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Unusual Reductive Deamination of 2,6-Dibromo-3,4,5-trimethylaniline by Alkyl Nitrites in N,N-Dimethylformamide. Simultaneous Side-chain Nitration[1)]

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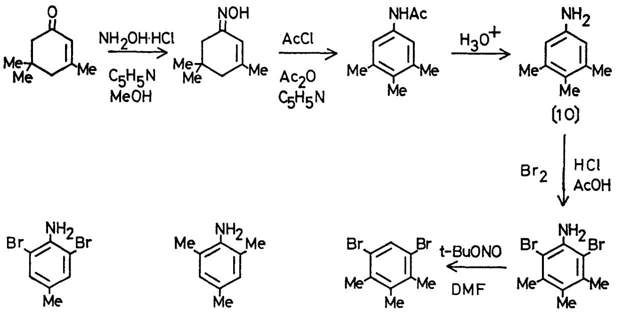
Synopsis. Treatment of 2,6-dibromo-3,4,5-trimethylaniline with *t*-butyl nitrite in *N,N*-dimethylformamide at 60—65 °C was found to give a significant amount of a side-chain nitration product, 3,5-dibromo-2,6-dimethylphenylnitromethane, in addition to the expected 4,6-dibromo-1,2,3-trimethylbenzene.

In the course of our studies of the reactions of polyalkyl aromatics, it became necessary to prepare 4,6-dibromo-1,2,3-trimethylbenzene (**2**). The synthesis of this compound was performed along the five-step sequence shown in Scheme 1. The outcome in the last step was unexpected, however. The solid material obtained from the reaction of 2,6-dibromo-3,4,5-trimethylaniline (**1**) with *t*-butyl nitrite in *N,N*-dimethylformamide (DMF) according to the procedure of Doyle[2)] was found to be a two-component mixture of an approximately 1: 1 composition. Chromatography of this mixture over silica gel using hexane as eluant gave the expected **2** as early eluate, mp 143—144 °C, and a pale yellow solid as late eluate, mp 134—136 °C. The elemental analysis and molecular weight of the latter compound were consistent with the formula $C_9H_9NO_2Br_2$. Its IR spectrum showed strong bands at 1550 and 880 cm^{-1}, indicating the presence of an aliphatic nitro group. Its PMR spectrum contained peaks at δ 2.48, 5.66, and 7.89 ppm, with a relative intensity ratio of 6: 2: 1, indicating the presence of two methyl groups, one methylene group, and one aromatic proton. These analytical and spectral data agree with the structure of 3,5-dibromo-2,6-dimethylphenylnitromethane (**3**). Its mass spectrum showed all the features expected for the assigned structure: characteristic triplet peaks centered at *m/e* 323 (M^+) and 277 (M^+-NO_2; base peak), and fragment peaks of these at *m/e* 242 and 244 (M^+-Br), 196 and 198 (M^+-NO_2-Br), and 117 (M^+-NO_2-2Br). The phenylnitromethane obtained was not contaminated with the isomeric 2,3-dimethyl-4,6-dibromophenylnitromethane (**7**) in any detectable amount.

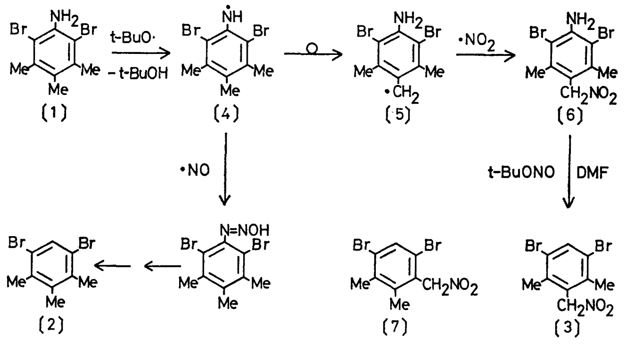


Scheme 1.

We tried to preclude this undesired side product by carrying out deamination in boiling tetrahydrofuran as a hydrogen donor.[3)] The product obtained was nearly identical with those derived from the corresponding reaction in DMF. The replacement of *t*-butyl nitrite by butyl nitrite did not have much influence on the product composition. Since the compound **2** was inert to the reagent under the reaction conditions employed, the unusual product **3** should have been formed from **1** through a pathway competing with the normal deamination.

