Chlorotyrosine N- and C-alkenylamine

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Abstract. Chloroacetylation of a number of N- and C-alkenylanilines was studied and some further transformations of the obtained compounds were considered; the reaction proceeds most smoothly upon acylation with chloroacetyl chloride. By heating chloroacetanilides with an equimolar amount of pyridine in benzene, quaternary pyridinium salts were obtained in good yield. Some of the pyridinium salts have been shown to be highly effective as inhibitors of acid corrosion of steel. The interaction of chloroacetanilides with primary and secondary amines leads to hydrochloric ammonium salts, which are of interest as biologically active compounds.

1. Introduction

Chloroacetanilides are of interest as compounds with biological activity. At the same time, the presence of a reactive chlorine atom in their molecule makes it possible to obtain from them products of further transformations with potentially useful properties. Condensation of chloroacetanilides with amines leads to substances that have a local anesthetic effect [1,2]. The presence of methyl substituents in the 2- and 4-positions of the benzene ring greatly increases their activity [3]. The effect of more complex hydrocarbon substituents, in particular, unsaturated ones, on the properties of drugs has practically not been studied. In [4,5], available methods for the preparation of N- and C-substituted arylamines containing unsaturated substituents of the allyl type are described. In this work, we studied the chloroacetylation of a number of N- and C-alkenylanilines and some further transformations of the obtained compounds.

We found that chloroacetylation of 2-(1-methyl-2-butenyl) anilines proceeds most smoothly when acylated with chloroacetyl chloride. Heating in a benzene solution in the presence of alkaline agents ensures the maximum yields of anilides.

Attempts to replace chloroacetyl chloride with the original acid did not lead to satisfactory results. The reaction of amine 1 with monochloroacetic acid occurs only at temperatures above 200 °C and leads to a strong resinification of the product. At the same time, chloroacetyl chloride easily reacts even at the boiling point of benzene, due to which a number of chloroacetyl derivatives of N-(1-methyl-2-butenyl) arylamines were obtained. By heating the latter with an equimolar amount of pyridine in benzene, quaternary pyridinium salts were obtained in good yield.
Figure 1. Scheme of chloroacetylation of 2-(1-methyl-2-butyl) anilines.

Figure 2. Scheme of chloroacetylation of N-(1-methyl-2-butyl) anilines followed by quaternization.

Quaternary pyridinium salts have also been obtained from some 2-(1-methyl-2-butyl)-N-chloroacetinilides.

Figure 3. Reaction of chloroacetic derivatives with pyridine.
The interaction of chloroacetanilides with primary and secondary amines is also easy. The reaction can be carried out in a solution of benzene or in an excess of amine with heating. In both cases, the precipitation of the ammonium salt occurs over a long time.

The structure of the obtained compounds was established by IR and $^1$H NMR spectroscopy, as well as by elemental analysis. In the IR spectra of chloroacetylated products 2, 4, 6, 8, 10, 12, one of the two broad bands disappears in comparison with the initial amines in the region of 3300 - 3500 cm$^{-1}$, which indicates the transformation of the primary amino group into the secondary one. This band is absent in tertiary amines 14, 17, 20, 23, 26, 29, 32. In the $^1$H NMR spectra of all chloroacetanilides, the protons of the methylene group included in the acyl component of the molecule resonate in the form of a singlet in the range 3.02 - 4.06 ppm. Otherwise, their spectra are consistent with the data given in [4, 5] for the starting N- and 2- (1methyl-2-buteryl) -substituted arylamines.

The identification characteristics of chloroacetylated compounds are given in table 1; quaternary pyridinium salts 15, 18, 21, 24, 27, 30-36 and ammonium salts 37-40 – are in table 2.

Table 1. Identification of chloroacetylated compounds.

| No | T. mlt., $^\circ$C, or $n_\text{D}^0$ | IR spectrum, $\nu$, cm$^{-1}$ | found calculated% | Formula |
|----|---------------------------------|-------------------------------|-------------------|---------|
| 2  | 64-66                           | 980, 1670, 3340               | C 65.80 H 6.72    | ClNO     |
| 4  | 71-73                           | 980, 1680, 3370               | C 66.80 H 7.11    | ClNO     |
| 6  | 77-78                           | 980, 1670, 3370               | C 66.80 H 7.16    | ClNO     |
| 8  | 86-88                           | 980, 1670, 3380               | C 66.80 H 7.16    | ClNO     |
| 10 | 89-90                           | 980, 1680, 3360               | C 67.80 H 7.46    | ClNO     |
| 12 | 90                              | 980, 1680, 3350               | C 57.51 H 5.45    | ClNO     |
| 14 | 1.5402                          | 984, 1680                    | C 65.81 H 6.79    | ClNO     |
| 17 | 1.5387                          | 985, 1680                    | C 66.64 H 7.05    | ClNO     |

