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# REACTIONS OF 1-TRICHLOROMETHYL-2,4,6-TRIMETHYLBENZENE WITH 2-AMINO- AND 2-AMINO-5-BROMOPYRIDINES

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*A new type of reaction has been discovered for trichloromethylarenes with pyridines. The reaction of 1-trichloromethyl-2,4,6-trimethylbenzene with 2-amino- and 2-amino-5-bromopyridines does not stop with formation of the pyridinium salt, but rather leads to unique amidines, namely, 1-[α-(2-pyridylimino)-2,4,6-trimethylbenzyl]-2-pyridonimine and its 5-bromo derivative.*

**Keywords:** 2-aminopyridine, 2-amino-5-bromopyridine, 1-[α-(5-bromo-2-pyridylimino)-2,4,6-trimethyl]-5-bromo-2-pyridonimine, 1-trichloromethyl-2,4,6-trimethylbenzene (mesitotrichloride), 1-[α-(2-pyridylimino)-2,4,6-trimethylbenzyl]-2-pyridonimine, reactions with 1-trichloromethyl-2,4,6-trimethylbenzene.

In previous work [1, 2], we have found that the nature of the products in the reaction of trichloromethylarenes with pyridines is a function of the reactants structure. Thus, trichloromethylbenzene, 1-trichloromethyl-2,4-dimethylbenzene, and 1-trichloromethyl-2,4,5-trimethylbenzene react with pyridine to give bispyridinium salts, which likely result from the reaction of initially formed unstable monopyridinium salts, namely, N-(α,α-dichloroarylmethyl)pyridinium chlorides with a second pyridine molecule. The monopyridinium salts generated in the reactions of pyridine and its 3-substituted derivatives with *o,o'*-dimethyl derivatives of trichloromethylbenzene, in particular, 1-trichloromethyl-2,4,6-trimethylbenzene (**1**) add a nucleophile, namely, a second pyridine molecule or chloride anion, at $C_{(4)}$ to give 4-pyridino-1,4-dihydropyridines or 4-chloro-1,4-dihydropyridines, respectively. Aromatization of the latter with hydrogen transfer from $C_{(4)}$ of the dihydropyridine ring to the benzylic dichloromethylene group leads to N-(α-chloroarylmethyl)-4-(pyridino)pyridinium dichlorides or N-(α-chloroarylmethyl)-4-chloropyridinium chlorides. The reaction of 1-trichloromethyl-2,4,6-trimethylbenzene with 4-picoline stops upon formation of the monopyridinium salt. Finally, 2-picoline and 2,6-lutidine are incapable of forming pyridinium salts with 1-trichloromethyl-2,4,6-trimethylbenzene.

We have discovered that the reactions of trichloromethylarenes with aminopyridines, which feature two nucleophilic sites, fail to give pyridinium or pyridylpyridinium salts, but rather lead to substitution products. The reaction of one molar equivalent of 1-trichloromethyl-2,4,6-trimethylbenzene **1** with two equivalents of 2-aminopyridine (**2a**) or 2-amino-5-bromopyridine (**2b**) leads to rather unusual amidines **3a** or **3b** in 50-60% yield. The structure of these compounds was supported by $^{1}H$ and $^{13}C$ NMR spectroscopy and mass spectrometry (see Scheme 1).

The formation of these rather anomalous products may be explained as follows. In the first step, the reaction of trichloride **1** with 2-aminopyridines **2a** or **2b** gives monopyridinium salt **4**, which, is incapable of adding a chloride ion due to reduced electrophilicity of the pyridine ring (in particular, the site at $C_{(4)}$) and is

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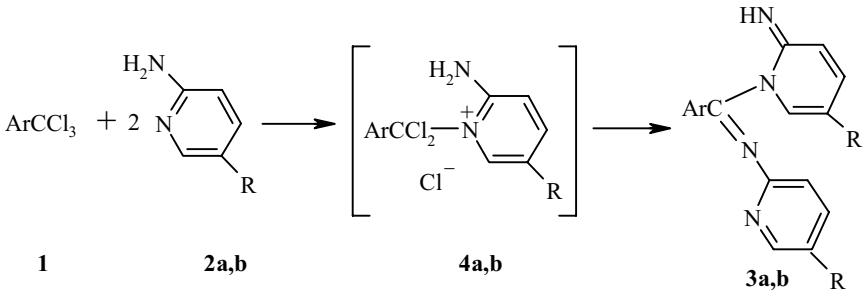
attacked by a second pyridine molecule with replacement of the labile chlorine atom of the dichlorobenzylic fragment. Nucleophilic substitution of this chlorine atom by a pyridinium group involving the endocyclic nitrogen atom of the pyridine ring is likely impossible due to steric hindrance produced by the *o*-methyl groups.

Scheme 1




Ar = 2,4,6-$Me_3C_6H_2$; **a** R = H, **b** R = Br

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were taken in a pulse mode with Fourier transformation on a Bruker WM-250 spectrometer at 250 MHz for the $^1H$ NMR spectra and an AM-300 spectrometer at 300 MHz for the $^1H$ NMR spectra and 75.5 MHz for the $^{13}C$ NMR spectra. The resonance conditions were stabilized using the $^1H$ signals of the solvent. The IR spectra were taken on a Perkin-Elmer 577 spectrometer for chloroform solutions. The mass spectra were taken on a Kratos MS-30 spectrometer with direct sample inlet into the ion source, 70 eV ionizing energy, and 100 μA emission current. The melting points were measured on a Boetius microscopic block and not corrected.