Alkyl nitrites have been successfully used in the aprotic diazotization of various arylamines.[4)] To the best of our knowledge, however, no report seems to have appeared on the simultaneous deamination and side-chain nitration during the reaction of alkylanilines with alkyl nitrites. In order to ascertain the scope of this anomaly, several other methylanilines were treated in a similar manner. 2,6-Dibromo-4-methylaniline (**8**) gave 3,5-dibromotoluene in a 50% isolated yield. Spectral inspection of the crude product mixture indicated the presence of a side-chain nitration product which, however, could not be isolated due to its small quantity. Both 2,4,6- and 3,4,5-trimethylanilines (**9** and **10**) yielded the expected hydrocarbons together with considerable amounts of polymeric substances, proving the Doyle's method to be synthetically less useful for the deamination of these reactive amines. The PMR spectrum of the crude product from **9** contained a minor peak (δ 5.21 ppm) in the region where phenylnitromethanes usually absorb.[5)] In contrast, no side-chain substitution product could be detected in the deamination product from **10**. The unusual course of deamination, therefore, seems to be important only for a narrow range of alkylanilines.

We have not made a mechanistic study of this unusual reaction, but a possible mechanism for the regiospecific side-chain nitration may be depicted by assuming the rearrangement of the hindered anilino radical (**4**) into the benzyl radical (**5**) (Scheme 2). Thus, alkyl nitrite decomposes homolytically to give alkoxyl radical and nitrogen oxide. The former abstracts a hydrogen atom from the amino group of arylamine, giving the assumed anilino radical intermediate **4**, while the latter is oxidized to nitrogen dioxide, as is evidenced by the liberation of brown fumes. In analogy to the conversion of hindered phenoxyl radicals to benzyl radicals,[6)] **4** would isomerize to 4-aminobenzyl radical **5** which combines with nitrogen dioxide to form the amine **6**; this will undergo further reductive deamination,



Scheme 2.

giving the arylnitromethane **3** as the final product. Although **6** could not be isolated as such, its intermediacy is highly probable.

Experimental

Melting points were determined on a hot stage apparatus and are uncorrected. IR spectra were obtained in Nujol mulls with a Hitachi 215 spectrophotometer. PMR spectra were run in deuteriochloroform on a Varian T-60 spectrometer using TMS as internal standard. Mass (MS) spectra were recorded on a Hitachi RMS-4 mass spectrometer with 70 eV ionizing current.

Butyl nitrites were prepared in the usual manner.[7] 2,4,6-Trimethylaniline (**9**; bp 145 °C/57 mmHg; lit,[8] bp 225—226 °C), 3,4,5-trimethylaniline (**10**; mp 77—78 °C; lit,[9] mp 78.5—79 °C), 2,6-dibromo-4-methylaniline (**8**; mp 74—75 °C; lit,[10] mp 79 °C), and 2,6-dibromo-3,4,5-trimethylaniline (**1**; mp 163—165 °C; lit,[9] mp 162.5—163.5 °C) were prepared as reported. *N,N*-Dimethylformamide was distilled from calcium hydride prior to its use.

Reaction of 2,6-Dibromo-3,4,5-trimethylaniline with t-*ButylNitrite in DMF.* To a stirred solution of *t*-butyl nitrite (0.74 g; 7.2 mmol) in dry DMF (10 ml) maintained at 60—65 °C, amine **1** (0.7 g; 2.4 mmol) in the same solvent (5 ml) was added dropwise over a 5 min period and the solution was stirred at this temperature for a further 20 min. After cooling, the mixture was diluted with ether (50 ml), washed successively with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and water, dried over sodium sulfate, and evaporated to leave a yellow residue (0.78 g), which was dried and chromatographed on silica gel. Elution with hexane gave **2** as early eluate; white needles, mp 143—144 °C. Yield, 0.28 g (42%). PMR: δ 2.31 (3H, s), 2.35 (6H, s), and 7.60 ppm (1H, aromatic H); IR: $\nu_{\max}$ 1560, 1000, 900, and 850 cm^{-1}. Found: C, 38.72; H, 3.60%. Calcd for $C_9H_{10}Br_2$: C, 38.88; H, 3.63%.

Further elution with the same solvent gave **3** as straw-colored needles, mp 134—136 °C. Yield, 0.25 g (32%). The ratio **2** to **3** in the crude product mixture as determined by PMR analysis was approximately 10 to 11. Found: C, 33.65; H, 2.84; N, 4.27%. Calcd for $C_9H_9NO_2Br_2$: C, 33.47; H, 2.81; N, 4.34%.

In the corresponding reaction of 2,6-dibromo-4-methylaniline **8** with *t*-butyl nitrite, the reddish brown oil obtained on removal of the solvent was shown by PMR (singlet peak at δ 5.31 ppm) and IR spectra (strong band at 1560 cm^{-1}) to contain a nitromethyl compound which, however, could not be isolated due to its small quantity. After passage in a pentane solution through an alumina column, 3,5-dibromotoluene was obtained as colorless plates, mp 36—37 °C (lit,[11] mp 36.8—37 °C). Yield, 50%.

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