Figure 4. Reaction of chloroacetic derivatives with various amines.
Table 2. Melting points and 1H NMR spectra compounds 15, 18, 21, 24, 27, 30, 33-40.

| No | T. ml., °C | 1H NMR spectrum, δ, ppm, solvent D-O |
|----|------------|--------------------------------------|
| 15 | 158        | 1.04 d (3H, CH₃), 1.56 d (3H, CH₃), 3.60 c (2H, CH₂), 5.08 m (1H, CH), 5.40 m (2H, CH=CH), 7.20 – 9.10 m (10H, Ar, Py) |
| 18 | 209(dec)   | 0.99 d (3H, CH₃), 1.53 d (3H, CH₃), 2.06 c (3H, CH₃), 3.07 c (2H, CH₂), 5.0 m (1H, CH), 5.43 m (2H, CH=CH), 7.25 – 7.78 m (4H, Ar), 8.2 – 9.0 m (5H, Py) |
| 21 | 303(dec)   | 1.06 d (3H, CH₃), 1.58 d (3H, CH₃), 2.05 c (3H, CH₃), 3.02 c (2H, CH₂), 5.10 m (1H, CH), 5.46 m (2H, CH=CH), 7.24 – 7.80 m (4H, Ar), 8.25 – 9.10 m (5H, Py) |
| 24 | 62-63      | 0.98 d (3H, CH₃), 1.60 d (3H, CH₃), 2.25 c (3H, CH₂), 3.40 c (2H, CH₂), 4.96 m (1H, CH), 5.34 m (2H, CH=CH), 7.15 – 8.95 m (9H, Ar, Py) |
| 27 | 48-49      | 1.13 d (3H, CH₃), 1.60 d (3H, CH₃), 2.26 c (6H, 2CH₃), 3.36 c (2H, CH₂), 5.16 m (1H, CH), 5.50 m (2H, CH=CH), 7.28 – 9.17 m (8H, Ar, Py) |
| 30 | 95         | 1.20 d (3H, CH₃), 1.58 d (3H, CH₃), 2.0 c (6H, 2CH₃), 4.26 c (2H, CH₂), 4.95 m (1H, CH), 5.40 m (2H, CH=CH), 7.10 – 9.10 m (8H, Ar, Py) |
| 33 | 193-194    | 1.18 d (3H, CH₃), 1.45 d (3H, CH₃), 3.56 c (2H, CH₂), 5.06 m (1H, CH), 5.35 m (2H, CH=CH), 6.90 – 7.35 m (4H, Ar), 8.20 – 8.90 m (5H, Py) |
| 34 | 90         | 1.10 d (3H, CH₃), 1.48 d (3H, CH₃), 3.60 m (1H, CH), 5.36 m (2H, CH=CH), 5.64 c (2H, CH₂), 7.10 – 7.30 m (4H, Ar), 8.0 – 8.7 m (5H, Py) |
| 35*| 172        | 1.10 d (3H, CH₃), 1.23 d (3H, CH₃), 2.15 c (3H, CH₃), 3.82 m (1H, CH), 4.55 m (1H, NH), 5.42 m (2H, CH=CH), 6.10 c (2H, CH₂), 7.0 – 10.6 m (8H, Ar, Py) |
| 36*| 59-61      | 1.05 d (3H, CH₃), 1.30 d (3H, CH₃), 1.95 c (3H, CH₃), 2.12 c (3H, CH₂), 3.56 m (1H, CH), 4.25c (1H, NH), 5.30 m (2H, CH=CH), 6.02 c (2H, CH₂), 6.60 c (1H, Ar), 6.70 c (1H, Ar), 7.7 – 9.1 m (5H, Py) |
| 37 | 150-151    | 1.25 d (3H, CH₃), 1.35 t (6H, 2CH₃), 1.60 d (3H, CH₃), 3.33 kw (4H, 2CH₂), 3.67 m (1H, CH), 4.25 c (2H, CH₂), 5.51 m (2H, CH=CH), 7.30 ush. with (4H, Ar) |
| 38*| 154-155    | 1.20 – 2.05 m (16H, 2CH₃, 2CH₂), 3.02 m (3H, CH, CH₂), 4.16 m (2H, NH, CH), 5.45 m (2H, CH=CH), 7.13 – 7.80 m (4H, Ar) |
| 39 | 159-160    | 1.21 d (3H, CH₃), 1.60 d (3H, CH₃), 2.42 m (4H, 2CH₂), 2.71 c (2H, CH₂), 3.50 m (5H, 2CH₂, CH), 5.33 m (2H, CH=CH), 6.93 – 7.99 m (4H, Ar) |
| 40*| 114-115    | 1.10 d (3H, CH₃), 1.30 t (6H, 2CH₃), 1.55 d (3H, CH₃), 2.05 c (3H, CH₃), 2.18 c (3H, CH₃), 3.23 m (4H, 2CH₂), 4.0 m (1H, CH), 4.28c (2H, CH₂), 5.27 m (2H, CH=CH), 6.75 c (2H, Ar) |