**Reaction of 1-Trichloromethyl-2,4,6-trimethylbenzene (1) with 2-Amino-5-bromopyridine (2b).** A sample of aminopyridine **2b** (1.22 g, 7.07 mmol) was added in portions with stirring to a solution of trichloride **1** (0.7 ml, 0.48 g, 3.54 mmol) in abs. $CHCl_3$ (6 ml), heated at reflux for 35 min, and then maintained for 25 days at room temperature to give 2-amino-5-bromopyridine hydrochloride as a precipitate (0.57 g, 38%); mp 186-188°C, M = 172 and 174 (1 Br atom). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 7.02 (1H, d, $J_{34}$ = 9.6 Hz, 3-H); 8.02 (1H, dd, $J_{46}$ = 2.5 Hz, 4-H); 8.24 (1H, d, 6-H); 8.15 (2H, br, $NH_2$). The precipitate was filtered off and the filtrate was evaporated. The residue was dissolved in ethanol (6 ml) and water (0.5 ml). Then, hydrazine hydrate (0.6 ml, 12 mmol) was added to the solution and the mixture was maintained at room temperature for 16 h. The precipitate formed was filtered off, washed with ethanol and, then, water, and dried to give 1-[α-(5-bromo-2-pyridylimino)-2,4,6-trimethylbenzyl]-5-bromo-2-pyridonimine **3b** (0.91 g, 54%); mp 189-191°C, M = 472, 474, 476 (2 Br atoms). Found, %: C 50.50; H 3.78; Br 32.78; N 11.89. $C_{20}H_{18}Br_2N_4$. Calculated, %: C 50.65; H 3.83; Br 33.70; N 11.82. IR spectrum, $cm^{-1}$ (0.005 M solution in $CHCl_3$): 3400 (νNH), 1630, 1615 (νC=N), 1565, 1455, 1415 (νC=$C_{arom}$). $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 2.24 (6H, s, 2- and 6-Me); 2.28 (3H, s, 4-Me); 6.43 (1H, d, $J_{34}$ = 8.6 Hz, 3-H); 6.75 (2H, s, 3- and 5-H mesityl); 6.77 (1H, br, NH); 7.44 (1H, dd, $J_{34}$ = 8.6, $J_{46}$ = 2.2 Hz, 4-H); 7.69 (1H, dd, $J_{3'4'}$ = 9.0, $J_{4'6'}$ = 2.0 Hz); 8.26 (1H, d, $J_{46}$ = 2.2 Hz, 6-H); 8.66 (1H, d, $J_{3'4'}$ = 9.0 Hz, 3'-H); 9.83 (1H, br. s, 6'-H). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 19.94 (2- and 6-Me mesityl), 21.47 (4-Me mesityl), 113.08, 113.94 ($C_{(5)}$, $C_{(5')}$), 116.03, 117.19 ($C_{(3)}$, $C_{(3')}$), 128.37 ($C_{(3)}$ and $C_{(5)}$ mesityl), 131.59 ($C_{(1)}$ mesityl), 135.22 ($C_{(2)}$ and $C_{(6)}$ mesityl), 139.44, 140.56 ($C_{(4)}$, $C_{(4')}$, 139.67 ($C_{(4)}$ mesityl), 147.97, 149.31 ($C_{(6)}$, $C_{(6')}$), 151.82 ($C_{(2)}$), 156.53 (C amidine), 160.24 ($C_{(2')}$).

**Reaction of 1-Trichloromethyl-2,4,6-trimethylbenzene (1) with 2-Aminopyridine (2a).** Using the conditions of the previous experiment, trichloride **1** (5.56 mmol) and 2-aminopyridine **2a** (11.11 mmol) gave 1-(α-(2-pyridylimino)-2,4,6-trimethylbenzyl]-2-pyridonimine **3a** (0.75 g, 51%); mp 180-182°C, $M^+$ = 316. Found, %: C 75.81; H 6.32; N 17.75. $C_{20}H_{20}N_4$. Calculated, %: C 75.92; H 6.37; N 17.71. IR spectrum (0.01 M solution $CHCl_3$): 3410 (νNH), 1635, 1617 (νC=N), 1580, 1465, 1417 (νC=$C_{arom}$). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.19 (3H, s, 4-Me); 2.28 (6H, s, 2- and 6-Me); 6.25 (1H, d, $J_{34}$ = 9.0 Hz, 3-H); 6.49 (1H, m, 5-H); 6.70 (2H, s, 3- and 5-H mesityl); 7.14 (1H, d, $J_{3'4'}$ = 9.0 Hz, 3'-H); 7.43 (2H, m, 4-H and 5'-H); 7.97 (1H, m, 4'-H); 8.24 (1H, d, $J_{56}$ = 5.4 Hz, 6-H); 8.61 (d, $J_{5'6'}$ = 5.4 Hz, 6'-H); 7.90 (1H, br, NH).

## REFERENCES


1. L. I. Belen'kii, I. S. Poddubnyi, and M. M. Krayushkin, *Tetrahedron Lett.*, **36**, 5075 (1995).
2. L. I. Belen'kii, I. S. Poddubnyi, and M. M. Krayushkin, *Khim. Geterotsikl. Soedin.*, 830 (1995).