, 2 CH_2); 2.70—2.90 (m, 4 H, 2 NCH_2); 2.90—3.50 (2 H, 2 NH); 6.40—6.80 (m, 4 H, H arom.).

8b. Found (%): C, 75.41; H, 10.47; N, 14.91. $C_{12}H_{20}N_2$. Calculated (%): C, 74.95; H, 10.48; N, 14.57. ^{1}H NMR, δ: 0.95 (t, 6 H, 2 Me, J = 7 Hz); 1.30—1.50 (m, 4 H, 2 CH_2); 2.70—2.90 (m, 4 H, 2 NCH_2); 2.90—3.30 (2 H, 2 NH); 6.00—6.20 (m, 3 H, H arom.); 6.85—6.95 (m, 1 H, H arom.).

8c. Found (%): C, 74.58; H, 10.90; N, 14.89. $C_{12}H_{20}N_2$. Calculated (%): C, 74.95; H, 10.48; N, 14.57. ^{1}H NMR, δ: 1.00 (t, 6 H, 2 Me, J = 7 Hz); 1.35—1.65 (m, 4 H, 2 CH_2); 2.60—2.80 (m, 4 H, 2 NCH_2); 3.00—3.60 (2 H, 2 NH); 6.70 (s, 4 H, H arom.).

9a. Found (%): C, 76.71; H, 11.35; N, 12.44. $C_{14}H_{24}N_2$. Calculated (%): C, 76.31; H, 10.98; N, 12.71. ^{1}H NMR, δ: 1.00 (t, 6 H, 2 Me, J = 8 Hz); 1.30—1.70 (m, 8 H, 2 $(CH_2)_2$); 2.60—2.80 (m, 4 H, 2 NCH_2); 2.80—3.70 (2 H, 2 NH); 6.50—6.90 (m, 4 H, H arom.).

9b. Found (%): C, 76.40; H, 10.45; N, 12.99. $C_{14}H_{24}N_2$. Calculated (%): C, 76.31; H, 10.98; N, 12.71. ^{1}H NMR, δ: 1.00 (t, 6 H, 2 Me, J = 8 Hz); 1.30—1.70 (m, 8 H, 2 $(CH_2)_2$); 2.60—2.80 (m, 4 H, 2 NCH_2); 2.90—3.40 (2 H, 2 NH); 6.10—6.30 (m, 3 H, H arom.); 6.85—6.95 (m, 1 H, H arom.).

9c. ^{1}H NMR, δ: 1.00 (t, 6 H, 2 Me, J = 7 Hz); 1.35—1.70 (m, 8 H, 2 $(CH_2)_2$); 2.60—2.80 (m, 4 H, 2 NCH_2); 2.90—3.30 (2 H, NH_2, NH); 6.70 (s, 4 H, H arom.).

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