* solvent CDCl₃

Water-soluble quaternary salts of pyridinium and a number of other amines have been tested as inhibitors of acid corrosion of steel. Some of them showed high efficiency in HCl solution at rather low concentrations (table 3).
Table 3. The results of laboratory tests of the obtained compounds as corrosion inhibitors of steel in hydrochloric acid.

| Compound                          | Mass fraction, % | Protective effect, % |
|-----------------------------------|------------------|---------------------|
|                                   | reagent | acid |
| 34                                | 0.01    | 10   | 88     |
|                                   | 0.05    | 10   | 93     |
|                                   | 0.05    | 15   | 98     |
|                                   | 0.05    | 20   | 95     |
|                                   | 0.10    | 15   | 95     |
|                                   | 0.10    | 20   | 99     |
| 35                                | 0.10    | 15   | 78     |
| 36                                | 0.10    | 15   | 89     |
| 39                                | 0.20    | 15   | 75     |
| 15                                | 0.05    | 15   | 78     |
| *para*-alkylbenzylpyridinium chloride | 1.00    | 20   | 95-98 [6] |

As follows from the table 3, compound 34 exhibits high efficiency (95-98%) at a significantly lower dosage than the known inhibitor, *para*-alkylbenzylpyridinium chloride. This substance dissolves well in hydrochloric acid of various concentrations, does not salty out when acid is neutralized by carbonate rocks of the formation, does not coagulate and does not reduce its efficiency in the presence of Fe$^{3+}$ ions, is convenient for transportation, storage and use. The test results allow us to recommend 2-[(1-methyl-2-butenyl) phenylamino-2-oxoethyl]pyridinium chloride 34 as an effective inhibitor of corrosion of carbon steels in acidic environments.

2. Experimental part
The starting N- and 2- (1-methyl-2-butenyl) arylamines were synthesized according to known methods, the physicochemical characteristics correspond to the literature data [4, 5].

$^1$H NMR spectra were recorded on a BrukerAM-300 instrument with an operating frequency of 300 and 75 MHz, internal standard HMDS. IR spectra were recorded on a UR-20 device. Elemental analysis was performed on a C-H-N-AnalyzerM-185B instrument. The reaction progress and the purity of the obtained products were monitored on a Chrom-5 chromatograph (flame ionization detector, 1.2 m column, SE-30 on chromatone, carrier gas helium).

N-Chloroacetyl-2-[(1-methyl-2-butenyl) aniline (2) and 2-[(1-methyl-2-butenyl) phenylamino-2-oxoethyl]pyridinium chloride (34). To a mixture of 4.8 g of potash and 16.1 g (0.1 mol) of amine 1 in 50 ml of benzene, a solution of 13.5 g (0.12 mol) of chloroacetyl chloride in 50 ml of benzene was added dropwise with stirring. The mixture was heated for 3 h on a water bath until the complete disappearance of the starting amine. The precipitate was filtered off, benzene and excess chloroacetyl chloride were distilled off. The residue, which solidified after distillation of benzene, was dried in a vacuum desiccator. 22.3 g (94%) of product 2 was obtained, which was redissolved in benzene, an equimolar amount of pyridine was added with stirring, heated for 1 - 2 h, and left overnight after cooling. There was obtained 28.7 g (89%) of compound 34.

The rest of the chloroacetanilides and their ammonium salts were obtained in a similar manner.

3. Conclusion
Degreased and dried to constant weight specimens measuring $20 \times 25 \times 0.5$ mm, made of steel St. 3 GOST 380-2005, kept in acid for 6 h at room temperature. In parallel, experiments were carried out with the addition of an inhibitor. After the exposure time, the samples were removed, washed with water, corrosion products were removed, kept for 1 h in a desiccator, and weighed on an analytical balance.

The corrosion rate ($\rho$) was determined by the formula:

$$\rho = \frac{\Delta m}{S \cdot t}$$
where: $\Delta m$ – change in sample weight (g), $S$ – sample area (m$^2$), $t$ – test time (h).

The degree of protection ($z$) was determined by the formula:

$$z = \frac{\rho_1 - \rho_2}{\rho_1}$$

where: $\rho_1$ – corrosion rate in an environment without inhibitor, g/(m$^2$h), $\rho_2$ – corrosion rate in an inhibited environment.

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